

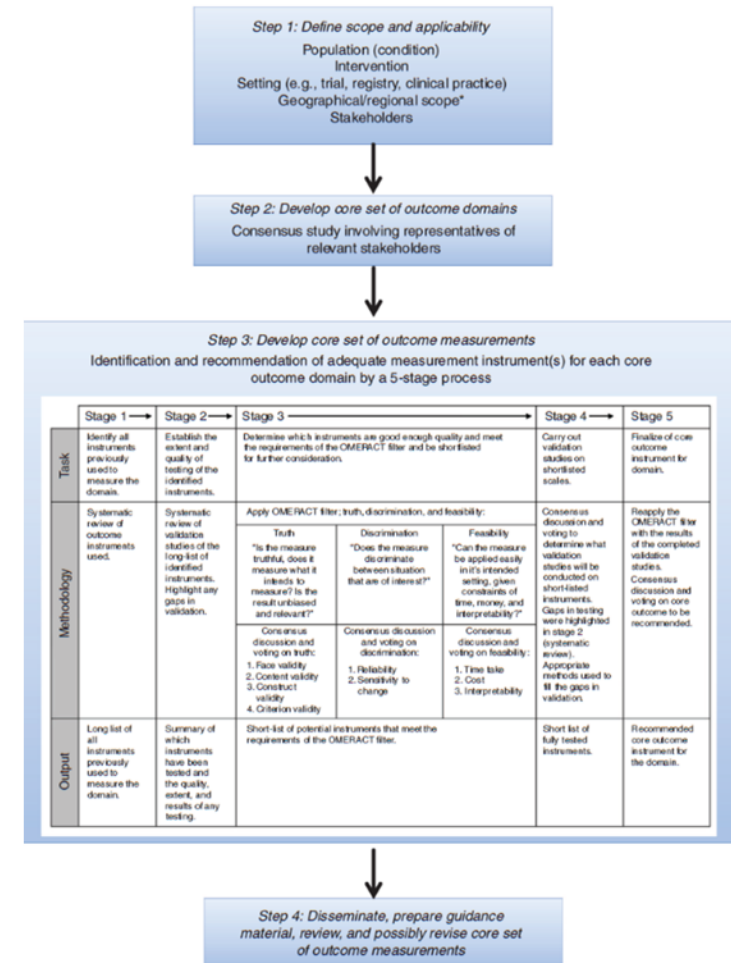
Guidance on how to develop a core outcome set for skin disease by the CS-COUSIN methods group

Summary

The Cochrane Skin Group - Core Outcome Set Initiative (CS-COUSIN) is a working group within the international Cochrane Skin Group. It recommends using the Harmonising Outcome Measures for Eczema (HOME) roadmap (Schmitt et al. 2015) to structure the core outcome set (COS) development process (or parts of it). The HOME roadmap provides guidance how to define, select and recommend the most important core outcome domains and how to identify the best outcome measurement instruments for these identified domains. Despite the existence of guidance on how to develop COS (e.g. Boers et al. 2015), optimal methods for COS development are not known and uncertainty exists (Kirkham et al. 2016, Gargon et al. 2017). For instance, there is no 'gold' standard on how to do consensus studies (e.g. which decision rules to use) and how to select/develop core outcome domains and outcome measurement instruments (e.g. Kirwan et al. 2015). This document is intended to provide guidance and essential references in order to ensure that a new COS is developed with 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 for COS development, outcome measurement instrument selection and for reporting for COS development studies are published and must be used (Kirkham et al. 2016, Kirkham et al. 2017, Prinsen et al. 2016) and a handbook by the Core Outcome Measures in Effectiveness Trials (COMET) initiative was published in 2017 (Williamson et al. 2017). The following outlines some key principles that need to be considered when developing a COS in a stepped fashion based on the current state of knowledge.

References

- Boers M et al. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf
- Gargon E et al. Improving Core Outcome Set Development: Qualitative Interviews with Developers Provided Pointers to Inform Guidance. *J Clin Epidemiol.* 2017 May 8. [Epub ahead of print]
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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 on the HOME and CS-COUSIN COS development process

	Step	Key questions/ tasks	To dos and explanations	Resources
1	Preparation	<ul style="list-style-type: none"> Do we really need a COS? 	<ul style="list-style-type: none"> Look into the literature and into epidemiological data The answer should be “yes” if <ol style="list-style-type: none"> there is a high incidence, prevalence, and/or high impact in terms of quality of life, costs and/or mortality of the disease or condition (burden of disease) various non-comparable outcomes are used in clinical research especially in clinical trials and/or systematic reviews/meta-analyses outcomes in clinical research are unlikely to be 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. Trials. 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 CSG-COUSIN homepage Consult the CSG-COUSIN coordinator Search the internet via common search engines Search electronic databases 	<ul style="list-style-type: none"> http://www.comet-initiative.org/ https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin 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 the CSG-COUSIN Submitting the proposal form implies that the COS will be developed according to CSG-COUSIN standards 	<ul style="list-style-type: none"> https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin
2	Protocol	<ul style="list-style-type: none"> Write a protocol for the COS domain development (after approval from CSG-COUSIN) 	<ul style="list-style-type: none"> Specify all relevant steps, tasks, expected results, planned people to involve and why Consider the protocol requirements for the domain development process according to CSG-COUSIN Register your initiative at COMET Set up the COS development group consisting of at least clinicians and methodologists and patients The protocol must include 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/ https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin Williamson et al. The COMET Handbook: version 1.0. Trials. 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 Make sure that you meet the 11 Core Outcome Set-Standards for Development (COS-STAP) Include experts in your group Look for (external) feedback for your protocol Include relevant stakeholders in a meaningful way 	<ul style="list-style-type: none"> Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol.</i> 2015;135(1):24-30. Boers M et al. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf 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. Williamson et al. The COMET Handbook: version 1.0. <i>Trials.</i> 2017;18(Suppl3):280.
3	Core Outcome domains	Identify possible outcome domains	<ul style="list-style-type: none"> Outcome domains define "what" to be measured Essential features of the disease/conditions e.g. in terms of mortality, life impact, resource use, pathophysiological manifestations Use and/or do a (systematic) review and make a preliminary selection of outcomes (domains) covering at least the two databases Medline and Embase When doing systematic reviews, register at PROSPERO Develop inductively and iteratively possible outcome domains Look for further input, e.g. from experts Involve patients/service users (What is important for them?) Consider to involve regulating authorities (FDA, EMA) Define the domains 	<ul style="list-style-type: none"> Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol.</i> 2015;135(1):24-30. Boers M et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. <i>J Clin Epidemiol.</i> 2014;67(7):745-53. Boers M et al. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf 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#
		Select the core outcome domains	<ul style="list-style-type: none"> Do a consensus study (Delphi or Nominal groups) involving relevant stakeholders (patients, clinicians, clinical researchers) 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 for outcome measurement development Present definitions of the domains Define decision rules a priori Select outcome domains Publish the results according to the COS-STAR Statement 	<ul style="list-style-type: none"> Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol.</i> 2015;135(1):24-30. Boers M et al. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf Sinha IP et al. 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. <i>PLoS Med.</i> 2011;8(1):e1000393. 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. http://www.comet-initiative.org/assets/downloads/Tips%20for%20Designing%20an%20Accessible%20Core%20Outcome%20Set%20Consensus%20Meeting%20final%2026-10-17.pdf



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"> • Identify all measurement instruments of the domain of interest using a systematic review covering at least the two databases Medline and Embase to create a list of existing instruments 	<ul style="list-style-type: none"> • Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol.</i> 2015;135(1):24-30. • Boers M et al. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf • http://www.cosmin.nl/ • 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. • 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.
		<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 of the scores or parameters • Consider to use the search algorithms and filters provided by COSMIN • Do a methodological and quality appraisal of the validation studies, by applying quality criteria. COSMIN is one of the best developed framework for doing this. • 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 the validation studies based on highest methodological standards (e.g. following STARD 2015; 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. • Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol.</i> 2015;135(1):24-30. • Kottner J et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. <i>J Clin Epidemiol.</i> 2011;64(1):96-106.
		<ul style="list-style-type: none"> • Evaluate the quality of the instruments 	<ul style="list-style-type: none"> • Appraise the validation evidence taking the methodological appraisal of the study quality into account (e.g. using COSMIN methodology and/or OMERACT filter) • Perform a best evidence synthesis / apply levels of evidence in order to come to a short list of instruments that have the potential to be included in the COS 	<ul style="list-style-type: none"> • 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. <i>J Invest Dermatol.</i> 2015;135(1):24-30. • 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. • Boers M, Kirwan, JR, Tugwell P. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf • http://www.cosmin.nl/
		<ul style="list-style-type: none"> • Define the core outcome measurement instruments 	<ul style="list-style-type: none"> • Do a consensus study (Delphi or Nominal groups) involving the relevant stakeholders (patients, clinicians, clinical researchers) to be followed by a face-to-face group meeting plus voting (anonymous voting pads are essential) to select one core outcome instrument per core outcome domain • Define decision rules a priori • Select one core outcome measurement instrument per core outcome domain 	<ul style="list-style-type: none"> • 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. <i>J Invest Dermatol.</i> 2015;135(1):24-30. • Boers M, Kirwan, JR, Tugwell P. The OMERACT Handbook. 2015. http://www.omeract.org/pdf/OMERACT_Handbook.pdf • 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. <i>PLoS Med.</i> 2011;8(1):e1000393. • Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. <i>Trials.</i> 2012;13:132.

5	Dissemination and implementation	Make your results available	<ul style="list-style-type: none"> • Publish your results in leading journals • Present at conferences, meetings, symposia • Register your results in COMET and at the CSG-COUSIN homepage • Make sure that the CSG knows about them so that it can encourage reviewers to adopt them in systematic reviews • Share your experience e.g. in the CSG-COUSIN group • Use the COS 	<ul style="list-style-type: none"> • http://www.comet-initiative.org/ • https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin • Williamson PR et al. Developing core outcome sets for clinical trials: issues to consider. <i>Trials</i>. 2012;13:132.
		Does your work make an impact?	<ul style="list-style-type: none"> • Monitor the use 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 • Weigh the decision to revise against the need that the COS should not change 	<ul style="list-style-type: none"> • Schmitt J et al. The Harmonizing Outcome Measures for Eczema (HOME) roadmap: a methodological framework to develop core sets of outcome measurements in dermatology. <i>J Invest Dermatol</i>. 2015;135(1):24-30. • Williamson PR et al. Developing core outcome sets for clinical trials: issues to consider. <i>Trials</i>. 2012;13:132. • Barnes KL et al. Citation analysis did not provide a reliable assessment of core outcome set uptake. <i>J Clin Epidemiol</i>. 2017 [Epub ahead of print]