The CHORD COUSIN Collaboration

# C3 Manual

## Methodology for the development and implementation of Core Outcome Sets in dermatology

Explanation & Elaboration of the C3 Checklist

*Cecilia AC Prinsen*
*Murad Alam*
*Phyllis I Spuls*
*Kim S Thomas*
*Viktoria Eleftheriadou*
*Khaled Ezzedine*
*Amit Garg*
*Jamie J Kirkham*
*John Ingram*
*Daniel Munblit*
*Linnea Thorlacius*
*Jan Kottner*

*December 2025*

# The CHORD COUSIN Collaboration

A collaboration of international stakeholders interested in
advancing outcome measurement for skin conditions

**The CHORD COUSIN Collaboration**

**Authors**: Prinsen C, Alam M, Eleftheriadou V, Ezzedine K, Garg A, Kirkham JJ, Ingram J, Munblit D, Spuls P, Thomas KS, Thorlacius L, Kottner J. The C3 Manual version 1.8. CHORD COUSIN Collaboration. Available from https://www.c3outcomes.org/

**Contact**: CHORD COUSIN Collaboration 1991 Marcus Ave, Suite 300, Lake Success NY 11042 USA. Email: chordcollab@gmail.com

# Content

# Introduction

## About C3

The CHORD COUSIN Collaboration (C3) is an international research organization focused on development, dissemination, and implementation of high-quality Core Outcome Sets (COS) for trials and practice in dermatology and related areas through the engagement of patients, clinical experts, methodologists, and industry partners.

## Our vision

C3's vision is the improved health of patients through robust assessment of interventions for skin conditions. Our mission is to develop, disseminate and implement COS for clinical trials and routine clinical care through the engagement of patients, clinical experts, methodologists, industry partners, and other stakeholders.

## Purpose of this manual

The C3 Manual is a practical, step-by-step guide for the development of Core Outcome Sets (COS) in dermatology. It serves as an explanation and elaboration of the C3 Checklist (**Appendix 1**), which outlines the minimum required steps for COS development. The manual provides detailed guidance on how to implement each step in practice, including clarifications, recommendations, and examples tailored to the dermatology context. It complements existing resources such as the COMET Handbook, which offers general recommendations for COS development, and the COSMIN methodology, which provides standards for selecting and evaluating outcome measurement instruments. By addressing practical decisions and challenges specific to dermatology, the C3 Manual supports consistent and high-quality application across COS projects.

**Appendix 1: C3 Core Outcome Set Development Checklist**:
https://www.c3outcomes.org/resources

Clinical trials for diseases of the skin are proceeding at a rapid pace, and we are witnessing the development of several new treatments which are safe and effective, and which reduce the impact that disease has on patients. However many trials, especially those for rare skin diseases with few regulatory approved drugs, have little consistency in the 'what to measure' and the 'how to measure' aspects in trial protocols. Moreover, measurements used in trials often lack input from an important stakeholder group, our patients. Some outcome measurement instruments used in trials also have insufficient validation, which makes the results difficult to interpret. Finally, use of disparate outcome measurement instruments restricts our ability to compare efficacy across trials.

C3 seeks to address these issues through establishing COS for skin diseases that support development of new therapies and improve the consistency and relevance of outcome measurement. A COS is a standardized minimum set of outcome domains and outcome measurement instruments that should be used across all relevant studies for a given condition, with the goal of ensuring robust and comprehensive measurement framework that also allows for comparisons of effectiveness across trials.
While clinical trials are a primary focus, COS can also be developed for and applied in other research and healthcare settings, such as observational studies, registries, routine clinical care, and public health surveillance. The C3 Manual is therefore relevant not only for COS developers working in clinical trial contexts, but also for those aiming to harmonize outcomes in broader dermatological research and care.

In order to achieve these goals, C3 brings together clinical experts, patients, methodologists, industry partners, and other stakeholders in the scientific process. A fundamental doctrine for our work is that disease measures and outcomes must be patient-centered, and in fact, must have direct input from patients.

Developing high-quality COS is a complex and iterative process that may take several years to complete. These sets should be seen as evolving resources: as new evidence emerges, updates may be needed, and the benefits and drawbacks of making changes should always be carefully weighed.

# The C3 Manual

## Version and updates

This document is version 2.0 of the C3 Manual with the latest edits made on December 30th, 2025.

The C3 Manual is a living document; it will be updated regularly to align with advancements in the field of COS development. The latest version of the C3 Manual is readily accessible at no cost on the website: https://www.c3outcomes.org/manual/

## Authors

The C3 Manual has been developed by the members of the C3 Methods Group:
Prinsen C[1], Alam M[2], Eleftheriadou V[3], Ezzedine K[4], Garg A[5], Kirkham JJ[6], Ingram J[7], Munblit D[8,9], Spuls PhI[10], Thomas KS[11], Thorlacius L[12], Kottner J[13].

## Affiliations

[1]Department of Dermatology, Amsterdam UMC, Academic Medical Center, University of Amsterdam, Amsterdam Public Health, Infection and Immunity, The Netherlands
[2]
[3]
[4]
[5]Department of Dermatology, Northwell Health, New York, USA
[6]Centre for Biostatistics, The University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom
[7]
[8]Care for Long Term Conditions Division, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London, United Kingdom
[9]Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, FSAEI HE I.M. Sechenov FMSMU of MoH of Russia (Sechenovskiy University), Moscow, Russia
[10]Department of Dermatology, Amsterdam UMC, Academic Medical Center, University of Amsterdam, Amsterdam Public Health, Infection and Immunity, The Netherlands
[11]
[12]
[13]Charité-Universitätsmedizin Berlin, Institute of Clinical Nursing Science, Berlin, Germany

## Editors

C.A.C. (Sanna) Prinsen

## Citation

This version of the C3 Manual can be cited as:

**Prinsen C, Alam M, Eleftheriadou V, Ezzedine K, Garg A, Kirkham JJ, Ingram J, Munblit D, Spuls P, Thomas KS, Thorlacius L, Kottner J.**
*The C3 Manual.* Version 2.0. CHORD COUSIN Collaboration; 2025. Available from: https://www.c3outcomes.org/manual/ (accessed December 2025).

## Disclaimer

The guidance documents referenced in this chapter are open-access methodology publications. They are reproduced here for educational and informational purposes only. We acknowledge the original authors for their contributions, and while we strive to accurately represent their content, this chapter does not claim authorship of these methodologies. The use of these documents should not be considered as an endorsement or replacement of the original works, and we assume no responsibility for their content.

# How to use the C3 Manual

The C3 Manual is divided into two main sections:

- Part A, which comprises of 18 steps in the Core Outcome Domain Set Development process
- Part B, which includes 23 steps in the Core Outcome Measurement Instrument Development process.

**Structure and purpose**

Part A focuses on establishing the core outcome domains that should be assessed and reported as a minimum in clinical trials involving a particular dermatological condition.

Part B offers guidance on the selection of outcome measurement instruments for assessing the identified core outcome domains. In addition, it addresses the planning and implementation of the COS in clinical research and practice.

While implementation is discussed in more detail in Part B, we recommend that considerations for implementation are considered from the beginning of the COS development process.

Together, these sections provide a comprehensive roadmap for developing high-quality COS.

**Guidance and Practical Support**

The Manual offers guidance on how to effectively implement the proposed steps, providing practical advice, examples, template documents, and best practices. This guidance aims to facilitate the consistent and rigorous development of COS, thereby enhancing the quality and comparability of research findings across clinical trials and other areas in dermatology. In doing so, we seek to achieve an optimal balance between rigorous methodology and practical considerations, such as workload and time investment.

Additionally, the C3 Manual aims to provide guidance and resources to assist COS developers in their work, allowing flexibility to adapt methods to specific needs and contexts. By adhering to the C3 Manual, COS developers can ensure that their work meets C3's standards of methodological rigor.

**Referencing Appendices and C3 Resources**

Appendices are highlighted in grey boxes throughout this manual for easy reference. When referring to appendices or downloadable C3 resources, please include the full title, version (if stated), and the source: CHORD COUSIN Collaboration, https://www.c3outcomes.org.

# Part A: Core Outcome Domain Set Development Standards

Part A describes the minimum standards that C3 COS developers should adhere to in the Core Outcome Domain Set Development process.

## COS Group

### Introduction

Creating a robust COS for dermatology requires the formation of a dedicated group of diverse and representative stakeholders. This chapter will guide you through the process of assembling an effective COS group, ensuring international representation, inclusion of key stakeholders, and comprehensive coverage of the disease state and COS development.

## Step 1. Assemble your COS group

Before initiating the COS development process, COS developers should first visit the C3 website to ensure that their topic of interest is not already part of an ongoing C3 COS project. In addition, we recommend searching the Core Outcome Measures in Effectiveness Trials (COMET) database for ongoing, on-hold or completed COS projects that address the same or a similar topic. This check helps to avoid duplication efforts and ensures that the proposed COS project addresses an unmet need or a unique aspect within the field of dermatology.

If there is potential overlap with an existing COS, developers are encouraged to contact the C3 Methods Group to discuss whether a full COS development process is warranted or if a more targeted 'top-up' project would be more appropriate. We also recommend reaching out to the authors of related COS projects to explore potential collaboration or alignment.

To further avoid duplication and ensure relevance, COS developers are advised to conduct initial landscape scans to identify existing COS-related work. This can include rapid searches in PubMed and Embase, in the COMET database, or exploratory inquiries via AI-assisted platforms (e.g. Google Gemini) that offer quick overviews of the current landscape. Where appropriate, these should be followed by more detailed searches of COS-related initiatives such as IDEOM and ICHOM.

#### Steering Committee: Leadership and Direction

The first step in forming your COS group is to establish a Steering Committee, which will provide strategic oversight and leadership throughout the development process. This

committee typically consists of a small group of individuals responsible for defining the scope and objectives of the COS, setting key milestones, and ensuring that the project adheres to ethical and methodological standards.

To avoid confusion, it is important to clarify that the Steering Committee may not be responsible for the day-to-day tasks of COS development. These activities, such as literature searches, preparing Delphi rounds, analyzing data, or drafting materials, are usually carried out by the Working Group(s). The Steering Committee may delegate specific tasks, offer guidance on key decisions, and help resolve methodological or stakeholder-related dilemmas.

The Steering Committee should represent a balanced mix of expertise, including dermatology, methodology, and patient perspectives, and consists of experts in the relevant clinical fields who have a proven track record in research and/or COS development, and whom can commit sufficient time and resources to the project.
Their primary responsibilities include chairing the group process, overseeing the entire development process, ensuring adherence to ethical and methodological standards and established guidelines, and facilitating communication among all stakeholders. Additionally, they are tasked with ensuring that the COS developed is comprehensive, relevant, and inclusive of diverse perspectives, particularly those of patients and caregivers.

### Working Groups: Focused Contributions

In addition to the Steering Committee, it may be beneficial to establish Working Groups to handle specific tasks or areas within the COS development process. These Working Groups operate under the guidance of the Steering Committee and should involve a multidisciplinary team of clinicians, researchers, patients, caregivers, and other relevant stakeholders. Key responsibilities of these groups include but are not limited to conducting reviews, gathering data, developing and refining outcome domains, and engaging with stakeholders to gather input and feedback. Members of the Working Groups should be selected based on their expertise relevant to the specific task or disease state, their ability to represent different stakeholder perspectives, and their willingness to collaborate and contribute to the project.

**Time Commitment and Expectations**

To ensure clarity and alignment, members of both the Steering Committee and Working Groups should be informed of the expected time investment. Steering Committee members should anticipate dedicating approximately 1-10 hours every 1 to 2 months (depending on the stage and activity of the project) for meetings, correspondence, and decision-making tasks. Working Group time commitment will vary depending on the tasks that they are working on and level of involvement by individual members. Tasks may include literature reviews, protocol development, or stakeholder engagement.

## Considerations for Group Composition

### International Representation

To enhance the applicability of the COS across different settings, we recommend considering the inclusion of stakeholders from multiple geographical regions. Skin conditions can vary by geographical region, ethnic background, and treatment approaches may differ, so diverse representation can help ensure broader relevance. Recruitment efforts may include outreach via professional networks, conferences, and patient advocacy groups.

### Stakeholder Inclusion

The group should include all relevant stakeholders, particularly patients and caregivers, who provide invaluable insights into the impact of skin conditions and treatments and the relevance of outcomes. To guide patient participation from the outset, developers are encouraged to consult the POPPIE (Patient Participation, Involvement and Engagement) guidance developed by COMET. POPPIE provides practical and ethical recommendations on involving patients throughout the COS development process. Engaging patient advocacy groups and using purposive sampling can ensure diverse patient representation. Stakeholder involvement is a dynamic process, and group composition may evolve over time. The group should remain open to the inclusion of new members as the project progresses, to ensure continued relevance and representativeness.

### Comprehensive Expertise

Comprehensive representation of all aspects relevant to the disease state and COS development is essential. This includes clinical and psychosocial perspectives, as well as economic expertise where appropriate. While health economics input can be valuable, it may not be necessary for every COS project.

Using a structured stakeholder mapping approach can help identify representatives from all relevant domains. This involves systematically identifying and engaging key stakeholders to ensure diverse perspectives are included in the COS development process. COS developers can achieve this by, for example, searching the literature to identify key opinion leaders, consulting expert panels, and engaging with patient organizations. A good example is the CORALS lichen sclerosis steering group, which includes representation from dermatology, gynecology, urology, sexual health, nursing, patients, and methodologists which is illustrating the value of broad, interdisciplinary input.

### Stakeholder Engagement Plan

To maintain active involvement and commitment from stakeholders throughout the COS development process, it is recommended to implement a stakeholder engagement plan. This may include regular updates via email, newsletters, or virtual meetings to share progress and gather feedback. The plan should also define expectations for active participation and describe how to respond if a stakeholder does not engage meaningfully. This could include

follow-up communication to clarify their availability or, if needed, replacing inactive members to maintain balanced and continuous input.

**Working Group Responsibilities**

Working group members play a crucial role in the COS development process by handling specific tasks. Their responsibilities may include:

- Participating actively in (online) working group meetings to collaborate with other members and discuss progress.
- Accepting specific responsibilities and share the workload, including writing study protocols, conducting scoping or other reviews, and (Part B:) developing and/or refining/validating outcome measurement instruments.
- Engaging in consensus processes to select and/or refine the core outcome domains.
- Contributing to dissemination and implementation activities, including evaluating the uptake of the COS in clinical research and practice, to ensure it is effectively communicated and applied in relevant settings.

**Conflict of Interest Declaration**

To promote transparency and prevent potential bias, all members of the Steering Committee and Working Groups should complete a Conflict of Interest (COI) declaration at the start of their involvement. This step ensures that any competing interests are disclosed and managed appropriately, safeguarding the integrity of the COS development process. Depending on the nature and extent of the declared COI, appropriate measures may be taken, such as restricting participation in specific discussions or excluding individuals from voting on certain decisions.

C3 aims to maintain a centralized COI log for all affiliated COS projects, which will allow for public access to relevant disclosures. This system is currently under development. To support appropriate management of declared conflicts of interest, C3 recommends aligning with established guidance from reputable sources, such as the Cochrane Conflict of Interest Policy (2020) (https://www.cochranelibrary.com/cdsr/editorial-policies#coi) and the WHO Guidelines for Declaration of Interests (https://www.who.int/about/ethics/declaration-of-interests). Depending on the nature and severity of the conflict, mitigation strategies may include transparency within the group, restriction from participation in certain decisions, or recusal from voting.

Examples of potential conflicts include financial relationships (e.g. funding from industry), intellectual property interests (e.g. development or ownership of an outcome measurement instrument), or professional roles that may influence objectivity (e.g. advisory roles or affiliations with commercial entities).

COI declarations should be updated whenever new relevant information becomes available, or a potential conflict arises. C3 recommends that project teams maintain an up-to-date COI log for all COS contributors and consider making this information publicly accessible to enhance transparency.

A **C3 Template COI Form** can be found in Appendix 2 and is available on the C3 website: [link to be included here]

**Appendix 2: C3 Template COI Form:**
[Link to be included here]

**Authorship Considerations**
It is recommended to establish clear authorship rules at the beginning of the COS development process. Early agreement on who qualifies for authorship, how the order will be determined (e.g. based on contribution, alphabetical order, or a combination), and how to handle group authorship and acknowledgements can prevent misunderstandings later on. Consideration should also be given to whether panelists or Delphi participants will be acknowledged or included under group authorship, and how transparency around contributions will be maintained.

We encourage COS developers to follow established guidelines such as the ICMJE authorship criteria (https://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html) and to document these decisions in writing, preferably as part of the protocol or project charter.

## Conclusion

Assembling a diverse and representative COS group is the first critical step in developing a robust and applicable COS for dermatology. By ensuring international representation, including key stakeholders, and addressing all relevant aspects of the disease state, COS developers establish a strong foundation for a successful and impactful development process.

### Introduction

COS developers are encouraged to familiarize themselves with existing C3 guidelines, resources, and C3 support available on the website.

## Step 2. Submit COS development Application Form to C3

The second step in the COS development process is to submit the COS Development **Application Form** to C3. This Application Form, available on the C3 website (see Appendix 3), captures key details about the proposed COS project, including the team composition, scope, objectives, methodology, and anticipated timelines. The Application Form will be reviewed by the Executive Committee and the Methods Group. The review focuses on the methodological quality, relevance of the topic, feasibility, and alignment with C3's principles and standards.

Note that completing this form requires planning and attention to detail to ensure that all relevant aspects of the project are addressed. Providing comprehensive information supports an effective review process, and applicants are therefore encouraged to complete all sections as thoroughly as possible.

**Appendix 3: C3 Application Form**:
https://www.c3outcomes.org/resources?download_file=eyJpZCI6IjEwMDIwMCJ9

*Please note that the C3 Application Form will soon also be available as an electronic form that can be completed directly on the website.*

## Step 3. Approval and registration within C3 obtained

Following a review by the C3 Executive Committee and Methods Group, C3 confirms that the project is aligned with its principles and formally registers the COS development project on the C3 website. Approval is based on the information provided in the Application Form and indicates that the proposed methodology is considered appropriate and feasible at this stage.

As part of this process, a C3 Methods Support person is assigned. This person acts as the primary point of contact for methodological questions and supports the COS developers in aligning the project with C3 standards. Early engagement helps COS developers navigate the process effectively and promotes methodological robustness from the outset.

Registration within C3 not only confirms alignment with C3's standards but also provides developers with access to C3's network, resources, and ongoing support. Additionally, it enhances the project's credibility and visibility within the research community.

## Conclusion

By verifying that the topic is not part of an existing C3 project, completing and submitting the C3 Application Form, and securing approval and registration from C3, a strong foundation for your COS project is established.

## Introduction

This chapter outlines the key steps for developing the protocol for Core Outcome Domain Set Development. These steps help COS developers define the scope and aim of their project and prepare a clear protocol that aligns with established methodological standards.

# Step 4. Define the Scope of the COS: Health Condition, Population, Intervention, and Context/Setting

The starting point in protocol development is to clearly define the scope of the COS. This involves specifying four key aspects: the health condition, population, intervention (if applicable), and context or setting for which the COS will be developed. A well-defined scope ensures that the COS is relevant and applicable to the intended target population.

- **Health Condition**: Identify the specific dermatological condition being addressed. For example, specify whether the COS targets a single disease (e.g., atopic dermatitis) or a broader category of related conditions. Use existing disease classification systems (e.g. WHO-ICD 11) or consensus definitions where possible.
- **Population**: Clearly describe the characteristics of the affected individuals. This includes age groups (e.g., pediatric vs. adult patients), disease severity, skin type (including skin of color), or any other relevant group characteristics.
- **Intervention (if applicable)**: Specify the type of intervention the COS is intended to evaluate. This could include pharmacological treatments, surgical procedures, or lifestyle interventions. If the COS is not developed for an interventional study context (e.g. for observational research, trial registries or routine clinical practice), this should be clearly stated, and the scope should reflect the intended use accordingly.
- **Context/Setting**: Define the context or setting where the COS will be applied. This may include clinical trial settings, routine care, observational studies, and registries. Include geographical or healthcare system considerations if relevant. Consider whether the COS is intended for international use or tailored to a specific healthcare system, region, or country. While international applicability may be ideal in some cases, a more limited geographical scope may be appropriate depending on the objectives and feasibility of the COS project.

## Step 5. Develop Core Outcome Domain Set development protocol using C3 Manual

The next step is to develop the Core Outcome Domain Set development protocol, using the **C3 Template Protocol for Core Outcome Domain Set Development** (see Appendix 4).

**Appendix 4: C3 Template Protocol for Core Outcome Domain Set Development**:
The C3 Template Protocol for Core Outcome Domain Set Development is currently being developed and will be uploaded to the C3 website as soon as this document is available.

Link to the C3 website to be included here.

This template provides a framework that outlines key steps for each stage of the COS development process, ensuring a structured, transparent, and methodologically sound approach.

The C3 Template Protocol for Core Outcome Domain Set Development not only helps to structure the development process but also integrates best practices and standards to ensure alignment with C3's guidelines. Additionally, it includes implementation strategies that support the uptake of the Core Outcome Domain Set in various research and clinical contexts, including but not limited to clinical trials, observational studies, and registries.

Implementation of the COS starts at the very beginning of the COS development process with different implementation strategies, such as raising awareness of the COS via newsletters and stakeholder engagement (Leshem, 2023). It is recommended to outline the intended implementation strategy in the protocol (also see Step 18).

For a COS to be feasible and widely implementable, it is generally recommended, where possible, to aim for four to five core outcome domains. This helps ensure that the COS is practical for use in clinical trials and routine practice while still capturing the most essential outcomes.

We encourage COS developers to refer to the C3 Template Protocol for Core Outcome Domain Set Development for detailed instructions and a step-by-step framework tailored to guide the development of your specific Core Outcome Domain Set. This protocol serves as a roadmap, ensuring that your project adheres to the C3 standards.

One example of a protocol on Core Outcome Set development from the COSEB (for Epidermolysis Bullosa) group can be found here:
https://link.springer.com/article/10.1186/s13063-025-09052-w

## Step 6. Review and apply to COS-STAD and COS-STAP guidance documents

During protocol development, it is essential to review and apply the **COS-STAD** (Core Outcome Set-STAndards for Development, see Appendix 5) and **COS-STAP** (Core Outcome Set-STAndardised Protocol Items, see Appendix 6) guidance documents. These documents outline the minimum standards and recommendations for COS development, helping to standardize the process and ensure that the protocol adheres to best practices.

### How to Apply the Guidance Documents

- **Familiarize yourself with COS-STAD and COS-STAP**: Begin by reviewing the COS-STAD standards, which outline 12 key criteria for high-quality COS development, such as stakeholder involvement, transparency, and consensus methods. Use the COS-STAP document as a checklist to ensure that all essential protocol items are included.
- **Draft Protocol**: Compare your protocol draft against the criteria in COS-STAD and COS-STAP. Highlight areas that align with the guidelines and identify any gaps or aspects that require further detail or adjustment.
- **Integrate Feedback**: Engage your Steering Committee and stakeholders to review the revised protocol and confirm that the COS-STAD and COS-STAP criteria are fully addressed.

By using the C3 Template Protocol (Appendix 4), which incorporates the COS-STAD and COS-STAP guidance documents, adherence to these standards is streamlined. This ensures that the resulting COS protocol is robust, transparent, and aligned with international best practices.

**Appendix 5: COS-STAD guidance document**
Kirkham JJ, Davis K, Altman DG, Blazeby JM, Clarke M, Tunis S, et al. (2017) Core Outcome Set-STAndards for Development: The COS-STAD recommendations. PLoS Med 14(11): e1002447.

https://doi.org/10.1371/journal.pmed.1002447

**Appendix 6: COS-STAP guidance document**
Kirkham, J.J., Gorst, S., Altman, D.G. et al. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. Trials 20, 116 (2019).

https://doi.org/10.1186/s13063-019-3230-x

## Step 7. Submit protocol to C3 Methods Group

Once the protocol is finalized, it must be submitted to the C3 Methods Group for review.

### How to Submit

- **Prepare Your Submission**: Ensure that your protocol is complete and follows the structure provided in the C3 Template Protocol (Appendix 4).
- **Submit via Email**: Protocols can be submitted directly to C3 via email at chordcollab@gmail.com.
- **Engage in the Review Process**: The review process by the Executive Committee and the Methods Group typically takes approximately two to four weeks. Be prepared to respond to queries or requests for clarification during this time. This collaborative review helps refine the protocol to meet C3's methodological standards.

### Purpose of the Review

The Methods Group will assess the Core Outcome Domain development protocol to evaluate its alignment with C3's methodological standards and principles of quality and transparency. Their feedback may include suggestions for improvement or refinement. Adhering to these recommendations ensures that the project is methodologically sound and consistent with C3's approach. Projects that meet these standards can formally align with C3 and benefit from its network, resources, and ongoing methodological support.

**Submit your protocol for review directly via the C3 website:**
A direct link to the C3 website will be included here. Until then, please use the provided email address: chordcollab@gmail.com

Please note that the protocol submission process will soon be fully online. Both the submission form and the protocol document can then be submitted directly via the C3 website.

## Step 8. Protocol reviewed by C3 Methods Group

Following submission, the C3 Methods Group will review the protocol to evaluate its methodological quality, feasibility, and overall alignment with current best practices in COS development. As methodological standards are continuously evolving, the Methods Group considers the use of state-of-the-art methods, and transparent and up-to-date approaches.

Key areas of focus during the review include: the justification and clarity of the proposed methodology, the feasibility of the planned activities, and the proposed strategies for implementation and dissemination.

**Review process and revisions**
The review process approximately takes 2 to 4 weeks. During this time, developers will receive detailed feedback highlighting strengths, potential gaps, or areas for improvement. Revisions may be requested as part of an iterative process to ensure that the protocol is methodologically sound, feasible, and consistent with C3's quality standards.
Engaging in this collaborative review enhances the overall quality and relevance of the protocol. Developers are advised to allocate sufficient time to incorporate feedback before proceeding to the next step.

## Step 9. Register protocol with COMET database and on C3 website

Early in the development process, COS developers should register their project with the COMET (Core Outcome Measures in Effectiveness Trials) database and on the C3 website. This can be done even before the full protocol is finalized, as COMET only requires key project information at the initial stage. Registering early helps prevent duplication of efforts and signals to the broader community that a COS is being developed for a specific topic.

Once the protocol is finalized and approved by the C3 Executive Committee and the Methods Group, the full protocol can then be uploaded to both platforms to ensure full methodological transparency and visibility.

**How to Register**
Upload your protocol via the COMET database at www.comet-initiative.org following the provided guidance and instructions. The C3 administrative team (chordcollab@gmail.com) will update the registration on the C3 website.

**COMET database:**
A direct link to the COMET database can be found here:
https://www.comet-initiative.org/About/SubmitNewStudy

**Registration link C3 website:**
A direct link to the C3 website will be included here. Until then, please use the provided email address: chordcollab@gmail.com

## Step 10. Publish protocol, preferably in open access format

The final step in the protocol development process is to is to ensure that the protocol is accessible in the public domain.

We recommend uploading the protocol to the C3 website and/or a public repository. This may include a preprint server (e.g. MedRxiv (https://www.medrxiv.org) or OSF (https://osf.io), which allows for early sharing of protocols prior to peer review. Publication in a peer-reviewed journal may be considered if appropriate, but is not required.

We appreciate it when COS development groups acknowledge C3 in their research presentations and publications. Authorships and declarations of Conflicts of Interest for publications resulting from C3 support should follow the recommendations of the International Committee of Medical Journal Editors (ICMJE) (see https://www.c3outcomes.org/memorandum-of-understanding).

If a C3 Methods Group member has made a substantial intellectual contribution to the design, analysis, or interpretation of the COS development project, their inclusion as a co-author should be considered in accordance with ICMJE criteria. We encourage COS development groups to discuss authorship expectations early in the process and revisit them as needed during manuscript preparation.

### Conclusion

A clear, accessible protocol lays the foundation for a rigorous and well-coordinated COS development process. By registering the project and making the protocol publicly available, COS developers strengthen the credibility, transparency, and future implementation of their

work. This practice also helps to protect against key risks of bias identified in the COS-STAD recommendations.

# Generate Candidate Core Domain Set

## Introduction

This chapter outlines the steps required to outline and define potential core outcome domains. The process involves conducting a scoping review, reviewing qualitative evidence, and generating a comprehensive long list of candidate outcome domains, ensuring a comprehensive and stakeholder-informed approach.

It is important to note that disagreement or concerns may arise during this phase. Developers should remain open to dissenting voices, while using transparent methods and clear criteria to guide decisions. The goal is not to reach consensus at this stage, but to ensure that the long list reflects the full range of potentially relevant domains.

To avoid unnecessary delays, COS developers are encouraged to take a structured but pragmatic approach, focusing on completeness and clarity without striving for perfection. The long list will be further refined during the consensus process.

In addition, it should be noted that for most inflammatory skin conditions, outcome domains such as signs and symptoms and health-related quality of life are already considered core. COS developers may choose to assume their inclusion and focus efforts on refining these domains during the eDelphi stage, or on identifying appropriate measurement instruments during the scoping review.

## Step 11. Conduct a scoping review to identify all potentially relevant outcomes

### Aim of a Scoping Review

Conducting a scoping review is the initial step in generating a candidate list of outcome domains. A scoping review is a systematic approach to identify and map the existing evidence available on a particular topic. In our case the focus is systematically collecting and categorizing reported outcome domains related to the specific dermatological condition of interest. This includes outcome domains reported across quantitative evidence (e.g. outcomes reported in clinical trials or observational studies) and qualitative evidence (e.g. themes and concepts identified in interviews, focus groups, or patient narratives).

**Note on terminology**

We acknowledge that distinguishing between outcome domains, concepts, contextual factors (e.g. baseline characteristics), domain items, and outcomes can be challenging. A standardized taxonomy for outcome domains in dermatology is currently being developed within C3 to support clarity and consistency across COS projects.

Until this taxonomy becomes available, COS developers are advised to clearly define the terms they use within their project and to apply them consistently throughout the scoping review and subsequent steps. Importantly, contextual factors such as baseline characteristics are not considered outcome domains, but may be relevant in developing a minimum dataset or in interpreting intervention effects.

### How to Conduct the Scoping Review

We recommend adhering to the *Joanna Briggs Institute Methodology for Scoping Reviews* (see Appendix 7) and the *Best practice guidance and reporting items for the development of scoping review protocols* (Peters et al. 2022) (see Appendix 8)

The PRISMA Extension for Scoping Reviews guidance and its checklist items (see Appendix 9) can be used when reporting the scoping review (Tricco et al. 2018).

**Appendix 7: Joanna Briggs Institute Methodology for Scoping Reviews**
https://jbi.global/scoping-review-network/resources

**Appendix 8: Best practice guidance and reporting items for the development of scoping review protocols**
Peters, Micah D.J.; Godfrey, Christina; McInerney, Patricia; Khalil, Hanan; Larsen, Palle; Marnie, Casey; Pollock, Danielle; Tricco, Andrea C.; Munn, Zachary. Best practice guidance and reporting items for the development of scoping review protocols. JBI Evidence Synthesis 20(4):p 953-968, April 2022.

https://doi.org/10.11124/JBIES-21-00242

**Appendix 9: PRISMA-ScR Checklist and Explanation**
Andrea C. Tricco, Erin Lillie, Wasifa Zarin, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med.2018;169:467-473

https://doi.org/10.7326/M18-0850

We recommend that a scoping review should involve at least two reviewers with experience in conducting systematic or scoping reviews, as well as expertise in the relevant dermatological condition.

Please note that PROSPERO does not accept the registration of scoping reviews. Instead, scoping reviews can be registered in the Open Science Framework (OSF) database, see: https://osf.io, or submitted as a standalone publication in a peer reviewed journal (e.g. BMJ Open).

In practice, the distinction between scoping reviews and systematic reviews is not always consistently applied. Many COS projects refer to their work as a 'systematic scoping review' to emphasize that the process was structured and reproducible, even if it does not meet all methodological requirements of a full systematic review (e.g. risk of bias assessment). Journal editors and peer reviewers may prefer the term "systematic review", or may require clarification on why a scoping approach was chosen. COS developers are therefore advised to be transparent in their methods section and to explain the rationale for using a scoping review (e.g. mapping concepts, identifying outcomes). The PRISMA-ScR guideline can be a helpful reference in such cases.

### Outcome of the Scoping Review

The outcome of a scoping review is a list of previously used or proposed outcome domains. This serves as the foundation for developing a comprehensive long list of candidate outcome domains.

Although the primary aim is to identify outcome domains, COS developers may also consider extracting the outcome measurement instruments (OMIs) used to assess these domains, especially for commonly reported areas such as signs, symptoms, and quality of life. This can improve efficiency and help inform subsequent steps in the COS development process. Relevant data sources include bibliographic databases (e.g. PubMed, Embase), trial registries (e.g. ClinicalTrials.gov, WHO ICTRP), and grey literature (regulatory documents, industry reports, conference abstracts). At present, C3 does not provide a standardized extraction template, but this has been identified as a potential future satellite project. COS developers

are encouraged to design and document their extraction methods transparently and consistently.

## Step 12. Review qualitative evidence and/or conduct qualitative work, including focus groups, surveys and/or interviews, as needed

Qualitative input is helpful to broaden the scope of outcome domains that might be missed if you rely solely on published trials, trial registries or systematic reviews (Brunton et al. 2020).

Following the scoping review, the next step is to review existing qualitative evidence (if not already done within the scoping review) and/or collect new stakeholder input to gain deeper insights into the outcome domains that matter most to patients and other relevant stakeholders. This may involve reviewing qualitative studies or conducting new qualitative work (e.g. interviews, focus groups, or surveys) to understand patients' and caregivers' perspectives.

Qualitative research in this context often explores broader themes, such as lived experiences, concerns, and treatment goals, rather than explicitly named outcomes. These themes need to be carefully analyzed and mapped to potential outcome domains using transparent and systematic methods (e.g., thematic analysis followed by conceptual mapping). This process helps translate rich qualitative data into candidate domains that are both meaningful and measurable in future studies.

A formal qualitative systematic review can be valuable, but is not always necessary. Before initiating new qualitative work, COS developers are advised to search for existing systematic reviews of qualitative evidence, as these may already provide rich insights into patients' experiences and priorities, potentially eliminating the need for new data collection. When no such reviews exist, meaningful patient and public involvement (PPI) activities can still provide sufficient insight into core outcome priorities, particularly when resources or time are limited. These may include focus groups, structured interviews, or surveys with patients and caregivers. The aim is to identify what truly matters without overcomplicating or delaying the process. At the same time, developers should remain mindful of the need for transparency and methodological rigor. Especially for those developing a COS for the first time, it is important to strike a careful balance: ensuring stakeholder input is systematically gathered and translated into outcome domains, while keeping the development process timely and feasible.

### When to Conduct New Qualitative Research

Before initiating new qualitative research, COS developers should first explore whether relevant stakeholder input is already available. This includes reviewing existing qualitative studies, reports of previous patient or public involvement (PPI) activities, and outcomes reported identified through initiatives such as Priority Setting Partnerships (PSPs). These sources may already provide insights into concepts and experiences that map onto potential outcome domains.

If existing input is insufficient, outdated or lacks representation of key stakeholder groups (e.g., patients with skin of color, caregivers, or clinicians from underrepresented regions), new engagement activities may be helpful. Depending on the context, this could include focus groups, interviews, or surveys with patients, caregivers, or professionals. The purpose of this step is not necessarily to determine what stakeholders find most important, but to ensure that all potentially relevant outcomes are captured, including those that may not have been reported in trials. New qualitative research can thus serve to broaden the outcome list and ensure that it reflects the lived experience of those most affected.

### How to Conduct Qualitative Work

- Engage Stakeholders Early: Collaborate with your Steering Committee and Working Groups to identify key participants and ensure culturally sensitive, inclusive and accessible approaches to recruitment and data collection.
- Develop a Topic Guide: Create a semi-structured guide to ensure consistency across interviews or focus groups, while allowing participants the space to raise new ideas and express their views freely.
- Analyze Qualitative Data: Apply established analytical methods such as thematic content analysis, grounded theory, or framework analysis to organize and interpret the data. We strongly recommend involving researchers with expertise in qualitative methods at this stage to ensure methodological rigor and appropriate interpretation of findings.

## Step 13. Generate long list of candidate outcome domains and provide established definitions, including lay descriptions

With the insights gained from the scoping review and qualitative research, the next step is to finalize the long list of candidate core outcome domains. This involves compiling a comprehensive list of potential outcome domains identified through the previous steps.

### Defining Outcome Domains

Each outcome domain should be clearly defined. Definitions should be concise, unambiguous, and based on existing evidence where possible. To support clarity and consistency across COS projects, developers are encouraged to use standardized

terminology. When available, the dermatology-specific taxonomy currently under development within C3 should be considered the preferred reference.
In the meantime, developers may wish to consult existing classifications or definitions from the literature (e.g., Nast et al. 2016, Dodd et al. 2018), while bearing in mind that these are not always tailored to dermatological conditions and may need adaptation.

At this stage make sure that the presented outcomes domains have a unique meaning. For example, outcomes that have different names, but the same meaning (e.g. wound healing, numbers of wounds healed) should be summarized under one outcome domain. The same applies to outcomes measured at different points in time (Young et al. 2019).

In addition, all outcome domains in the long list should ideally be defined at a comparable level of granularity (Kottner et al. 2024). This helps avoid conceptual overlap and supports clarity in subsequent prioritization steps. Listing both a broad outcome domain (e.g., "disease severity") and its specific components (e.g., erythema, scaling) may confuse participants and artificially inflate the relative importance of overlapping concepts during voting.

While some variation in granularity may be acceptable, depending on the scope of the COS (see Steps 2 and 4)., developers are advised to be explicit about their choices and provide a clear rationale when including domains at different levels of abstraction.

The COS group should define and agree on a consistent level of granularity for all outcome domains, to avoid mixing broad categories (e.g. disease activity) with specific items (e.g. itch, scaling).

All domains should be defined at a comparable hierarchical level to support conceptual clarity and ensure meaningful instrument selection. For example, a higher-level domain such as clinical signs may encompass erythema, pustules, and erosion. Alternatively, if a more granular approach is chosen, these individual signs may each be treated as separate outcome domains. Regardless of the chosen approach, the group should clearly describe what each domain entails and explain the rationale behind the level of granularity. In addition, practical considerations such as participant burden, time commitment, and potential impact on retention during consensus processes should be taken into account when deciding on the level of detail.

Some COS groups distinguish between outcome domains, subdomains, or domain items, representing different levels of granularity rather than entirely separate constructs. For example, pain may be considered a domain, whereas burning sensation may be a more specific domain or subdomain within that category. Whatever level of granularity is chosen, it is important to apply it consistently across all domains and to ensure comparability.

### Incorporating Plain Language Descriptions

Alongside technically correct definitions, plain language descriptions should be provided to make the outcome domains understandable to non-experts, such as patients and caregivers. These descriptions should be written using understandable terminology, avoiding medical jargon, and reviewed by patient representatives to ensure clarity and accessibility.

Including well-defined plain language descriptions helps ensure that all stakeholders, including those without specialized knowledge, can meaningfully engage with and provide feedback on the proposed outcome domains.

In certain contexts, specific considerations may merit the involvement of children and young people themselves. Their perspectives can provide unique insights into how outcomes are understood and prioritized, and further adaptations (e.g. age-appropriate wording, visual aids, or alternative formats) may be needed to ensure that the material is accessible and meaningful across different developmental stages.

### How to Proceed

- **Review and Refine**: Collaborate with your Steering Committee and stakeholders to ensure all relevant outcomes have been included in the long list of potential outcome domains for the COS.
- **Validate Definitions**: Share the draft list and definitions with patients, patient representatives and other stakeholders for feedback before moving to the next step.
- **Consider Translations**: If the COS project involves stakeholders from different countries or language regions, consider where translations may be needed, such as outcome definitions, Delphi instructions, or consensus meeting materials. Translating key documents supports meaningful participation, accurate interpretation, and inclusivity throughout the process.

Translation is not only a matter of accessibility but also of equity, ensuring that stakeholders from diverse linguistic and cultural backgrounds can engage fully and equally throughout all stages of COS development.

## Conclusion

The process of generating the long list of candidate Core Outcome Domains is fundamental to the COS development process. By conducting a thorough scoping review, engaging in qualitative research, and developing a detailed list of candidate outcome domains with clear definitions, you establish a robust foundation for refining and prioritizing of core outcome domains.

# Consensus Process

## Introduction

To ensure that the outcomes selected from the candidate Core Outcome Domain Set are relevant and widely accepted, it is essential to engage in a robust consensus process that involves appropriate representation from all relevant stakeholders. For meaningful involvement of patients throughout this process, COS developers are encouraged to consult the POPPIE (Patient Participation, Involvement and Engagement) guidance developed by COMET, which offers practical recommendations for involving patients in all phases of COS development.

This chapter provides an overview of the key elements and methodologies for achieving consensus on the core outcome domains to be included in the final COS. In particular, it highlights the **eDelphi consensus process** and the **international consensus meeting** as effective methods for gathering and synthesizing diverse perspectives among stakeholders.

## Step 14. Select Core Outcome Domains using a consensus process that includes an appropriate representation of stakeholders

The consensus process should be designed to ensure that the views and expertise of all stakeholders (i.e. patients, clinicians, and other relevant a priori agreed upon stakeholder groups) are adequately represented. This representation is crucial to ensure that the selected core outcome domains genuinely reflect the priorities of those involved. To facilitate broad participation and thorough discussion, the consensus process may incorporate both virtual and in-person methods.

A common pathway for achieving consensus on the core outcome domains involves initially employing the eDelphi consensus process, followed by a consensus meeting. While the eDelphi is a widely used method, there are several variations in how it can be conducted, including the number of rounds, rating scales, feedback formats, and definition of consensus. COS developers are advised to select and document their approach carefully, and to consult available C3 resources or methodological experts if needed.

## Key Methods for Achieving Consensus

### *1. eDelphi consensus process*

C3 recommends the use of eDelphi studies in the consensus process, particularly for engaging a diverse, international group of stakeholders. The eDelphi method is widely used for consensus-building as it facilitates anonymous input and iterative feedback from a broad range of participants, including e.g. patients, patient representatives, clinicians, researchers, and methodologists (see below paragraph on 'Stakeholder Representation').

Stakeholders can be recruited through professional networks, patient advocacy groups, clinical registries, and relevant scientific or patient organizations. Clear eligibility criteria should be defined to ensure appropriate representation, and purposive sampling may be used to include underrepresented groups (e.g., patients with skin of color or caregivers). Invitations should clearly describe the study purpose, expected time commitment, and how participant input will be used.

This method is particularly advantageous for engaging geographically dispersed stakeholders. By minimizing the influence of group dynamics and promoting equal participation, the eDelphi process enables all voices to be heard.

We recommend adhering to existing methodological guidance when conducting and reporting eDelphi studies. This includes the CREDES guideline (Jünger et al., 2017 and Niederberger et al., 2024), which offers practical recommendations for conducting Delphi studies (see Appendix 10), and the more recent ACCORD reporting guideline (Tong et al., 2024), which provides a broader framework for the transparent reporting of consensus methods across health research (see Appendix 11).

**Appendix 10: CREDES Guideline**

Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: Recommendations based on a methodological systematic review. Palliative Medicine. 2017;31(8):684-706.

https://doi.org/10.1177/0269216317690685

Niederberger M, Schifano J, Deckert S, Hirt J, Homberg A, Ko ¨berich S, et al. (2024) Delphi studies in social and health sciences - Recommendations for an interdisciplinary standardized reporting (DELPHISTAR). Results of a Delphi study. PLoS ONE 19(8): e0304651.

https://doi.org/10.1371/journal.pone.0304651

**Appendix 11: Accord Reporting Guideline**
Gattrell WT, Logullo P, van Zuuren EJ, Price A, Hughes EL, Blazey P, et al. (2024) ACCORD (ACcurate COnsensus Reporting Document): A reporting guideline for consensus methods in biomedicine developed via a modified Delphi. PLoS Med 21(1): e1004326.

https://doi.org/10.1371/journal.pmed.1004326

### Evaluating Outcome Domains

The primary goal of the eDelphi consensus process is to achieve agreement on the core outcome domain set (i.e. 'what' to measure). Participants are asked to rate the importance of each candidate outcome domain based on three criteria:

- **Relevance**: Are the most critical outcome domains included in the core outcome domain set?

  Example question:
  *How important do you consider the inclusion of 'outcome domain X' in the core outcome domain set? (Not important – Important but not critical – Critically important – Not able to score)*
  *Please provide your reasoning in the free text box.*

- **Comprehensibility**: Is the definition of the outcome domain clear and easy to understand?

  Example question:
  *Is the definition of 'outcome domain X' clearly worded and easy to understand? (Strongly disagree – Disagree – Neutral – Agree – Strongly agree – I wish not to rate this item)*
  *Please suggest any improvements to the wording in the free text box.*

- **Comprehensiveness**: Does the definition cover all relevant aspects of the domain?

  Example question:
  *Does the definition of 'outcome domain X' include all relevant aspects? (Strongly disagree – Disagree – Neutral – Agree – Strongly agree – I wish not to rate this item)*
  *Please suggest any improvements to the definition in the free text box.*

To ensure the comprehensiveness of the core outcome domain set, the first-round eDelphi questionnaire should ask for suggestions for additional outcome domains:

Example question:
Are there any key outcome domains missing? (no – yes)
If yes, please suggest any additional outcome domains you think should be included and explain your rationale in the free text box.

Depending on the scope and purpose of the eDelphi, it is also advisable to collect key variables on e.g. stakeholder group, expertise, years of experience, and country of residence. This information is essential to assess panel diversity and representativeness and should be reported in the study results.

**Item generation**

Evidence suggests that the number of items in the questionnaire affects response rates, with larger numbers of items leading to lower engagement (Gargon et al., 2018). Although it depends on the granularity and topic (see Step 13), C3 recommends aiming for no more than 50-70 candidate domains in the first Delphi round, to balance comprehensiveness and participant retention. This recommendation is line with the OMERACT Handbook v2.1 (Beaton et al., 2021).

Where possible, pre-screening should be conducted before item generation to remove outcome domains that are clearly not suitable for inclusion in a COS. Examples include domains that are not applicable to most people affected by the condition or outcomes that can only be measured using highly specialized equipment or expertise. To ensure transparency, we recommend that COS developers outline this pre-screening approach in their protocol, including the criteria used and the rationale for excluding any domains. These decisions should also be reported when disseminating the COS development process and results. Such pre-screening helps keep the Delphi questionnaire focused and manageable, while maintaining methodological rigour.

**Response options**

Evidence indicates that the number of response options (e.g. 3, 5, or 9-point scales) influence the response behavior (e.g. De Meyer et al. 2019, Remus et al. 2021). However, the optimal number of response options is unknown.

### Iterative Feedback and Consensus

The eDelphi consensus process is iterative, allowing participants to refine their responses based on feedback from the group. To qualify as a Delphi survey, a minimum of two rounds (including at least one round of feedback) is required (Williamson et al., 2017).

The eDelphi process typically begins with participants rating the importance of outcome domains from the comprehensive list of candidate domains. After each round, the aggregated results and a summary of key arguments are shared with participants. This structured feedback promotes thoughtful re-evaluation of ratings.

In the second eDelphi round, participants who have completed the first round are presented with the group's aggregated responses from the first round. There is some evidence that the presentation of summarized voting results per stakeholder group may facilitate the consensus process of the entire group. It is very often observed that different stakeholder groups have different views and priorities, for example there might be differences between clinicians and patients.

Alongside these results, they receive a summary of reasoning provided by other participants, which may include arguments for or against the inclusion of specific outcome domains, as well as suggestions for refining domain definitions. Participants are asked to reconsider their initial ratings considering this feedback and can either maintain or adjust their scores.

If consensus is not achieved after the second round, a third round may be conducted. In this round, participants who have completed the first and second rounds are asked to focus on the remaining contentious outcome domains. The third round may serve to narrow down the list of outcome domains further, clarify definitions of outcome domains that remain ambiguous, or to confirm agreement with the overall results of the previous round. This step helps consolidate consensus while avoiding unnecessary discussion.

Any outcome domains or definitions that fail to reach consensus can be discussed further during an international consensus meeting for final decision-making.

### Reporting of eDelphi studies

To ensure methodological transparency and allow for critical appraisal, it is recommended to follow established reporting standards when reporting eDelphi studies. In particular, we recommend adherence to the CREDES guidelines (Jünger et al., 2017), the updated CREDES reporting guidance (Niederberger et al., 2024) and, where applicable, the ACCORD reporting guideline for Delphi-based consensus studies (Gattrell et al., 2024).

These resources complement each other and together support rigorous design and transparent reporting of Delphi consensus processes.

### Examples of eDelphi software includes:

Several platforms can be used to conduct eDelphi studies, ranging from purpose-built Delphi software to customizable survey tools. The following list provides examples of commonly used platforms:

- **REDCap (via COMET)**: The COMET Initiative currently uses REDCap for conducting eDelphi studies. REDCap is a secure, web-based application designed for data collection in research studies and can be adapted for structured Delphi processes. More information: https://projectredcap.org
- **DelphiManager**: Previously used by COMET, DelphiManager is a specialized eDelphi software tool designed for conducting and managing Delphi studies. It provides structured support for consensus-building and is available at: https://www.comet-initiative.org/delphimanager/
- **Qualtrics**: A widely used, user-friendly survey platform that can be customized for Delphi studies. It offers flexible survey design, data tracking, and export options, making it a practical choice for many research teams.
- **STAT59**: STAT59 is an all-in-one eDelphi software solution that supports the entire Delphi process, from study design to data analysis. It offers automated workflows and statistical tools to streamline consensus-building. More information: https://www.stat59.com/about/delphi-method-software
- **eDelphi**: A web-based platform specifically designed for Delphi studies, facilitating expert discussions and structured consensus-building through multiple rounds. It provides an interactive environment for real-time collaboration.
  See: https://www.edelphi.org
- **Welphi**: A cloud-based platform designed for Delphi studies, offering interactive surveys, customizable rounds, and real-time monitoring of responses.
  See: https://www.welphi.com

*Disclaimer: these examples are provided for information purposes only. C3 does not endorse any specific software tool and cannot guarantee their functionality, quality, or suitability for individual projects.*

### Stakeholder Representation

Ensuring appropriate representation of stakeholders is critical to the success of the consensus process. Stakeholders should be selected based on their expertise, experience, and relevance to the health condition of interest. This includes, but is not limited to:

- *Patients and Patient Representatives*: To ensure that the selected outcomes reflect the priorities and experiences of those directly affected by the condition. Ideally, patients from different countries and cultural backgrounds should be included; however, we acknowledge that this may not always be feasible due to practical or financial constraints. Where international representation is limited, efforts should be made to ensure diversity within the available patient group and to transparently report any limitations in representation.

- *Clinicians and Healthcare Providers*: To incorporate practical insights on the relevance and feasibility of the outcome domains in clinical practice.
- *Researchers, systematic reviewers, guideline developers*: To ensure that the outcomes are scientifically valid and make sense in the context of evidence-based practice.
- *Industry and Policy Representatives*: To provide perspectives on the broader impact of the COS, including regulatory and implementation considerations. Participation should be limited to scientific or medical representatives rather than commercial roles.
- *Regulatory Agency Representatives*: To ensure that selected outcomes are relevant for regulatory decision-making and can support clinical trial approval and product registration.
- *Journal Editors*: To ensure that the selected outcome domains align with publication standards and priorities, facilitating the dissemination and adoption of the COS in scientific literature.

To ensure robust stakeholder participation, COS developers are advised to set realistic recruitment and retention targets, tailored to the condition and stakeholder groups involved. Recent evidence suggests that panels of 60–80 participants can provide stable consensus results under certain conditions (Manyara et al 2024, https://www.jclinepi.com/article/S0895-4356(24)00241-5/fulltext).

Retention strategies should be clearly outlined in the protocol, and attrition rates reported transparently, as high drop-out may bias results.

**Note on Industry Involvement**
Industry participants can offer valuable scientific and regulatory insights. However, to minimize potential conflicts of interest, participation should be limited to science-based roles (e.g. clinical researchers, regulatory experts) and may exclude voting rights, depending on the project's governance and declared COI policy.

### Defining consensus

A clear and pre-defined definition of consensus is essential to the integrity of the consensus process in selecting core outcome domains. Consensus refers to the level of agreement among stakeholders on which outcome domains should be included in the COS. The threshold for defining consensus must be established before the process begins, based on both quantitative and qualitative criteria, in accordance with the COS-STAD recommendations (Kirkham et al., 2017).

There is no reference standard as how many outcome domains should be included in COS. We recommend including no more than four to five outcome domains, with seven as the

absolute maximum. It is important to explain to all stakeholders that all identified outcome domains may be important and can still be measured in individual studies, but the core outcome domains are those considered crucial and should always be measured and reported in all relevant trials. This distinction should be clearly communicated to all stakeholder groups.

### Thresholds for Agreement

In eDelphi consensus processes, a common a priori defined threshold is that at least 80% of participants must rate an outcome domain as "critical" or "important" to be included in the COS depending on the used scoring system. Several stricter or less stringent criteria may be applied including proportions for disagreement and combinations of proportions for agreement/disagreement (Williamson et al. 2017). It is always important to keep the overall goal of COS development in mind: identifying the critically important outcomes to be measured in all clinical trials or clinical practice. Therefore, the scoring system must help to fulfill this aim.

In general, the primary goal of the first eDelphi round is to gather a broad range of perspectives on potential outcome domains. Subsequent rounds should focus on analyzing differences in stakeholder group ratings, as variations in perspectives are common.

To prioritize the most critical domains, it is recommended to apply strict criteria for selection. Domains that remain undefined or borderline should be brought forward to the consensus meeting for further discussion. This is particularly important for outcomes where stakeholder group ratings differ significantly.

It is important to note that there is no universal threshold for determining which outcomes should be retained or excluded. Instead, COS developers should transparently define their selection criteria and refer to relevant methodological guidance. A comprehensive review of consensus methods in Delphi studies is provided by Diamond et al. (2014), which serves as a valuable reference document. The criteria used to define consensus in the eDelphi do not necessarily need to be identical to those applied in the consensus meeting; different rules may be appropriate depending on the stage of the process. However, any differences in thresholds or criteria between phases must be clearly predefined and documented in the protocol.

C3 recommends that all outcomes that are problematic, ambiguous, or subject to disagreement between stakeholder groups be considered for further discussion in the consensus meeting.

### Handling Dissenting Views

Dissensus occurs when there is disagreement among stakeholders, particularly when an outcome domain is rated as important by one stakeholder group but not by others. When this happens, it is crucial to carefully examine the reasons behind the disagreement. For example, if a domain is deemed important by patients but not by clinicians, this discrepancy should be discussed further. The consensus process may involve additional rounds of deliberation during the eDelphi or structured discussions at the international consensus meeting. During these meetings, participants with dissenting views should be encouraged to explain their rationale so that others can understand their perspective. Dissenting views should be documented in the meeting minutes to ensure transparency.

If dissensus persists and the outcome domain is not deemed critical by the majority of stakeholder groups, it may be appropriate to exclude the outcome domain from the final COS, provided there is clear documentation of the reasons for this decision.

### Addressing "No Consensus"

In some cases, no clear consensus may be reached on certain outcome domains, even after multiple rounds of discussion and deliberation. When "no consensus" occurs (i.e. if the domain does not achieve consensus by the final round), and no stakeholder group has supported this domain by at least 80%, the domain will not be endorsed for the final COS.

It is recommended to clearly document the lack of consensus, including the differing perspectives and the rationale for any decisions made.

### *2. International Consensus Meeting*

Following the completion of the eDelphi process, any remaining issues or outcome domains for which consensus was not achieved or where disagreement persists should be addressed in a face-to-face international consensus meeting.
Organizing a successful meeting requires thorough preparation and structured facilitation. Develop a detailed protocol that clearly defines the meeting's objectives, agenda, and expected outcomes, along with logistical details such as the date, location, participant list, and voting procedures. This ensures transparency and provides clear guidance to all participants.

For meaningful patient participation throughout the COS development process, developers are encouraged to consult the POPPIE (Patient Participation, Involvement and Engagement) guidance developed by COMET. This resource provides practical recommendations for effective patient involvement at all stages of COS development, including protocol design, Delphi surveys, consensus meetings, and dissemination activities.

For general guidance on organizing a face-to-face consensus meeting, we refer to the HOME V Meeting Protocol, which provides a comprehensive, practice-oriented framework, including preparatory steps, timelines, roles, and practical considerations for planning and facilitating an international consensus meeting.

For online consensus meetings, we refer to COMET guidance on issues to consider for online consensus meetings, which offers practical, evidence-informed recommendations on planning, preparing, facilitating, and documenting virtual consensus processes, including preparatory activities, technological setup, participant support, and considerations for effective engagement in a COS development context.

When planning online meetings, careful consideration should be given to time zone differences to maximize participation across regions. If multiple meetings are required to accommodate time zones, the results of voting should remain confidential until all meetings are completed, after which the combined results can be revealed to avoid influencing subsequent votes. Hybrid meetings (a mix of in-person and online participation) are generally not recommended for consensus building, as differences in participation format may affect discussion dynamics and decision-making.

**During the meeting**

Diverse stakeholder representation is essential to ensure that a wide range of perspectives are considered (see below paragraph on **Stakeholder Representation**). To optimize engagement, consider organizing pre-meeting material and sessions for specific groups, such as patients or non-specialists, to align participants on key topics and review findings from previous rounds. Background materials, including summaries of eDelphi results and supporting evidence, should be distributed in advance to help participants prepare.

It is crucial to foster a structured and inclusive environment. Techniques like the Nominal Group Technique (NGT) can be used to facilitate discussions in smaller groups. NGT is a structured method in which participants first generate ideas individually, then share them in a round-robin format, followed by a group discussion and private ranking or voting. This technique ensures that all voices are heard, including those who may be less comfortable speaking in larger settings.

Anonymous electronic voting systems should be employed to make final decisions, reducing peer pressure and encouraging honest input. Real-time feedback on voting results and key discussion points helps maintain transparency and focus.

**After the meeting**

After the meeting, compile a comprehensive summary report documenting key decisions, consensus reached, and any action items. Share this report with all participants for review and confirmation.

## Conclusion

The eDelphi process promotes broad participation and equal input by providing iterative feedback, while the consensus meeting enables focused, in-depth discussions to address and resolve remaining disagreements.

Both methods rely on meticulous planning, inclusive stakeholder representation, and predefined consensus criteria. Together, they ensure that the final core outcome domain set is scientifically robust, practically relevant, and widely endorsed by all stakeholders.

# Dissemination and Implementation

## Introduction

Once the Core Domain Set (CDS) has been agreed upon, it is important to begin planning for its dissemination and implementation to ensure its future impact. Early dissemination helps raise awareness among key stakeholders, while proactive planning supports the eventual integration of the CDS into clinical research and practice.

This chapter outlines the essential steps for sharing the CDS with stakeholders, registering it in key databases, and publishing it following established guidelines. It also provides guidance on planning further strategies to promote adoption, which should start during the domain stage to facilitate seamless transition to the later Core Outcome Measurement Instrument phase.

## Step 15. Share the Core Outcome Domain Set among the stakeholder groups that participated in the Delphi consensus process

Once the CDS has been agreed upon through the consensus process, it is essential to share the results with all stakeholder groups that participated in the Delphi survey and other consensus activities. This step ensures transparency, acknowledges contributions, and strengthens stakeholder engagement for future implementation efforts.

### How to Share the CDS

- **Direct Communication**: Send a detailed summary of the CDS and the consensus process to all participants and stakeholders via email or other communication platforms. Include a clear explanation of how the COS was developed and how stakeholder input influenced the outcomes.
- **Webinars or Meetings**: Organize webinars or virtual meetings to present the final CDS, discuss the results, and outline the next steps for implementation. Use these sessions to address any questions or concerns from stakeholders.
- **Tailored Reports**: Create customized reports for different stakeholder groups, such as patients, clinicians, researchers, policy makers, and journal editors. Highlight specific areas where their input was critical to the final CDS to emphasize their impact on the process.

- Dedicated Project Website: If available, publish the final COS and supporting materials on a dedicated project website or webpage. This allows broader access to the COS and supports ongoing dissemination.
- Encourage Dissemination via Stakeholder Networks: Ask stakeholders to actively share the CDS within their own professional or patient networks, organizations, or societies. This helps raise awareness and supports early adoption of the CDS.
- Engage with Regulators: Where appropriate, consider proactively engaging with regulatory bodies to present the finalized COS and explore opportunities for alignment with regulatory requirements. This can strengthen the position of the COS in clinical trial design and approval processes.

By effectively sharing the finalized COS among stakeholders, their involvement is reinforced, fostering a sense of ownership that is critical for successful implementation of the CDS.

## Step 16. Register the Core Outcome Domain Set in COMET database and on C3 website (i.e. update work as completed)

Upon finalizing the CDS, the next step is to register the final COS with the COMET (Core Outcome Measures in Effectiveness Trials) database and on the C3 website.

### How to Register

- **COMET Database**: Update the work as completed in the COMET database at www.comet-initiative.org.
- **C3 Website**: Send the finalized CDS and relevant documentation to the C3 administrative team via chordcollab@gmail.com for inclusion on the C3 website.

Registering the finalized CDS ensures transparency and accessibility, allowing researchers, clinicians, and other stakeholders to learn about the CDS and its development process. This step enhances the visibility and credibility of the CDS and promotes its adoption and use in dermatological research.

**COMET database:**
A direct link to the COMET database can be found here:
https://www.comet-initiative.org/About/SubmitNewStudy

**Registration link C3 website:**
A direct link to the C3 website will be included here. Until then, please use the provided email address: chordcollab@gmail.com

## Step 17. Publish Core Outcome Domain Set following COS-STAR

Publishing the CDS is a key step in sharing your work with the scientific community and promoting its adoption in dermatological research. To ensure transparency and consistency, publications should follow the Core Outcome Set-STAndards for Reporting (**COS-STAR**) guidelines (Kirkham et al., 2016), which can also be applied to the reporting of the CDS. COS-STAR provides a structured framework for describing the development process in a clear and standardized way (see Appendix 12).

**Appendix 12: COS-STAR guidance document**
Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Devane D, et al. (2016) Core Outcome Set–STAndards for Reporting: The COS- STAR Statement. PLoS Med 13(10): e1002148. doi:10.1371/journal.pmed.1002148

https://doi.org/10.1371/journal.pmed.1002148

### How to Apply the COS-STAR Guidelines

- **Familiarize Yourself with COS-STAR early**: Review the COS-STAR guidelines before starting the CDS process and incorporate relevant aspects into your protocol. This ensures that key information, such as stakeholder involvement, methods, and decision-making processes, is systematically captured from the outset, making it easier to produce a complete and transparent report.
- **Draft Manuscript**: Draft your manuscript to include:
    - A clear explanation of the need for the CDS and its relevance to dermatology.
    - A detailed account of the consensus process, including the eDelphi survey, stakeholder involvement, and any consensus meetings.
    - The final CDS, with justifications for included and excluded domains.
    - A discussion of the implications for research, clinical practice, and patient care.

- **Select the Appropriate Journal**: Identify a peer-reviewed journal that aligns with your target audience and consider open-access options to maximize visibility. Tools such as the Journal/Author Name Estimator (JANE) (https://jane.biosemantics.org) can help identify suitable journals based on your manuscript's title or abstract.
- **Engage Stakeholders in the Review**: Share the draft manuscript with your Steering Committee and key stakeholders for feedback to ensure accuracy and completeness.

By adhering to COS-STAR guidelines, your publication enhances the credibility and transparency of the CDS and ensures that it is accessible to an international audience. This step is essential for encouraging the adoption and implementation of the CDS in future research and clinical settings.

## Step 18. Plan and conduct further implementation and dissemination strategies following the HOME Implementation Roadmap

Effective implementation and dissemination of the CDS require ongoing efforts beyond its initial publication and registration. Following the principles of the **HOME** (Harmonising Outcome Measures for Eczema) **Implementation Roadmap**, a structured approach can enhance the adoption of the CDS in both research and clinical settings, see Appendix 13. This includes identifying potential facilitators and barriers to implementation early on, as understanding these factors helps to tailor strategies that maximize uptake and address possible resistance.

**Appendix 13: HOME Implementation Roadmap**
Yael A Leshem, Eric L Simpson, Christian Apfelbacher, Phyllis I Spuls, Kim S Thomas, Jochen Schmitt, Laura Howells, Louise A A Gerbens, Michael E Jacobson, Norito Katoh, Hywel C Williams, on behalf of the Harmonising Outcome Measures for Eczema (HOME) initiative, The Harmonising Outcome Measures for Eczema (HOME) implementation roadmap, British Journal of Dermatology, Volume 189, Issue 6, December 2023, Pages 710–718

https://doi.org/10.1093/bjd/ljad278

### Engage with Professional Societies

Collaborate with dermatological societies and professional organizations to promote the integration of the CDS into clinical practice guidelines and research protocols. This collaboration may involve presentations at conferences, inclusion in policy documents, and advocacy efforts to encourage widespread adoption.

In addition, engage with key external stakeholders such as research funders, regulatory agencies, and health policy bodies to support the recognition and implementation of the CDS in clinical trial design, funding criteria, and regulatory guidance.

### Develop Training and Education Initiatives

Create educational materials and workshops tailored to researchers, clinicians, and other stakeholders. These resources should focus on how to effectively implement the CDS, providing practical examples and case studies to illustrate its application.

### Establish Monitoring and Evaluation Mechanisms

Develop systems to track the adoption and use of the CDS over time. This could include conducting surveys, organizing follow-up studies, or analyzing trends in published research to assess its impact on dermatological research and practice.
In addition, monitor the inclusion of CDS domains in trial registries, systematic reviews (SRs), Cochrane SRs, network meta-analyses (NMAs), and clinical guidelines, as these sources provide valuable insights into how widely the CDS is being adopted.
Regular feedback from users can help identify barriers to adoption and areas for refinement.

### Strengthen Networks and Collaboration

Build and expand networks of researchers, clinicians, and patient groups committed to using and promoting the CDS. These networks provide a platform for sharing best practices, exchanging ideas, and supporting the ongoing evolution of the CDS. Engaging stakeholders regularly through meetings or online forums ensures sustained interest and collaboration.

By implementing these strategies, the CDS can achieve widespread adoption, improving the quality and comparability of research in dermatology and, ultimately, contributing to better patient outcomes.

## Conclusion

The successful dissemination and implementation of the CDS are critical to its impact on dermatological research and patient care. By systematically sharing the CDS with stakeholders, registering it in accessible databases, and publishing it following established guidelines, a solid foundation is established for its broad adoption. Additionally, planning for ongoing implementation and dissemination ensures that the CDS remains relevant and widely utilized.

These steps not only guarantee that the CDS reaches its intended audience but also support its sustained use, fostering collaboration and advancing dermatological science. Ultimately, this process contributes to improved research quality, enhanced comparability across studies, and better patient outcomes.

# Part B: Core Outcome Measurement Instrument Development Standards

Part B describes the minimum standards that C3 COS developers should adhere to in the Core Outcome Measurement Instrument Development process. These standards ensure that selected instruments are feasible, reliable and valid for use in clinical trials and other research contexts, thereby improving the quality and comparability of dermatological research. In addition, COS developers are encouraged to document any gaps in validation evidence, as these can inform priorities for future research and continuous improvement of outcome measurement instruments (OMIs).

**Check Before Starting Part B: Are All Core Domain Definitions Clear?**
Before moving to the selection of Core Outcome Measurement Instruments (COMIs), take a moment to confirm with your COS development team that all core outcome domains are clearly defined. This means agreeing on what each domain encompasses and, where relevant, specifying essential sub-domains or components.

If some definitions still feel unclear or incomplete, it may be helpful to revisit Step 13 in Part A (Generate long list of candidate outcome domains and provide established definitions) to refine them first. In most cases, this involves only minor adjustments, but if substantial changes are needed, consider whether parts of the consensus process (e.g., the eDelphi) should be updated to ensure that all stakeholders share the same understanding.
A clear and shared definition at this stage will make the selection of instruments much more straightforward and increase confidence in the final Core Outcome Measurement Set.

## Working Group(s)

### Introduction

Developing a fully specified COS including core outcome domains and core OMIs requires a collaborative effort guided by specialized expertise. This chapter outlines the steps to assemble and organize Working Groups that will review, evaluate, select and possibly develop, and/or validate OMIs for each Core Outcome Domain. By ensuring diverse stakeholder representation, international applicability, and comprehensive expertise, these Working Groups form the foundation for creating or selecting scientifically robust and clinically relevant measurement instruments.

# Step 1. Assemble Core Outcome Measurement Instrument Working Group(s) (e.g. one for each Core Outcome Domain)

The first step in developing the Core Outcome Measurement Instruments (COMIs) is to establish one or more working groups, particularly if multiple Core Outcome Domains are being addressed. These working groups will then be responsible for evaluating the OMIs for their assigned Core Outcome Domain. They may also develop and/or validate instruments if required.

### Leadership and Structure

Each working group should have a clear leadership structure, with a designated leader or chair to guide the group's activities and ensure alignment with the overall COS development objectives. The leader should be an expert in the relevant field, which may include dermatology, outcome measurement, or instrument development, depending on the focus of the working group.
In addition, the working group should include or consult members with expertise in evidence synthesis (e.g., systematic reviews following COSMIN guidance), as this expertise is crucial for reviewing and selecting appropriate outcome measurement instruments.

Their responsibilities include setting the direction, overseeing the development process, ensuring adherence to C3 standards, and facilitating communication among all group members.

In addition to the leader, the working group should include a diverse range of members with expertise relevant to the assigned core outcome domain. This multidisciplinary composition ensures that all aspects of the measurement instrument development process, primarily evaluation, but also development or validation if required, are comprehensively addressed.

### Important Considerations for Group Composition

- **International Representation**: To enhance the international applicability of the measurement instruments, it is essential to include international representation in the working groups. Members should ideally come from at least three different continents to ensure relevance across various cultural and healthcare contexts. Recruitment can be facilitated through professional networks, international conferences, and collaboration with international patient advocacy organizations.
- **Stakeholder Inclusion**: Key stakeholders, such as patients, patient representatives, and caregivers, should play an integral role in the working groups. Their perspectives are crucial for ensuring that the measurement instruments reflect outcomes that are meaningful from a patient-centered viewpoint. Engaging with patient advocacy groups and employing purposive sampling techniques can help achieve diverse and representative patient involvement.

- **Comprehensive Expertise**: The working group should aim to collectively represent all aspects relevant to the disease state and COS development. By incorporating expertise from various domains, the group can evaluate or, if required, develop measurement instruments that are both scientifically robust and practically applicable. However, full representation may not always be feasible in practice; working groups can collaborate with or delegate specific tasks to other experts or groups when needed. A structured approach to stakeholder mapping and recruitment can help identify and include experts from all relevant fields.

### Responsibilities of Working Group Members

Working group members are essential to the development process and are expected to:

- Actively participate in meetings to collaborate with other members and discuss progress.
- Take on specific tasks such as drafting study protocols, conducting literature reviews, and evaluating, refining, or developing Outcome Measurement Instruments.
- Engage in consensus processes to select, validate, or refine Outcome Measurement Instruments.
- Contribute to dissemination and implementation activities to ensure that the Outcome Measurement Instruments are effectively communicated and adopted in relevant research and clinical settings.

## Conclusion

Assembling a well-structured and diverse Core OMI Working Group is a crucial step in the process of evaluating and/or developing OMIs. By ensuring international representation, incorporating the perspectives of key stakeholders, and including expertise across all relevant aspects of the disease state, you create a solid foundation for the selection of the core OMIs.

In practice, much of the detailed work is often carried out by a smaller core group, but broad representation remains important for ensuring transparency, stakeholder buy-in, and methodological rigor.

### Introduction

This chapter outlines the steps for developing a protocol for the Core Outcome Measurement Instrument development process. By following these steps, COS developers ensure that their work adheres to established standards, as outlined in the C3 Template Protocol and supporting guidance documents. This structured approach enhances the scientific rigor and transparency of the process.

## Step 2. Develop Core Outcome Measurement Instrument development protocol

The next step is to develop a detailed protocol for the Core Outcome Measurement Instrument development process. A well-structured protocol ensures methodological transparency and consistency in the selection and evaluation of OMIs. To support this process, we recommend following the PRISMA-COSMIN guidance, specifically the Guideline for Reporting Systematic Reviews of Outcome Measurement Instruments (Elsman et al., 2024), see Appendix 14.

**Appendix 14: PRISMA-COSMIN Guideline for reporting systematic reviews of OMIs**

Elsman, E.B.M., Mokkink, L.B., Terwee, C.B. et al. Guideline for reporting systematic reviews of outcome measurement instruments (OMIs): PRISMA-COSMIN for OMIs 2024. Qual Life Res 33, 2029–2046 (2024).

https://doi.org/10.1007/s11136-024-03634-y

Although originally developed for reporting systematic reviews of OMIs, the PRISMA-COSMIN guideline also provides a valuable framework for designing protocols that guide the identification and evaluation of OMIs for each Core Outcome Domain.

For guidance on conducting a consensus process and planning for dissemination and implementation that should be included in the protocol, refer to Part A of this manual. These sections provide detailed recommendations on engaging stakeholders, achieving consensus, and ensuring the effective adoption of COS.

## Step 3. Review and apply C3 guidance documents

During the development of your core OMI protocol, it is essential to review and apply the C3 guidance document. At this stage, we recommend referring to clear examples from the literature (e.g., published OMI development protocols such as those from the HOME initiative), as no dedicated C3 template is currently available.

A standardized C3 Protocol Template for Core Outcome Measurement Instrument Development is planned for future development to support consistency and streamline the C3 approval process once established.

## Step 4. Submit protocol to C3 Methods Group

Once finalized, the core OMI development protocol should be submitted to the C3 Methods Group for review. The submission and review follow the same process as described for the Core Domain Set (CDS) protocol in Part A, Step 7.

Where possible, it is recommended to continue working with the same C3 Methods Support person assigned during the CDS phase to ensure consistency and alignment across both parts of the COS development process.

Depending on the number and complexity of domains, a separate protocol may be developed for each Core Outcome Domain, as has been done in initiatives such as HOME.

## Step 5. Protocol review by C3 Methods Group

The review of the core OMI development protocol follows the same process as described for the Core Domain Set (CDS) protocol in Part A, Step 8.

As with the CDS phase, the Methods Group will assess whether the proposed methodology is robust, feasible, and aligned with C3 standards. If the same C3 Methods Support person is involved, they can help ensure continuity and consistency across both phases of the COS development process.

## Step 6. Register protocol with COMET database and on C3 website

The registration process for the Core OMI development protocol follows the same procedure as described for the Core Domain Set (CDS) protocol in Part A, Step 9.

**COMET database:**
A direct link to the COMET database can be found here:
https://www.comet-initiative.org/About/SubmitNewStudy

**Registration link C3 website:**
A direct link to the C3 website will be included here. Until then, please use the provided email address: chordcollab@gmail.com

As with the CDS, registration ensures transparency and accessibility, allowing other researchers and stakeholders to learn about your project. Make sure to clearly indicate that this registration refers to the OMI phase of your COS development project.

## Step 7. Publish study protocol, preferably in open access format

The Core OMI development protocol should be made publicly accessible, following the same recommendations as outlined for the Core Domain Set (CDS) protocol in Part A, Step 10.

This can be done through registration on the C3 website or other platforms that provide a persistent public record (e.g., COMET database, OSF, Figshare). Open-access publication in a peer-reviewed journal is encouraged but not required, as long as the protocol is accessible to the broader research community.

### Conclusion

Developing a robust and methodologically sound protocol is a critical step in the Core OMI development process. By following the outlined steps, creating a protocol using the C3 Template Protocol, incorporating relevant guidance documents, and submitting the protocol for rigorous review by the C3 Methods Group, you ensure that your project meets C3's

methodological standards, and supports the implementation and adoption of the Core Outcome Measurement Instrument Set

## Generate Candidate List of Instruments

### Introduction

This chapter will guide you through the process of generating a list of relevant instruments, assessing their alignment with the core outcome domains, evaluating their feasibility, and determining whether new OMIs need to be developed.

Before starting this process, it is crucial to ensure that each Core Domain is clearly defined, including what essential sub-domains or components need to be captured. For example, if "quality of life" has been agreed as a Core Domain, developers should consider which specific aspects are most relevant for people with the condition of interest. Similarly, for signs and symptoms, the essential sub-domains that reflect meaningful change in disease status should be specified. Empirical evidence may need to be identified or, if unavailable, new work may be required to support these decisions.

## Step 8. Conduct a scoping review to find all available relevant Outcome Measurement Instruments per Core Outcome Domain

Conducting a scoping review is the initial step in generating a candidate list of OMIs for each identified core outcome domain. Some information may already have been collected during the systematic or scoping review conducted for the Core Domains (Part A, Step 11). However, the search for OMIs generally needs to be broader, as it should also include instrument development and validation studies, not just randomized controlled trials.

### Aim of a Scoping Review

A scoping review is used to map the existing evidence and identify all relevant OMIs for the core outcome domains(s) of interest. Conducting a scoping review ensures that all potential instruments are considered, allowing for a comprehensive assessment of their suitability for inclusion in the COS (Steps 9-18).

### How to Conduct the Scoping Review

We recommend adhering to the *Joanna Briggs Institute Methodology for Scoping Reviews* (see Appendix 7) and the *Best practice guidance and reporting items for the development of scoping review protocols* (Peters et al. 2022) (see Appendix 8)

Compared to the scoping review for Core Domains (Part A, Step 11), the search strategy for OMIs should be broader and specifically tailored to identify measurement instruments and their measurement properties. We recommend using the COSMIN search strategy for identifying studies on measurement properties, see: https://www.cosmin.nl/tools/pubmed-search-filters/.

The PRISMA Extension for Scoping Reviews guidance and its checklist items (see Appendix 9) can be used when reporting the scoping review (Tricco et al. 2018).

We recommend that a scoping review should involve at least two reviewers with experience in conducting systematic or scoping reviews, as well as expertise in the relevant dermatological condition. In addition, working group members/reviewers may suggest OMIs they are aware of within the scoping review process (other sources).

Please note that PROSPERO does not accept scoping reviews or literature scans. Instead, scoping reviews can be registered in the Open Science Framework (OSF) database, see: https://osf.io.

### Outcome of the Scoping Review

The scoping review describes all OMIs, that may be potentially helpful to measure the core outcome domain of interest.

## Step 9. Assess whether the instruments match the target domain (is the instrument likely to capture the outcome of interest?)

After compiling a long list of potential OMIs, it is essential to assess whether identified instruments capture the Core Outcome Domains.

This assessment is often easiest to conduct per domain, but there can be efficiencies in performing an initial broader screening across domains, particularly when instruments are relevant to multiple domains (e.g., quality of life or symptom scores). The results of this initial screening can then be shared with the relevant CDS working groups for further domain-specific evaluation.

It involves evaluating whether the content and purpose of the instrument covers the definition and/or conceptual framework of the core domain. This requires a very clear and detailed understanding of what the domain encompasses.

Instruments that do not align with the domain content should be excluded from further consideration. This decision should be made by the OMI Working Group, ideally using predefined criteria based on the agreed domain definition. Where uncertainty exists, consensus should be sought within the group, and methodologists or other domain experts may be consulted.

## Step 10. Assess whether the instruments are feasible to implement based on a priori criteria

The next step is to evaluate the feasibility of implementing each instrument based on predefined criteria, which need to be specified by each specific COS group individually. Feasibility refers to the ease of application of the outcome measurement instrument in its intended setting, considering constraints such as time, resources, and accessibility (Prinsen et al. 2016). Key feasibility aspects include completion time, cost, instrument length, and the type and ease of administration.

Feasibility should also be considered cumulatively: even if individual instruments are quick and easy to complete, the overall burden across all selected instruments can become significant, particularly if there is overlap in what they measure. This cumulative burden should be carefully weighed to avoid overloading participants, researchers, or clinicians.

Table 1 provides an overview of relevant feasibility aspects, as adopted from Prinsen et al. (2016).

| **Feasibility aspects** | |
|---|---|
| Patient's comprehensibility | Type of outcome measurement instrument |
| Interpretability | Cost of an outcome measurement instrument |
| Ease of administration | Required equipment |
| Length of the outcome measurement instrument | Type of administration |
| Completion time | Availability in different settings |
| Patient's mental ability level | Copyright |
| Ease of standardization | Patient's physical ability level |
| Clinician's comprehensibility | Regulatory agency's requirement for approval |
| | Ease of score calculation (if applicable) |

***Table 1: Overview of Feasibility Aspects***

## Step 11. If #9 AND #10 are Yes, continue with quality assessment. If #9 and #10 are No, instrument should not be taken into further consideration

Only instruments that meet both the **relevance** (Step 9) and **feasibility** (Step 10) criteria are eligible for quality assessment, i.e. a detailed assessment of their measurement properties (see Step 14 and Step 15 for the assessment of measurement properties). Instruments failing to meet these criteria should be excluded from further consideration to maintain focus on the most promising outcome measurement instruments.

Decisions on whether an instrument meets these criteria should be made by the OMI Working Group, using predefined relevance and feasibility criteria. Where there is uncertainty or disagreement, consensus should be sought within the group, and expert consultation (e.g., from methodologists or clinical experts) may be required.

For guidance on evaluating measurement properties, we recommend using the COSMIN methodology in a *stepwise approach*, starting with content validity and subsequently assessing other relevant measurement properties such as reliability, validity, and responsiveness (see Step 14 and Step 15). To ensure consistency with these evolving standards and avoid duplication, we refer to the original COSMIN resources: the COSMIN Risk of Bias Checklist for PROMs (see Appendix 15), and the COSMIN Risk of Bias tool to assess the quality of studies on reliability or measurement error of outcome measurement instruments (see Appendix 16).

**Appendix 15: The COSMIN Risk of Bias Checklist for PROMs v3.0**
https://www.cosmin.nl/wp-content/uploads/COSMIN-RoB-checklist-for-PROMs-V3_1.pdf

**Appendix 16: COSMIN Risk of Bias tool to assess the quality of studies on reliability or measurement error of outcome measurement instruments**

https://www.cosmin.nl/wp-content/uploads/COSMIN-RoB-tool_reliability-and-measurement-error_1.pdf

## Step 12. If either no instruments are available, or none pass #9 and #10, a new instrument should be developed

If no existing instruments are available or if none meets the criteria for relevance (Step 9) and feasibility (Step 10), it may be necessary to refine, adapt or modify an existing OMI, or to develop a new instrument. However, instrument development is not considered a core task within the COS or COMS development process, as it often requires substantial time, resources, and psychometric expertise beyond the scope of most COS teams.

Instead, COS developers are encouraged to recommend the best available instrument, even if it does not meet all criteria. This should be accompanied by a clear description of its limitations and the rationale for its selection. Highlighting such gaps can help inform the research and clinical communities about areas where further instrument development is needed.

Before pursuing new development efforts, consider whether suitable generic instruments (e.g., PROMIS CAT) or tools developed for other conditions could be adapted to fit the target domain. Using existing tools, where appropriate, can enhance feasibility and support implementation across settings.

**Guidance on Developing or Refining Outcome Measurement Instruments**
The development of new outcome measurement instruments or the refinement of existing ones falls outside the scope of this manual. If COS developers have the necessary expertise and resources, they may consider instrument development or adaptation.

For Patient-Reported Outcome Measures (PROMs), we recommend consulting:

- The COSMIN Methodology for Content Validity (User Manual v1): https://cosmin.nl/wp-content/uploads/COSMIN-methodology-for-content-validity-user-manual-v1.pdf
- The FDA Guidance for Industry: Patient-Reported Outcome Measures (Use in Medical Product Development to Support Labeling Claims): https://www.fda.gov/media/77832/download

For other types of instruments, formal guidance is more limited. COS developers are advised to follow available best practices where applicable (e.g. see www.cosmin.nl for other resources).

## Conclusion

By systematically generating a comprehensive list of OMIs through conducting a scoping review, assessing their alignment with Core Outcome Domains, evaluating their relevance

and feasibility, and, if necessary, developing new instruments you provide a solid foundation for further consideration of the identified outcome measurement instruments in the subsequent steps of the Core Outcome Measurement Instrument development process.

## Introduction

This chapter provides guidance on how to evaluate the quality of outcome measurement instruments (OMIs) identified or developed for the COS. The approach to evaluation depends on the type of outcome. For example, some outcomes (e.g. mortality, hospitalizations, or complications) may not require extensive psychometric evaluation and can be assessed based on clear clinical definitions and data availability.
For patient-reported outcome measures (PROMs), and to some extent for clinician-reported outcomes (CROMs), a more structured evaluation of measurement properties is needed. This is addressed using the COSMIN methodology, which is introduced in detail in a subsequent section of this chapter.

# Step 13. Conduct a systematic review of instruments in accordance with guidance depending on the type of instruments

The next step is to perform a systematic review of the pre-selected instruments, i.e., those that meet the criteria for relevance and feasibility. This review aims to assess:

1) the quality of the studies on measurement properties of each instrument, and
2) the quality of the instruments themselves according to predefined quality criteria.

In some projects, it may be efficient to combine this systematic review with the earlier scoping review (Step 8), especially if information on measurement properties is extracted during the same literature search. This combined approach can help reduce workload and duplication of effort. However, COS developers should ensure that the formal evaluation of measurement properties still follows a structured and transparent process at this stage.

High quality systematic reviews can provide a useful overview of the measurement properties of OMIs and support evidence-based recommendations in the selection of the most suitable instrument for the core outcome domains.

In summary, getting an overview of the quality of the assessed OMIs consists of three parts:

1) evaluating the methodological quality of studies on measurement properties (i.e. rating the risk of bias)
2) assessing the quality of the instruments (i.e. rating the results against quality criteria of good measurement properties), and

3) grading the quality of the evidence (i.e. performing a best evidence synthesis by using a modified GRADE approach.

When conducting this review, include not only validation and measurement property studies but also the original inauguration papers describing the development and initial testing of the instrument, as they often provide essential information on its content and measurement properties.

### Systematic Reviews of OMIs

The COSMIN group developed a comprehensive methodological guideline for systematic reviews of PROMs, including the COSMIN Risk of Bias checklist, criteria for good measurement properties, and a modified GRADE approach to conduct a systematic review of PROMs. Although it focuses on PROMs, it can be used with adaptions for systematically reviewing all other OMI types such as ClinROMs (Clinician-Reported Outcome Measures), PerFOMs (Performance-Based Outcome Measures), and laboratory values.

Therefore, we recommend following the **COSMIN guideline for systematic reviews of PROMs version 2.0**, as it provides a comprehensive framework for summarizing measurement properties (Appendix 17). When planning the systematic review, we strongly recommend using the COSMIN search strategy for validation studies to ensure that all relevant evidence is identified (see: https://www.cosmin.nl/tools/pubmed-search-filters/). For non-PROMs, the Risk of Bias tool for reliability and measurement error is recommended for use (Appendix 18).

**Appendix 17: COSMIN guideline for systematic reviews of PROMs**

Mokkink, L.B., Elsman, E.B. & Terwee, C.B. COSMIN guideline for systematic reviews of patient-reported outcome measures version 2.0. Qual Life Res 33, 2929–2939 (2024).

https://doi.org/10.1007/s11136-024-03761-6

**Appendix 18: COSMIN guideline for conducting systematic reviews of other types of instruments**

Mokkink, L.B., Boers, M., van der Vleuten, C.P.M. *et al.* COSMIN Risk of Bias tool to assess the quality of studies on reliability or measurement error of outcome measurement instruments: a Delphi study. *BMC Med Res Methodol* **20**, 293 (2020).

https://doi.org/10.1186/s12874-020-01179-5

### Registration and Reporting of Systematic Reviews

To enhance transparency and ensure methodological rigor, systematic reviews should be registered in the PROSPERO database (https://www.crd.york.ac.uk/prospero/). Registration allows researchers to publicly document their review protocol, reducing the risk of duplication and promoting accountability.

Upon completion, systematic reviews should be reported following the **PRISMA-COSMIN Guideline for reporting systematic reviews of OMIs**, which provides a standardized framework for presenting systematic reviews of OMIs, see Appendix 14. Adhering to this guideline ensures comprehensive and transparent reporting.

**Appendix 14: PRISMA-COSMIN Guideline for reporting systematic reviews of OMIs**
Elsman, E.B.M., Mokkink, L.B., Terwee, C.B. et al. Guideline for reporting systematic reviews of outcome measurement instruments (OMIs): PRISMA-COSMIN for OMIs 2024. Qual Life Res 33, 2029–2046 (2024).

https://doi.org/10.1007/s11136-024-03634-y

## Step 14. Evaluate content validity first to avoid wasted effort, if applicable

Content validity refers to the extent to which the content of an instrument adequately reflects the construct to be measured. It is considered the most important measurement property, as it ensures that all content (e.g. items, tasks, observations or parameters) of an outcome measurement instrument is relevant, comprehensive, and comprehensible with respect to the construct of interest and the target population.

Evaluating content validity early in the process is crucial to avoid investing time and resources in assessing other measurement properties for instruments that may ultimately fail to meet these foundational requirements. Content validity should be assessed for PROMs, ClinROMs, PerFOMs, and other multi-item outcome measurement instruments, whenever applicable.

While relevance was initially assessed in Step 9 as a first screening step, content validity provides a more detailed, evidence-based evaluation to confirm that the instrument truly captures the essential aspects of the core outcome domain. Evaluating content validity early in the process is crucial to avoid investing time and resources in assessing other

measurement properties for instruments that may ultimately fail to meet these foundational requirements.

Content validity should be assessed for PROMs, ClinROMs, PerFOMs, and other multi-item outcome measurement instruments, whenever applicable. For PROMs we recommend using the COSMIN methodology for assessing content validity, which provides structured guidance for evaluating the relevance, comprehensiveness, and comprehensibility of PROM content. With appropriate adaptations this checklist can be also used to evaluate content validity of other OMIs.

**COSMIN methodology:**
https://www.cosmin.nl

### Next Steps if Content Validity is 'Inadequate' or Missing Evidence on Content Validity

If the content validity of an OMI is found to be 'inadequate' regarding the construct to be measured, the instrument should not proceed to further evaluations of other measurement properties. Instead, proceed to Step 17, that provides guidance on how to address gaps in validation evidence and develop strategies for improving or replacing inadequate instruments.

If the content validity of an OMI is missing, we recommend conducting a study on content validity. Assessing content validity involve input from multiple stakeholders, preferably including patients, clinicians, and other experts in the field. This approach ensures that the instrument is relevant to key stakeholders and accurately reflects the construct of interest. Techniques such as structured interviews, focus groups, or expert panel reviews can be used to gather evidence. The COSMIN Risk of Bias Checklist for content validity can be used for guidance purposes.

## Step 15. If #14 is Yes, continue with the assessment of other measurement properties. If #14 indicates inadequate or missing content validity, proceed to step 17

If the instrument has demonstrated 'very good' or 'adequate' content validity, the next step is to assess the other measurement properties, if applicable, to ensure that the instrument is suitable for inclusion in the Core OMI Set.

When moving to this step, keep in mind that not all measurement properties are relevant for every type of instrument. For example, internal consistency is only applicable to reflective

models, while responsiveness is relevant for instruments intended to detect change over time. Focusing only on the properties that are truly applicable to the instrument type helps to reduce unnecessary workload and allows resources to be concentrated on the most critical evaluations.

### Assessment of Measurement Properties of PROMs

For the assessment of the measurement properties of PROMs, we recommend using the COSMIN guideline for systematic reviews of Patient-Reported Outcome Measures (PROMs) (Appendix 17) and the COSMIN Risk of Bias checklist for systematic reviews of PROMs (Appendix 15), which can be found on the COSMIN website: https://www.cosmin.nl

The evaluation should follow the COSMIN taxonomy of measurement properties, grouped into three main categories:

**Reliability**:

- Reliability (test–retest, inter-rater, intra-rater)
- Internal consistency
- Measurement error (test–retest, inter-rater, intra-rater)

**Validity**:

- Content validity (face validity)
- Criterion validity (concurrent validity, predictive validity)
- Construct validity, including structural validity, hypotheses testing for construct validity, and cross-cultural validity (measurement invariance)

**Responsiveness**:

- Ability of the instrument to detect change over time

Further guidance on how to assess these measurement properties is provided in the following steps, following the COSMIN methodology. However, depending on the type of domain and possible OMIs, not all measurement properties apply. For example, clinical outcomes such as hospitalization, complications or mortality may only require a clear, standardized definition and do not need evaluation of internal consistency or construct validity. By contrast, PROMs typically require a full evaluation of content validity, structural validity, reliability, and responsiveness. For CROMs or other clinician-assessed tools, some but not all COSMIN properties may apply, and should be interpreted with caution. COS developers are encouraged to use a proportionate and fit-for-purpose approach tailored to the type of OMI. Thus, not all boxes of the COSMIN Risk of Bias Checklist may apply, as it depends on the type of OMI being evaluated.

The COSMIN methodology for PROMs can also be used for systematic reviews on other types of outcome measurement instruments (e.g. clinician-reported outcome measures or performance-based outcome measures), but the methodology may need to be adapted for these other purposes. For that purpose, the COSMIN group developed additional methodology and standards for assessing the quality of studies on reliability and measurement error (see below).

### Assessment of Measurement Properties of Other Types of Outcome Measurement Instruments

To assess the quality of the included studies on reliability and measurement error of other types of outcome measurement instruments, we recommend using the adapted version of the COSMIN Risk of Bias Checklist, i.e. **COSMIN Risk of Bias Checklist for other types of outcome measurement instruments**, specifically developed for other types of outcome measurement instruments, see Appendix 16.

**Appendix 16: COSMIN Risk of Bias Checklist for other types of outcome measurement instruments**

Mokkink, L.B., Boers, M., van der Vleuten, C.P.M. *et al.* COSMIN Risk of Bias tool to assess the quality of studies on reliability or measurement error of outcome measurement instruments: a Delphi study. *BMC Med Res Methodol* **20**, 293 (2020).

https://doi.org/10.1186/s12874-020-01179-5

**Rating the results against quality criteria of good measurement properties**

After rating the risk of bias (i.e. rating the quality of studies on measurement properties), the quality of the instruments needs to be assessed (i.e. rating the results against quality criteria of good measurement properties).

Refer to the COSMIN user manual that will guide you through this part of the quality assessment, see: https://www.cosmin.nl/wp-content/uploads/COSMIN-manual-V2_7_4_final.pdf

### How to evaluate the quality of the selected OMIs

A clear example of a systematic review on the evaluation of the measurement properties of symptom measurement instruments for atopic eczema, can be found here: https://onlinelibrary.wiley.com/doi/10.1111/all.12959

## Step 16. Perform evidence synthesis and define gaps in validation evidence

**Grading the quality of the evidence**

In the final step of the systematic review on measurement properties, the level of confidence in the final rating of the measurement properties (per PROM) is assessed. In accordance with the COSMIN methodology, a modified GRADE approach is used to perform a best evidence synthesis and indicate whether there are concerns about the quality of the evidence per measurement property per PROM.

In practice, the results are often summarized in a table, presenting for each instrument: (1) the overall rating of each measurement property (e.g., “sufficient,” “insufficient,” “inconsistent,” or “indeterminate”), (2) the quality of the evidence (e.g., “high,” “moderate,” “low,” “very low”), and (3) key considerations such as sample size or risk of bias. These evidence tables can be shared with the consensus group to inform decision-making on which instruments are most suitable for inclusion in the core OMI set.

Refer to the COSMIN user manual that provides guidance on grading the quality of the evidence of the measurement properties, see: https://www.cosmin.nl/wp-content/uploads/COSMIN-manual-V2_7_4_final.pdf

### Identifying Gaps in Validation Evidence

Following the synthesis, gaps in validation evidence can be identified. For example, an instrument might lack evidence on responsiveness, have inadequate data on cross-cultural validity, or show uncertainty regarding measurement error. These gaps need to be documented in a structured way (e.g. in an evidence table or the final report) and discussed within the COS Working Group to decide which gaps are most critical to address. Prioritizing these gaps helps direct future validation research toward the most promising instruments and can inform future updates of the Core OMI Set as new evidence emerges.

### Reporting the systematic review

We recommend publishing your systematic review in a peer-reviewed scientific medical journal, preferable in an open access format. The PRISMA-COSMIN Reporting Guideline helps you to accurately report your systematic review (Appendix 14).

## Step 17. If gaps in validation evidence exist, consider performing additional instrument development studies or studies on measurement properties (optional)

If gaps in validation evidence are identified during the synthesis process (Step 16), consider conducting additional studies to address these deficiencies. These may include instrument development studies to refine or adapt existing instrument, or validation studies to evaluate missing measurement properties.

The decision to perform additional studies depends on the importance of the instrument, its potential applicability to the core outcome domain, and the feasibility of conducting the research within the COS development timeline. When undertaking these studies, ensure adherence to established guidelines for instrument development and validation, such as those provided by COSMIN, to maintain methodological rigor and consistency.
By addressing these gaps, you enhance the robustness and credibility of the Core Outcome Measurement Instrument Set.

## Step 18. Identify candidate instruments for each Core Outcome Domain

Based on the evidence synthesized in Step 16, outcome measurement instruments should be categorized into predefined categories to guide their selection for inclusion in the Core Outcome Measurement Instrument Set:

- **Category A** includes instruments with adequate evidence for all required measurement properties and deemed suitable for inclusion in the COS.
- **Category B** comprises instruments with promising but incomplete validation evidence. These tools show potential for future use but require further studies to confirm their suitability.
- **Category C** includes instruments that fail one or more critical quality criteria. Such tools are not recommended for use due to concerns about their reliability and validity.
- **Category D** consists of instruments with insufficient validation evidence overall. These instruments require significant additional research before they can be considered for inclusion.

### Application of Findings

Instruments categorized as **Category A** should be prioritized for inclusion in the COS, as they meet the required standards for measurement properties and feasibility. Instruments in **Category B** may be cautiously included as provisional tools, provided that additional validation studies are planned to address gaps in evidence. Instruments in **Category C** should be excluded from the COS, as their methodological limitations preclude reliable use. Instruments in **Category D** require further research and development before any consideration for inclusion.

### Preparing for the Consensus Meeting

The categorization of instruments, along with a clear summary of the supporting evidence and rationale, will form the basis for discussions during the consensus meeting (see Chapter 11). At this stage, it is generally recommended to present only high-level information, such as overall ratings of measurement properties and key strengths and limitations, to keep discussions focused and manageable. Detailed evidence tables should be made available in advance for those who wish to review them, but they do not need to be discussed in full during the meeting.

This approach ensures that stakeholders can make well-informed decisions while keeping the process efficient and focused on selecting the most appropriate instruments for inclusion in the COS.

## Conclusion

Evaluating the measurement properties of outcome measurement instruments is a critical step in ensuring the quality of the Core Outcome Measurement Instrument Set. By systematically reviewing existing instruments, assessing their measurement properties, synthesizing evidence, and addressing gaps in validation evidence, COS developers can confidently identify instruments that are feasible, valid, and reliable. The categorization of instruments into A, B, C, and D category instruments, ensures a robust and transparent development process of the Core Outcome Measurement Instrument Set.

# Consensus Process

## Introduction

The consensus process plays a pivotal role in the selection of the most suitable outcome measurement instrument for each core outcome domain. Engaging stakeholders through structured consensus-building ensures that the final selection reflects a broad range of perspectives. This chapter outlines the steps to achieve consensus, emphasizing the importance of stakeholder representation and the use of transparent, inclusive methods. Both virtual and in-person approaches, such as eDelphi processes, workshops, and consensus meetings, are explored to support this critical step.

## Step 19. Whenever possible, select one instrument per domain through a consensus process that includes an appropriate representation of stakeholders

Once the quality of the outcome measurement instruments has been evaluated and categorized (see Step 18), the next step is to select the most appropriate instrument for each core outcome domain through a robust consensus process. Consensus meetings generally address one domain at a time to allow for focused discussions and well-considered decisions. The goal is to achieve agreement among stakeholders on a single instrument per outcome domain that is both scientifically sound and practical for use.

Whenever possible, include participants from as many countries and cultural backgrounds as feasible to identify potential cultural or contextual issues with specific instruments and to ensure that the selected tools are broadly applicable.

### Methods for Achieving Consensus

The consensus process should incorporate a structured approach to decision-making, ensuring equal participation from all stakeholders. Key methods include:

1. **eDelphi Process**
   For detailed information on eDelphi processes, we refer to Chapter 5, Step 14.
2. **Workshops**
   Workshops provide an opportunity for stakeholders to engage in collaborative discussions about the candidate instruments. However, in many cases (e.g., the HOME initiative), these discussions are integrated into the consensus meeting rather than held as a separate step. When used, workshops may include brief presentations

of evidence, breakout groups for focused discussions, and facilitated plenary sessions to synthesize findings and build agreement.

3. **Consensus Meetings**
   A face-to-face or virtual consensus meeting allows stakeholders to review the results of previous deliberations (e.g., eDelphi surveys or workshops) and vote on the final selection of instruments. Anonymous electronic voting can be used to reduce bias and peer pressure, ensuring that decisions are made transparently and equitably.

### Stakeholder Representation

To ensure that the selected instruments are relevant and widely accepted, it is essential to include a diverse group of stakeholders in the consensus process. This includes e.g. patients, clinicians, researchers, policymakers, and representatives from industry. Stakeholder engagement should be balanced across these groups to capture varying perspectives and priorities. For detailed information on stakeholder engagement, we refer to Chapter 5, Step 14.

## Conclusion

Selecting the most appropriate outcome measurement instruments for each core domain through a consensus process ensures that the final instruments are not only scientifically rigorous but also broadly accepted by the research and clinical community. By employing transparent and inclusive methods such as the eDelphi process, workshops, and consensus meetings, COS developers can foster collaboration and build stakeholder ownership of the Core Outcome Measurement Instrument Set. This structured approach ensures that the selected instruments are ready for effective implementation in clinical trials and research, ultimately enhancing the quality and consistency of outcome measurement in dermatology.

# Dissemination and Implementation

## Introduction

Once the Core Outcome Measurement Instrument Set is finalized, it is essential to ensure its effective dissemination and implementation to enhance its impact on research and clinical practice. This chapter outlines the critical steps required for sharing the Core Outcome Measurement Instrument Set with stakeholders, registering it in relevant databases, and publishing it in accordance with established guidelines. Furthermore, it provides guidance on planning and executing strategies to promote its adoption and integration into clinical research and practice, ensuring its widespread use and sustainability.

## Step 20. Share the Core Outcome Measurement Set among all participating stakeholder groups

Once the Core Outcome Measurement Instrument Set has been finalized through the consensus process, it is essential to share the results with all stakeholder groups that participated in the Delphi survey, consensus meetings, or other related activities. This ensures transparency, acknowledges contributions, and strengthens stakeholder engagement, which is crucial for the successful adoption and implementation. The same principles as described for sharing the Core Outcome Domain Set apply here (see Part A, Step 15).

## Step 21. Register the Core Outcome Measurement Set in COMET database and on C3 website (i.e. update work as completed)

Once finalized, the Core Outcome Measurement Instrument Set should be registered in the COMET database and on the C3 website to ensure transparency and visibility, and to signal that the work is complete. The registration process follows the same procedure as described for registering the Core Outcome Domain Set (see Part A, Step 16).

**COMET database:**
A direct link to the COMET database can be found here:
https://www.comet-initiative.org/About/SubmitNewStudy

**Registration link C3 website:**
A direct link to the C3 website will be included here. Until then, please use the provided email address: chordcollab@gmail.com

## Step 22. Publish Core Outcome Measurement Instrument Set following COS-STAR

Publishing the finalized Core Outcome Measurement Instrument Set is a pivotal step in disseminating your work to the scientific community and promoting its adoption in dermatological research. To ensure transparency and consistency, publications should follow the Core Outcome Set-STAndards for Reporting (COS-STAR) guidelines, which provide a structured framework for reporting COS development (see Appendix 12).

**Appendix 12: COS-STAR guidance document**

Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Devane D, et al. (2016) Core Outcome Set–STAndards for Reporting: The COS-STAR Statement. PLoS Med 13(10): e1002148. doi:10.1371/journal.pmed.1002148

https://doi.org/10.1371/journal.pmed.1002148

### How to Apply the COS-STAR Guidelines

- **Familiarize Yourself with COS-STAR**: Begin by reviewing the COS-STAR guidelines, which outline the key components of a high-quality publication. These include the rationale for the Core Outcome Measurement Instrument Set, methods used, stakeholder involvement, results, and implications for future research and practice. Most of these elements will already have been addressed if COS-STAP and COS-STAD guidance have been followed during protocol development, but keeping COS-STAR in mind early on can help ensure that all necessary details are captured for future reporting.
- **Draft Manuscript**: Structure your manuscript to include:
  - Introduction: Clearly state the need for the Core Outcome Measurement Instrument Set and its relevance to dermatology and the specific core outcome domains.

    - Methods: Provide a detailed description of the process, including systematic reviews, stakeholder involvement, consensus methods (e.g., eDelphi surveys or meetings), and instrument evaluation.
    - Results: Present the finalized Core Outcome Measurement Instrument Set with explanations for included and excluded instruments.
    - Discussion: Highlight the implications for research, clinical practice, and patient care, as well as any gaps or limitations in the current validation evidence.
- **Select an Appropriate Journal**: Choose a peer-reviewed journal that aligns with the target audience for the Core Outcome Measurement Instrument Set. Consider open-access options to maximize accessibility and visibility.
- **Engage Stakeholders in the Review**: Share the draft manuscript with your Steering Committee and relevant stakeholders for feedback to ensure accuracy and completeness.

By following the COS-STAR guidelines, your publication enhances credibility and transparency, encouraging the adoption of the Core Outcome Measurement Instrument Set in research and clinical settings internationally. Publishing your work in a respected journal enhances its impact and fosters widespread implementation.

## Step 23. Plan and conduct further implementation and dissemination strategies following the HOME Implementation Roadmap

The effective implementation and dissemination of the Core Outcome Measurement Instrument Set require sustained efforts beyond its initial publication and registration. Drawing on the principles outlined in the HOME (Harmonising Outcome Measures for Eczema) Implementation Roadmap, a structured approach is key to ensuring the widespread adoption and use of the Core Outcome Measurement Instrument Set in research and clinical practice.

### Engage with Professional Societies

Collaborate with dermatological societies and professional organizations to promote the integration of the Core Outcome Measurement Instrument Set into clinical practice guidelines and research protocols. These efforts may include delivering presentations at conferences, incorporating the Core Outcome Measurement Instrument Set into policy documents, and engaging in advocacy initiatives to encourage adoption.
In addition, COS developers should actively communicate with regulatory bodies to align on expectations for outcome measurement in clinical trials and support regulatory acceptance.

Early dialogue with regulators can improve the credibility, uptake, and long-term impact of the Core Outcome Measurement Instrument Set.

### Develop Training and Educational Initiatives

Create targeted educational materials and workshops tailored for researchers, clinicians, and other stakeholders. These resources should provide practical guidance on implementing the Core Outcome Measurement Instrument Set, including examples and case studies that illustrate its application in diverse research and clinical contexts.

### Establish Monitoring and Evaluation Mechanisms

Set up systems to track the adoption and use of the Core Outcome Measurement Instrument Set over time. Conduct surveys, follow-up studies, or analyze trends in published research to assess its impact on dermatological research and practice. Regular feedback from users can help identify challenges and inform future refinements to the Core Outcome Measurement Instrument Set.

### Strengthen Networks and Collaboration

Foster and expand networks of researchers, clinicians, and patient groups who are committed to the use and promotion of the Core Outcome Measurement Instrument Set. These networks facilitate the exchange of best practices, innovation, and continuous engagement. Regular meetings, forums, or online communities can sustain interest and encourage collaboration among stakeholders.

By following these strategies, the Core Outcome Measurement Instrument Set can achieve widespread implementation, enhancing the quality and comparability of dermatological research.

## Conclusion

The successful dissemination and implementation of the Core Outcome Measurement Instrument Set are essential to its impact on dermatological research and patient care. By systematically sharing the Core Outcome Measurement Instrument Set with stakeholders, registering it in accessible databases, and publishing it according to established guidelines, a strong foundation is laid for its broad adoption. Furthermore, planning for ongoing implementation and dissemination ensures that the Core Outcome Measurement Instrument Set remains relevant, accessible, and widely utilized.

These steps not only ensure that the Core Outcome Measurement Instrument Set reaches its intended audience but also promote its sustained use, fostering collaboration among researchers, clinicians, and patient groups. This process enhances the quality of dermatological research, improves comparability across studies, and contributes to better

patient outcomes through the consistent use of reliable and valid measurement instruments.

# Final Word

The C3 Manual represents a collective effort to standardize and elevate the development of Core Outcome Sets and Measurement Instruments in dermatology. By adhering to the methodologies and best practices outlined in this manual, researchers and stakeholders can ensure that their work meets the highest standards of quality, relevance, and transparency. This fosters comparability across studies, improves research efficiency, and ultimately enhances patient care.

It is important to recognize that COS, CDS, and OMIs are always provisional. New evidence may emerge over time, and the pros and cons of updating should be carefully balanced to ensure that revisions are both necessary and feasible.

However, the manual is not a static document; it is intended to evolve with advancements in the field and feedback from its users. We encourage COS developers to engage with the C3 community, contribute their insights, and share their experiences to refine and strengthen this resource.

We also acknowledge that developing high-quality COS, CDS, and OMIs is a complex and iterative process that may take several years to complete. Patience, planning, and collaboration are essential to move these projects forward while maintaining strong methodological standards.

Finally, the success of the C3 Manual depends not only on its rigorous methodologies but also on the collaboration, dedication, and shared vision of its users. Together, we can create meaningful, impactful COS that drives progress in dermatological science and improve the health outcomes of dermatological patients worldwide.

The authors.
December, 2025

# References


Beaton D, Maxwell L, Grosskleg S, Shea B, Tugwell B (editors). The OMERACT Handbook Version 2.1 [updated March 2021]. OMERACT. Available from https://omeract.org/handbook/.

Brunton G, Webbe J, Oliver S, Gale C. Adding value to core outcome set development using multimethod systematic reviews. Res Synth Methods. 2020 Mar;11(2):248-259. doi: 10.1002/jrsm.1391.

Campbell F, Tricco AC, Munn Z, Pollock D, Saran A, Sutton A, White H, Khalil H. Mapping reviews, scoping reviews, and evidence and gap maps (EGMs): the same but different- the 'Big Picture' review family. Syst Rev. 2023 Mar 15;12(1):45. doi: 10.1186/s13643-023-02178-5.

Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, Irwig L, Levine D, Reitsma JB, de Vet HC, Bossuyt PM. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. BMJ Open. 2016 Nov 14;6(11):e012799. doi: 10.1136/bmjopen-2016-012799.

Dodd S, Clarke M, Becker L, Mavergames C, Fish R, Williamson PR. A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. J Clin Epidemiol. 2018 Apr;96:84-92. doi: 10.1016/j.jclinepi.2017.12.020.

Elsman EBM, Mokkink LB, Terwee CB, Beaton D, Gagnier JJ, Tricco AC, et al. Guideline for reporting systematic reviews of outcome measurement instruments (OMIs): PRISMA-COSMIN for OMIs 2024. Quality of Life Research (2024), doi: https://doi.org/10.1007/s11136-024-03634-y.

Gerbens LA, Prinsen CA, Chalmers JR, Drucker AM, von Kobyletzki LB, Limpens J, Nankervis H, Svensson Å, Terwee CB, Zhang J, Apfelbacher CJ, Spuls PI; Harmonising Outcome Measures for Eczema (HOME) initiative. Evaluation of the measurement properties of symptom measurement instruments for atopic eczema: a systematic review. Allergy. 2017 Jan;72(1):146-163. https://onlinelibrary.wiley.com/doi/10.1111/all.12959.

Keeley T, Williamson P, Callery P, Jones LL, Mathers J, Jones J, Young B, Calvert M. The use of qualitative methods to inform Delphi surveys in core outcome set development. Trials. 2016 May 4;17(1):230. doi: 10.1186/s13063-016-1356-7. PMID: 27142835; PMCID: PMC4855446.

Kirkham JJ, Davis K, Altman DG, Blazeby JM, Clarke M, Tunis S, Williamson PR. Core Outcome Set STAnDards for Development: the COS-STAD Recommendations. PLOS Med. 2017;14(11):e1002447.

Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, Moher D, Schmitt J, Tugwell P, Tunis S, Williamson PR. Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. PLoS Med. 2016 Oct 18;13(10):e1002148.

Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Tunis S, Williamson PR and for the COS-STAP Group. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. Trials 2019 20:116.

Leshem YA, Simpson EL, Apfelbacher C, Spuls PI, Thomas KS, Schmitt J, Howells L, Gerbens LAA, Jacobson ME, Katoh N, Williams HC, on behalf of the Harmonising Outcome Measures for Eczema (HOME) initiative. The Harmonising Outcome Measures for Eczema (HOME) implementation roadmap. Br J Dermatol. 2023 Dec;189(6):710-718. doi: 10.1093/bjd/ljad278.

Maxwell LJ, Beaton DE, Boers M et al. The evolution of instrument selection for inclusion in core outcome sets at OMERACT: Filter 2.2. Semin Arthritis Rheum. 2021;51(6):1320-1330. doi: 10.1016/j.semarthrit.2021.06.012.

Meyer D, Kottner J, Beele H, Schmitt J, Lange T, Van Hecke A, Verhaeghe S, Beeckman D. Delphi procedure in core outcome set development: rating scale and consensus criteria determined outcome selection. Clin Epidemiol. 2019 Jul;111:23-31. doi: 10.1016/j.jclinepi.2019.03.011.

Mokkink LB, Elsman E, Terwee CB. The COSMIN guideline for systematic reviews of Patient-Reported Outcome Measures (PROMs). Qual Life Res. 2024. doi: 10.1007/s11136-024-03761-6.

Mokkink LB, de Vet HCW, Prinsen CAC, et al. COSMIN Risk of Bias checklist for systematic reviews of Patient-Reported Outcome Measures. Qual Life Res. 2018;27:1171–1179. doi: 10.1007/s11136-017-1765-4.

Mokkink LB, et al. COSMIN Risk of Bias tool to assess the quality of studies on reliability or measurement error of outcome measurement instruments: a Delphi study. BMC Med Res Methodol. 2020;20:293. doi: 10.1186/s12874-020-01179-5.

Nast A, Griffiths CE, Hay R, Sterry W, Bolognia JL. The 2016 International League of Dermatological Societies' revised glossary for the description of cutaneous lesions. Br J Dermatol. 2016 Jun;174(6):1351-8. doi: 10.1111/bjd.14419. Epub 2016 Apr 3. PMID: 26801523.

Niederberger M, Schifano J, Deckert S, Hirt J, Homberg A, Köberich S, et al. Delphi studies in social and health sciences—Recommendations for an interdisciplinary standardized reporting (DELPHISTAR). PLoS ONE 19(8): e0304651. doi: 10.1371/journal.pone.0304651.

Peters MDJ, Godfrey C, McInerney P, Khalil H, Larsen P, Marnie C, Pollock D, Tricco AC, Munn Z. Best practice guidance and reporting items for the development of scoping review protocols. JBI Evidence Synthesis. 2022 Apr;20(4):953-968. doi: 10.11124/JBIES-21-00242.

Prinsen CAC, Mokkink LB, Bouter LM, Alonso J, Patrick DL, de Vet HCW, Terwee CB. COSMIN guideline for systematic reviews of patient-reported outcome measures. Qual Life Res. 2018 May;27(5):1147-1157. doi: 10.1007/s11136-018-1798-3.

Prinsen CA, Vohra S, Rose MR, Boers M, Tugwell P, Clarke M, Williamson PR, Terwee CB. How to select outcome measurement instruments for outcomes included in a Core Outcome Set - a practical guideline. Trials 2016; 17:449. doi: 10.1186/s13063-016-1555-2.

Remus, A., Smith, V. & Wuytack, F. Methodology in core outcome set (COS) development: the impact of patient interviews and using a 5-point versus a 9-point Delphi rating scale on core outcome selection in a COS development study. BMC Med Res Methodol 21, 10 (2021). https://doi.org/10.1186/s12874-020-01197-3

Schmitt J, Apfelbacher C, Spuls PI, Thomas KS, Simpson EL, Furue M, et al. The harmonizing outcome measures for eczema (HOME) roadmap: A methodological framework to develop core sets of outcome measurements in dermatology. J Invest Dermatol 2015;135:24-30.

Schünemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. Ann Intern Med 2015; 163:548–53.

Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. PLoS Med 2011; 8:e1000393.

Terwee CB, Jansma EP, Riphagen II, de Vet HC. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. Qual Life Res. 2009 Oct;18(8):1115-23. doi: 10.1007/s11136-009-9528-5.

Terwee CB, Prinsen CAC, Chiarotto A, et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures: a Delphi study. Qual Life Res 2018; 27:1159–70. doi: 10.1007/s11136-018-1829-0.

Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med 2018; 169:467–73. doi: 10.7326/M18-0850.

# Appendices

*We refer to the following original resources that are helpful in developing Core Outcome Sets in dermatology:*

## Appendix 1. C3 Core Outcome Set Development Checklist

https://www.c3outcomes.org/resources

## Appendix 2. C3 Template COI Form

Online link to the C3 website to be included here.

## Appendix 3. C3 Application Form

https://www.c3outcomes.org/resources?download_file=eyJpZCI6IjEwMDIwMCJ9

## Appendix 4. C3 Template Protocol for Core Outcome Domain Set Development

Online link to the C3 website to be included here.

## Appendix 5. COS-STAD (Core Outcome Set-STAndards for Development) guidance

https://doi.org/10.1371/journal.pmed.1002447

## Appendix 6. COS-STAP (Core Outcome Set-STAndardised Protocol Items) guidance

https://doi.org/10.1186/s13063-019-3230-x

## Appendix 7. Joanna Briggs Institute Methodology for Scoping Reviews

https://jbi.global/scoping-review-network/resources

## Appendix 8. Best practice guidance and reporting items for the development of scoping review protocols

https://journals.lww.com/jbisrir/fulltext/2022/04000/best_practice_guidance_and_reporting_items_for_the.3.aspx

## Appendix 9. PRISMA-ScR checklist

https://www.acpjournals.org/doi/10.7326/M18-0850

https://static1.squarespace.com/static/65b880e13b6ca75573dfe217/t/65b9e60d891cf662fa5f7c13/1706681870986/PRISMA-ScR-Fillable-Checklist_11Sept2019.pdf

## Appendix 10. CREDES Guideline

https://doi.org/10.1177/0269216317690685

## Appendix 11. Accord Reporting Guideline

https://doi.org/10.1371/journal.pmed.1004326

## Appendix 12. COS-STAR (Core Outcome Set-STAndards for Reporting) guidance

https://doi.org/10.1371/journal.pmed.1002148

## Appendix 13. HOME Implementation Roadmap

https://doi.org/10.1093/bjd/ljad278

## Appendix 14. PRIMSA-COSMIN guideline for reporting systematic reviews of OMIs

https://doi.org/10.1007/s11136-024-03634-y

## Appendix 15. COSMIN Risk of Bias Checklist v3.0

https://www.cosmin.nl/wp-content/uploads/COSMIN-RoB-checklist-for-PROMs-V3_1.pdf

## Appendix 16. COSMIN Risk of Bias Tool to assess the quality of studies on resliability or measurement error of outcome measurement instruments

https://www.cosmin.nl/wp-content/uploads/COSMIN-RoB-tool_reliability-and-measurement-error_1.pdf

## Appendix 17. COSMIN guideline for systematic reviews of PROMs version 2.0

https://doi.org/10.1007/s11136-024-03761-6

## Appendix 18. COSMIN guideline for conducting systematic reviews of other types of instruments

https://doi.org/10.1186/s12874-020-01179-5

**The CHORD COUSIN Collaboration**

**Authors**: Prinsen C, Alam M, Eleftheriadou V, Ezzedine K, Garg A, Kirkham JJ, Ingram J, Munblit D, Spuls P, Thomas K, Thorlacius L, Kottner J. The C3 Manual version 2.0. CHORD COUSIN Collaboration. Available from https://www.c3outcomes.org/

**Contact**: CHORD COUSIN Collaboration 1991 Marcus Ave, Suite 300, Lake Success NY 11042 USA. Email: chordcollab@gmail.com