

Guidance on how to develop a core outcome set for skin disease by the CS-COUSIN methods group

Summary

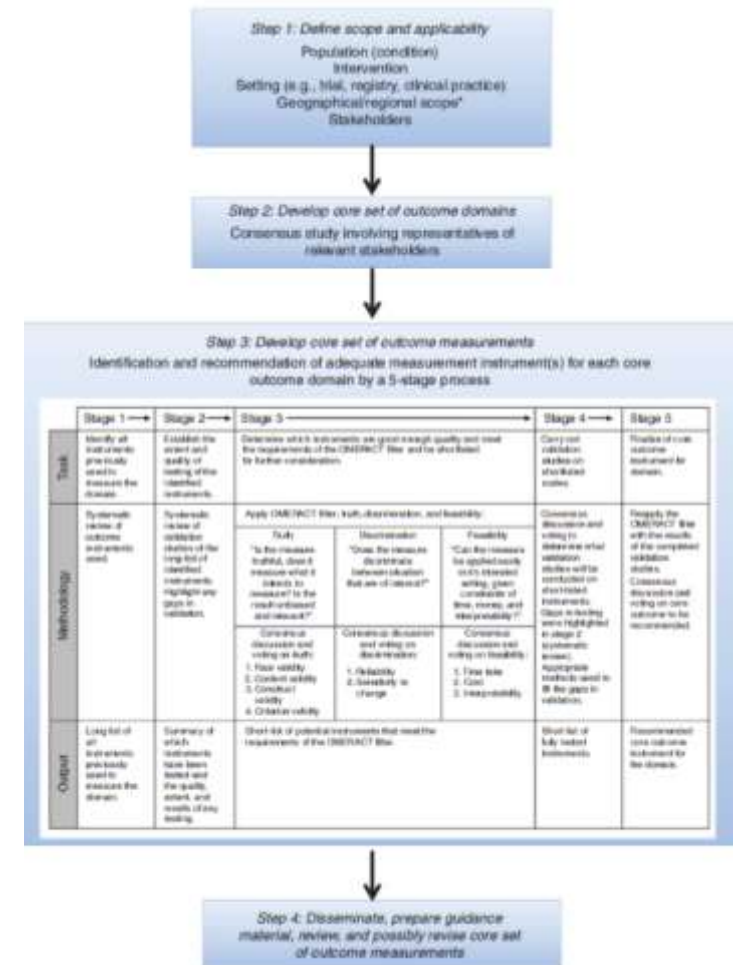
The Cochrane Skin - Core Outcome Set Initiative (CS-COUSIN) is a collaboration between Cochrane Skin and a wide range of groups interested in develop core outcome sets for diverse skin diseases (Prinsen et al. 2019). We recommend planning, structuring and conducting core outcome set (COS) development based on the Harmonising Outcome Measures for Eczema (HOME) roadmap (Schmitt et al. 2015) and latest international guidance (e.g. Williamson et al. 2017). CS-COUSIN provides practical support and follows standards on how to define, select and recommend core outcome domains and how to identify the best outcome measurement instruments for these identified domains within dermatology and associated fields. In the context of a clinical trial, an outcome domain/domain refers to *what* is being measured on trial participants to examine the effect of exposure to a health intervention. An outcome measurement instrument refers to *how* the outcome is being measured. It is a tool to measure a quality or quantity of the outcome (Prinsen et al. 2016).

Despite the existence of guidance on how to develop a COS, optimal methods for COS development are not known and uncertainty exists. For instance, there is no 'gold standard' on how to conduct consensus studies (e.g. which decision rules to use) and how to best select and develop core outcome domains and outcome measurement instruments.

This document is intended to provide guidance and essential references to ensure that a new COS is developed at an appropriate, high quality, methodological level. Among others, developing a protocol *a priori* for the COS development is mandatory. Inappropriately developed and published COS are potentially worse than no COS if they end up measuring the wrong things in the wrong way. Formal guidelines, if available, must be used when developing COS. The following outlines some key principles that need to be considered when developing a COS in a step-wise fashion based on the current state of knowledge.

References

- Prinsen et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. *Trials*. 2016;17(1):449.
- Prinsen et al. Navigating the landscape of core outcome set development in dermatology. *J Am Acad Dermatol*. 2019 Jul;81(1):297-305.
- Williamson et al. The COMET Handbook: version 1.0. *Trials*. 2017;18(Suppl3):280.



Schmitt J, Apfelbacher C, Spuls PI, 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(1):24-30.

Specific guidance CS-COUSIN COS development process

	Step	Key questions/ tasks	To dos and explanations	Resources and key references
1	Preparation	<ul style="list-style-type: none"> Do we really need a COS? 	<ul style="list-style-type: none"> Review the literature and epidemiological data The answer should be “yes” if <ol style="list-style-type: none"> there is a high incidence or prevalence, and/or high impact in terms of quality of life, costs and/or mortality of the disease or condition (i.e., high burden of disease) various non-comparable outcomes are used in clinical research, especially clinical trials and/or systematic reviews/meta-analyses outcomes currently used in clinical research and/or practice are insufficiently relevant and meaningful (e.g. for patients or service users) 	<ul style="list-style-type: none"> Electronic databases (e.g. Medline) Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280.
		<ul style="list-style-type: none"> Is there already a COS of interest available and/or under development? 	<ul style="list-style-type: none"> Check the COMET database Check with the COMET project coordinator Visit the CS-COUSIN homepage Consult the CS-COUSIN coordinator Search the internet via common search engines Search electronic databases 	<ul style="list-style-type: none"> http://www.comet-initiative.org/ http://cs-cousin.org/ Electronic databases (e.g. Medline)
		<ul style="list-style-type: none"> Proposal 	<ul style="list-style-type: none"> Download, complete and submit the proposal form to CS-COUSIN Submitting the proposal form implies that the COS will be developed according to CS-COUSIN standards Set up the COS development group consisting of at least clinicians, methodologists, and patients 	<ul style="list-style-type: none"> http://cs-cousin.org/resources/
2	Protocol	<ul style="list-style-type: none"> Write a protocol for the COS domain development (after approval from CS-COUSIN of the proposal) 	<ul style="list-style-type: none"> Specify all relevant steps, tasks, expected results, methodological experts and stakeholder types to be involved, and why Plan domain development in accordance with rules promulgated by CS-COUSIN and in accordance with COS-STAP Register your initiative at COMET The protocol must describe at least the domain development process. It may also contain steps for instrument selection but this can also be done later. 	<ul style="list-style-type: none"> http://www.comet-initiative.org/ http://cs-cousin.org/resources/ Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Tunis S, Williamson PR; COS-STAP Group. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. <i>Trials</i>. 2019 Feb 11;20(1):116. Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280.

		<ul style="list-style-type: none"> Does the protocol follow current best practice for COS development? 	<ul style="list-style-type: none"> Clearly define the health problem, the population, setting and intervention types (e.g. 'all interventions,' 'pharmacological interventions,' etc.) Study the latest methodological recommendations for COS development Ensure you satisfy the 11 Core Outcome Set-Standards for Development steps (COS-STAP) Include relevant stakeholders in a meaningful way Include content and methodological experts in your group Get some external feedback on your protocol from professional colleagues and patients outside your COS group and from CS-COUSIN Methods group 	<ul style="list-style-type: none"> Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Tunis S, Williamson PR; COS-STAP Group. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. <i>Trials</i>. 2019 Feb 11;20(1):116. Kirkham JJ et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. <i>PLoS Med</i>. 2017;14(11):e1002447. Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280.
3	Core Outcome domains	<ul style="list-style-type: none"> Identify possible outcome domains 	<ul style="list-style-type: none"> Outcome domains define "what" to be measured Possible outcome domains should cover essential features of the disease/conditions e.g. in terms of mortality, life impact, resource use, pathophysiological manifestations. Use an existing systematic review and/or initiate a systematic review in order to develop a preliminary list of outcome domains/domains based on at least the two databases Medline and Embase Include quantitative and qualitative research in the systematic review If performing a systematic review, register this at PROSPERO Develop inductively and iteratively possible outcome domains Look for further input, and additional outcome domains Consult experts Involve patients/service users (What is important for them?) Consider contacting national or international regulatory authorities (FDA, EMA) Define and describe the domains in as detailed a manner as possible 	<ul style="list-style-type: none"> Brunton G, Webbe J, Oliver S, Gale C. Adding value to core outcome set development using multimethod systematic reviews. <i>Res Synth Methods</i>. 2020;11(2):248-259. 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. <i>J Clin Epidemiol</i>. 2018;96:84-92. Gorst S, Young B, Williamson P, Wilding J, Harman N. Incorporating patients' perspectives into the initial stages of core outcome set development: a rapid review of qualitative studies of type 2 diabetes. <i>BMJ Open Diabetes Res Care</i>. 2019;7(1):e000615. Kirkham JJ et al. Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. <i>PLoS Med</i>. 2016;13(10):e1002148. Keeley T et al. The use of qualitative methods to inform Delphi surveys in core outcome set development. <i>Trials</i>. 2016;17(1):230. Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280. COMET PoPPiE Working Group, http://www.comet-initiative.org/ppi/poppie#
		<ul style="list-style-type: none"> Select the core outcome domains 	<ul style="list-style-type: none"> Perform a consensus study (Delphi or Nominal groups) involving relevant stakeholders (e.g. patients, clinicians, clinical researchers, industry representatives) to be followed by a face-to-face group meeting (if possible) plus voting (anonymous voting pads are essential) to define and/or select outcome domains Limit the number of outcome domains and present clear definitions of each Guide and support patients and healthcare participants to ensure meaningful participation Define decision rules <i>a priori</i> Publish the results according to the Core Outcome Set-STAndards for Reporting (COS-STAR) Statement 	<ul style="list-style-type: none"> Biggane AM, Williamson PR, Ravaud P, Young B. Participating in core outcome set development via Delphi surveys: qualitative interviews provide pointers to inform guidance. <i>BMJ Open</i>. 2019;9(11):e032338. Kirkham JJ et al. Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. <i>PLoS Med</i>. 2016;13(10):e1002148. Kirkham JJ et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. <i>PLoS Med</i>. 2017;14(11):e1002447.

4	Outcome measurement instruments to measure core outcome domains	<ul style="list-style-type: none"> • What instruments exist per domain? 	<ul style="list-style-type: none"> • Create a list of existing measurement instruments of the outcome domain of interest using a systematic review covering at least the two databases Medline and Embase. 	<ul style="list-style-type: none"> • https://www.cosmin.nl/tools/guideline-conducting-systematic-review-outcome-measures/ • Prinsen CA et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. <i>Trials</i>. 2016 Sep 13;17(1):449. • 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. <i>Qual Life Res</i>. 2018;27(5):1147-1157. • Terwee CB, Jansma EP, Riphagen II, et al. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. <i>Qual Life Res</i>. 2009 Oct;18(8):1115-23. • Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280. 	
		<ul style="list-style-type: none"> • What are the measurement properties of these instruments? 	<ul style="list-style-type: none"> • Identify the empirical evidence supporting the validity, reliability and feasibility of the scores or parameters • Consider using the search algorithms and filters provided by the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) • Do a methodological appraisal of the validation studies, by applying quality criteria. COSMIN is one of the best developed frameworks for this purpose. • Identify missing validation evidence. 		
		<ul style="list-style-type: none"> • Generate missing validation evidence (if needed) 	<ul style="list-style-type: none"> • Plan, conduct, and report validation studies based on highest methodological standards (e.g. following Standards for Reporting Diagnostic accuracy studies [STARD 2015]; Guidelines for reporting reliability and agreement studies [GRRAS]; COSMIN) 		<ul style="list-style-type: none"> • Bossuyt PM et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. <i>BMJ</i>. 2015;351:h5527. • Kottner J et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. <i>J Clin Epidemiol</i>. 2011;64(1):96-106. • Mokkink LB, de Vet HCW, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, Terwee CB. COSMIN Risk of Bias checklist for systematic reviews of Patient-Reported Outcome Measures. <i>Qual Life Res</i>. 2018 May;27(5):1171-1179. doi: 10.1007/s11136-017-1765-4.
		<ul style="list-style-type: none"> • Evaluate the quality of the instruments 	<ul style="list-style-type: none"> • Appraise the validation evidence taking study quality into account (e.g. using COSMIN methodology) • Perform a best evidence synthesis, and consider levels of evidence, in order to derive a short list of instruments that have the potential to be included in the COS 		<ul style="list-style-type: none"> • Prinsen CA et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. <i>Trials</i>. 2016 Sep 13;17(1):449. • 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. <i>Qual Life Res</i>. 2018;27(5):1147-1157. • http://www.cosmin.nl/
		<ul style="list-style-type: none"> • Define the core outcome measurement instruments 	<ul style="list-style-type: none"> • Complete a consensus study (Delphi or nominal group process) involving relevant stakeholders (e.g. patients, clinicians, clinical researchers, industry representatives), to be followed by a face-to-face group meeting with voting, to select core outcome instruments. • Define decision rules <i>a priori</i> • Select <u>one</u> core outcome measurement instrument per core outcome domain 		<ul style="list-style-type: none"> • Williamson et al. The COMET Handbook: version 1.0. <i>Trials</i>. 2017;18(Suppl3):280.

5	Dissemination and implementation	Make your results available	<ul style="list-style-type: none"> • Publish your results in leading journals (protocols, systematic reviews, core outcome domains, and core outcome measurement instruments may be published separately) • Present at conferences, meetings, symposia, including both those specific for core outcome sets and those that devoted to the disease or condition being studied. • Register your COS in COMET and at the CS-COUSIN homepage • Make sure that the CS knows about your work product so that it can encourage reviewers to include it in systematic reviews • Share your experience in developing your COS (e.g. in the CS-COUSIN group) • Use the COS in your own research and encourage others to use it in theirs 	<ul style="list-style-type: none"> • http://cs-cousin.org/ • Williamson et al. The COMET Handbook: version 1.0. Trials. 2017;18(Suppl3):280.
		Does your work make an impact?	<ul style="list-style-type: none"> • Monitor the use (i.e., uptake) of the COS (e.g. using citation databases Scopus, Web of Science, clinical trial registries) • Does the COS need revision (e.g. due to new measurement instruments, new evidence, emerging problems of COS usage)? <ul style="list-style-type: none"> • Weigh the decision to revise against the need that the COS should not change 	<ul style="list-style-type: none"> • Williamson et al. The COMET Handbook: version 1.0. Trials. 2017;18(Suppl3):280.