

University of Groningen

## Protocol for the development of a core domain set for hand eczema trials

Ronsch, H.; Apfelbacher, C.; Brans, R.; Ofenloch, R.; Schuttelaar, M. L. A.; Weisshaar, E.; Bauer, A.

*Published in:*

Journal of the European Academy of Dermatology and Venereology

*DOI:*

[10.1111/jdv.16429](https://doi.org/10.1111/jdv.16429)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2020

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Ronsch, H., Apfelbacher, C., Brans, R., Ofenloch, R., Schuttelaar, M. L. A., Weisshaar, E., & Bauer, A. (2020). Protocol for the development of a core domain set for hand eczema trials. *Journal of the European Academy of Dermatology and Venereology*, 34(12), 2871-2876. <https://doi.org/10.1111/jdv.16429>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*



## ORIGINAL ARTICLE

# Protocol for the development of a core domain set for hand eczema trials

H. Rönisch,<sup>1,\*</sup> C. Apfelbacher,<sup>2</sup> R. Brans,<sup>3</sup> R. Ofenloch,<sup>4</sup> M.L.A. Schuttelaar,<sup>5</sup> E. Weisshaar,<sup>4</sup> A. Bauer<sup>1</sup>

<sup>1</sup>Department of Dermatology, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany

<sup>2</sup>Institute of Social Medicine and Health Systems Research, Medical Faculty, Otto von Guericke University, Magdeburg, Germany

<sup>3</sup>Institute for Interdisciplinary Dermatological Prevention and Rehabilitation (iDerm) at the University of Osnabrück, Osnabrück, Germany

<sup>4</sup>Occupational Dermatology, Department of Dermatology, Ruprecht-Karls-University, Heidelberg, Germany

<sup>5</sup>Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

\*Correspondence: H. Rönisch. E-mail: henriette.roensch@tu-dresden.de

## Abstract

**Background** Clinical hand eczema trials measure a variety of outcome domains to determine the success of interventions. This considerably limits the comparability and overall confidence in the study results, and thereby the strength of recommendations for clinical practice.

**Objectives** The Hand Eczema Core Outcome Set (HECOS) initiative aims to develop a core outcome set (COS) for the standardized evaluation of interventions in future hand eczema trials and reviews. This COS will define the minimum that should be measured and reported in controlled and randomized-controlled trials of therapeutic hand eczema interventions. The objective of this protocol is to specify the methods to develop a core domain set.

**Methods** In Phase 1, a list of candidate domains will be derived from a systematic literature review concerning previously measured outcomes in hand eczema trials, from qualitative patient interviews and from expert interviews. In Phase 2, a consensus study about core domains will be conducted by an online 3-round Delphi survey and a face-to-face meeting, applying predefined consensus criteria. HECOS involves hand eczema and methods experts as well as patients and further stakeholders with an interest in the initiative.

**Outlook** When a set of core domains has been defined, HECOS is going to identify appropriate outcome measurement instruments in a development process that will be detailed in another protocol. The COS will considerably enhance the methodological quality, comparability and usefulness of hand eczema trials for clinical decision-making and the development of new therapeutic options for hand eczema, and also reduce the effort of planning, conducting, and reporting individual hand eczema studies, reviews and meta-analyses.

Received: 30 December 2019; Accepted: 24 March 2020

## Conflicts of interest

Christian Apfelbacher, Elke Weisshaar and Robert Ofenloch were involved in the development of the Quality Of Life in Hand Eczema Questionnaire (QOLHEQ) and Marie L.A. Schuttelaar was involved in its validation. Christian Apfelbacher is member of the executive committee of the HOME COS initiative. Andrea Bauer is involved in clinical trials on hand eczema (LEO Pharma); she received speaker honoraria from LEO Pharma, Novartis Pharma and Sanofi. The other authors have no conflicts of interest.

## Funding sources

The European Academy of Dermatology and Venereology (EADV) has granted funding for conducting qualitative patient interviews within the HECOS initiative.

## Introduction

### Scientific background and relevance

Hand eczema (HE) is an inflammatory skin disease that can be caused by several factors. Its typical clinical signs include

erythema, scaling, oedema, vesicles, fissures, erosions and hyperkeratosis.<sup>1</sup> In the general population, it is a common disease with a one-year prevalence of nearly 10%.<sup>2</sup> By affecting the hands, which are highly visible and vital for many everyday activities, HE has an immense social and economic impact on

individuals and societies.<sup>3</sup> Due to its high prevalence, poor prognosis and high burden of disease, HE is an important field of research.<sup>4</sup>

HE trials measure a variety of outcome domains to determine the effect of interventions. The problems arising from such heterogeneity have been explained in detail by the Core Outcome Measures in Effectiveness Trials (COMET) initiative.<sup>5</sup> In short, it considerably limits the comparability of results from different trials and hampers the synthesis of these in systematic reviews, which are the cornerstone of evidence-based decision making. This limitation was encountered in a recent Cochrane review of interventions for HE.<sup>4</sup> To help overcome these problems and enhance the efficiency of HE research, the Hand Eczema Core Outcome Set (HECOS) initiative was formed. In this protocol, we propose a process to develop and agree on a core domain set (CDS) for HE trials.

Currently, there exist no broadly agreed definitions of key terms applied in core outcome set (COS) development. Based on the usage in the Cochrane Skin Core Outcome Set Initiative (CS-COUSIN, <http://cs-cousin.org>), HECOS applies the nominal definitions given in Table 1.

## Objectives

The objectives of the domain development process are:

- to create a long list of efficacy/effectiveness domains as candidates for the CDS, and
- to reach consensus among stakeholders about which efficacy/effectiveness domains should be part of the CDS.

## Scope and applicability of the CDS

- Population of interest: Adult people with HE (regardless of HE type or general health status).

- Intervention: All therapeutic interventions that aim to ease the burden of HE (e.g. topical treatment, UV therapy, systemic treatment)
- Setting: Interventional controlled HE trials, both randomized and non-randomized, excluding laboratory experiments and observational studies. HECOS does not make a distinction between efficacy and effectiveness trials because there exists a continuum between both.
- Area: International.

## Materials and methods

HECOS is part of CS-COUSIN. This initiative provides structured guidance for developing COSs in the field of dermatology.<sup>6</sup> This includes the application of current formal guidelines<sup>7–9</sup> and the COMET handbook.<sup>5</sup> HECOS has been registered at the COMET website (<http://www.comet-initiative.org/studies/details/1405>).

## COS development group

In accordance with the international scope, HECOS aims to involve stakeholders from at least 4 continents and 15 countries. Anyone who has an interest in the development of a HE core outcome set can join HECOS.

- Patients will be contacted through patient associations, through university and general hospitals, through flyers at dermatology practices and through internet forums.
- HE researchers and methodologists will be identified through previous collaboration, from relevant publications listed at PubMed, and at congresses.
- Dermatologists who are not researchers will be contacted through national dermatologists associations, or via collaboration with HE experts from university hospitals.

**Table 1** Nominal definitions of key terms in HECOS

Term	Short form	Definition	Example
Outcome domain <sup>†</sup>	Domain	A concept that is or could be measured in a study	Physical functioning, signs of HE, itch, health-related quality of life
Outcome measurement instrument <sup>†</sup>	OMI	An instrument that is or could be applied to measure a domain	Visual analog scale, Osnabrueck Hand Eczema Severity Index (OHSI), Tewameter
Fully specified outcome <sup>†</sup>	–	The entirety of domain, OMI, metric, aggregation and time frame investigated in a study	Mean group difference of HE severity as measured with the OHSI at week 36
Outcome <sup>†</sup>	–	An outcome domain with or without further specifications (e.g. OMI, metric)	Change in HE severity, trans-epidermal water loss (TEWL)
Core domain set	CDS	A set of domains constituting the minimum that should be measured in a specified field of research	Core Outcome Set for Multimorbidity Research (COSmm)
Core outcome set <sup>†</sup>	COS	A CDS with corresponding OMIs	OMERACT core set of outcome measures for clinical trials in antineutrophil cytoplasmic antibody-associated vasculitis
Candidate domain	–	A domain that will be considered for inclusion in a CDS	–
Efficacy/effectiveness domain	–	Any domain that is potentially suitable to investigate the efficacy or effectiveness of an intervention	HE severity, health-related quality of life, pain

<sup>†</sup>In accordance with usage of these terms in CS-COUSIN.

- Representatives of pharmaceutical and cosmetic companies involved in research and development of products for the prevention and therapy of HE will be identified through an online search.
- Regulatory authorities, insurance representatives and journal editors will be identified through an online search.
- Nurses and other health care professionals will be contacted through personal contact or at appropriate conferences.

The *steering committee* will consist of a range of stakeholders from all continents. Its tasks are to ensure that HECOS is conducted according to protocol and CS-COUSIN guidelines and to make any decisions that are not predefined by protocol. The HECOS *initiative* consists of the steering committee and further members. Its main tasks are to conduct the steps and projects described in this protocol and to provide feedback concerning the work of the steering committee. The *consensus panel* involves the members of the initiative as well as a larger amount of stakeholders. Their tasks are to participate in the e-Delphi survey, the face-to-face meeting (optional) and the online confirmation survey of the meeting's results.

HECOS receives *methodological advice* from CS-COUSIN, represented by Dr Jan Kottner.

### Phase 1: Identification of candidate core domains

*Defining domains* There are several hierarchical levels of domains.<sup>10</sup> 'Erythema', for example, could be defined as a domain of its own or as part of the domain 'clinical signs of hand eczema' or as part of the even broader domain 'skin'. As a starting point, HECOS applies the taxonomy developed by Dodd *et al.*<sup>11</sup> to categorize all domains that are identified in the three projects of phase 1. In this taxonomy, the 'skin' domain is not yet differentiated, but Dodd *et al.*<sup>11</sup> propose to develop subcategories within each domain to provide finer classification.

Before initiating the actual consensus process (phase 2), the steering committee is going to decide which domain levels should be discussed by the panel as candidate core domains. These decisions and others that concern the merging and dividing of domains will be made by the steering committee throughout phase 1. Domains will not be merged or divided after commencing the consensus process (phase 2) unless there is an important reason. If it is nevertheless required, the steering committee will seek approval from CS-COUSIN.

*Systematic review.* This review has already been completed and its methods and results have been published.<sup>12</sup> Its objective was to identify outcomes that were measured in previous trials, to group them in domains and to identify their measurement instruments. We conducted a systematic review of controlled and randomized-controlled HE trials published between 2000 and 2017, including therapeutic as well as preventive interventions.

The trial outcomes were categorized according to the domain taxonomy developed by Dodd *et al.*<sup>11</sup> The initiative is going to discuss if and how the outcomes that were identified within the domain 'skin' should form more differentiated domains. The final decision will be made by the steering committee.

*Qualitative patient interviews.* The interviews focus on the population that is usually included in clinical hand eczema trials: patients with chronic hand eczema. Adult patients with chronic HE (persisting for more than three months or recurring two or more times within 12-months<sup>13</sup>) will be recruited in outpatient dermatological and occupational medicine clinics. In each participating country, ideally, 12–15 patients will be recruited and interviewed. We are going to apply purposive sampling by age, sex, employment status, education and HE severity.

We will conduct topic-guided patient interviews. As opposed to standardized interviews, this qualitative method applies open questions concerning key issues and will thereby ensure that the interviews are able to identify relevant domains from the patient's perspective. A topic guide has been prepared based on previous topic-guides<sup>14,15</sup> and following recommendations for patient interviews in the development of PRO measures.<sup>16</sup>

We apply a primarily deductive approach with inductive elements to inform the HECOS initiative about domains that patients consider relevant. All efficacy/effectiveness domains will be categorized according to the taxonomy of Dodd *et al.*<sup>7</sup> If a domain is identified during the interviews but not covered by Dodd's taxonomy, it will be defined inductively. This means that all patient statements that refer to a previously non-existent domain will be gathered and the domain will be named and defined according to these statements.

All interviews will be coded by the same researcher. A second researcher is going to independently re-code at least 10% of the interview transcripts. Deviations will be discussed. If the second researcher determines that 5% or more of the domains in this sample were overlooked or coded incorrectly, all remaining patient interviews will be coded in duplicate as well.

The domains gathered from these interviews will be considered in the consensus study (phase 2). In addition, candidate domains that are derived from patient interview studies with methods that deviate from this protocol can be accepted by the steering committee. Such studies need to be in accordance with local data protection laws and approved by the appropriate ethical board.

Efficacy/effectiveness domains emerging from the patient interviews will be compared domains gathered in a previous systematic review of HE trials.<sup>12</sup>

*Interviews with HE experts.* The objectives of this project are to identify gaps in the long list of candidate domains and to involve more experts from Australia, Africa, Asia and the Americas in the CDS and COS development. The interviews will be

conducted by several project group members applying various techniques (face-to-face, telephone, email). The interviewers are going to take notes about:

- newly identified domains
- other useful input.

## Phase 2: Agreeing on a CDS

**E-Delphi procedure** We aim to reach consensus by a 3-round online Delphi survey (Fig. 1) followed by a face-to-face consensus meeting with an online confirmation survey and further online Delphi rounds if required. Panellists will receive targeted background information about the rationale of COS. The form will include plain language descriptions, examples and pictures, where appropriate.

Before initiating round 1 of the online Delphi procedure, the steering committee reviews and discusses the consensus criteria (Table 2) and the criteria for excluding domains from consideration in subsequent rounds (Fig. 1) that are predefined in this protocol. The steering committee may decide to modify these criteria before round 1.

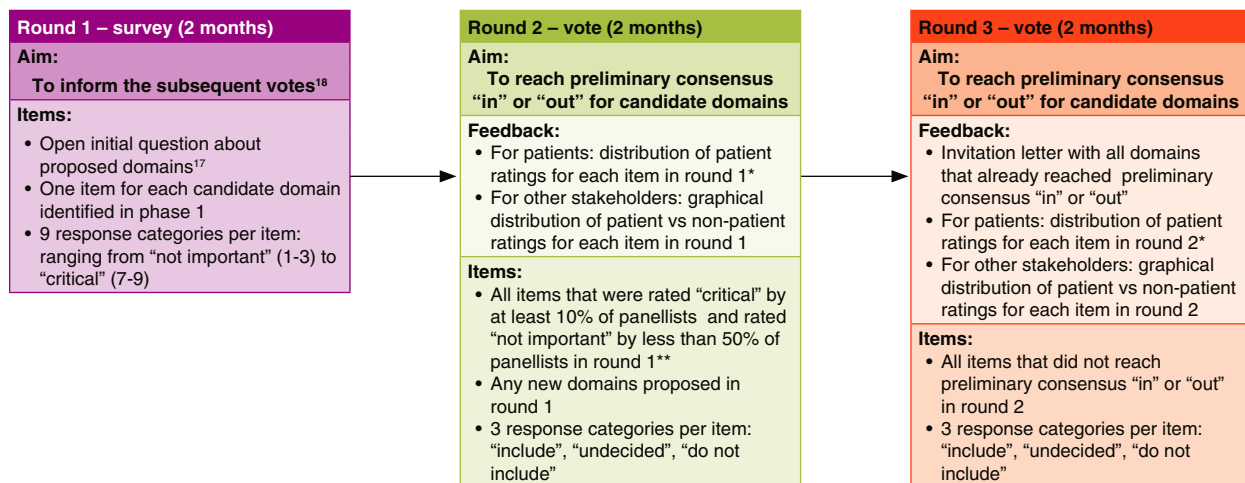
The e-Delphi form will include one item for each domain identified in phase 1. In the first e-Delphi round, participants may propose additional domains.<sup>17</sup>

**Face-to-face consensus meeting** The panellists are going to discuss all items in a face-to-face consensus meeting, including items that did reach consensus 'in' our 'out' during the e-Delphi procedure.

**Table 2** Consensus definition

<b>Consensus 'in':</b>	rated 'do not include' by <30% of panellists (across stakeholder groups)
<b>Consensus 'out':</b>	rated 'include' by <30% of panellists (across stakeholder groups)
<b>No consensus:</b>	rated 'include' by at least 30% and rated 'exclude' by at least 30%

- The panellists will be invited to join a premeeting session that explains the background of HECOS and the relevant terminology.
- At the beginning of the plenary session, the evidence gathered from the systematic review, patient interviews and expert interviews will be presented.
- In an open discussion, the participants will be able to speak about their perspectives concerning the CDS development.
- Results of the e-Delphi study will be presented and meaning/definition of all domains will be explained again.
- The panellists will be divided into groups with roughly similar representation of all stakeholder groups. With the assistance of moderators, applying nominal group techniques, all items that did not reach consensus 'in' or 'out' will be discussed.
- In a series of life anonymous votings applying the Delphi procedure, consensus on all items is sought.
- There will be a vote about the whole set of items that reached consensus 'in'. If <30% disagree, this will be the meetings' agreed preliminary CDS. If 30% or more disagree, the reasons will determined by a life multiple-choice survey (too many outcomes, too few outcomes, other reasons).



**Figure 1** Online Delphi to reach preliminary consensus about core efficacy/effectiveness domains.<sup>17</sup> \*Patients will only be shown results of their own stakeholder group so that they are not influenced by other groups that may be over-represented or perceived as more authoritative.<sup>19</sup> \*\*These criteria have been chosen to ensure that the majority of panellists can discard any item unless a minority of 10% or more considers the item critical.

- If 30% or more panellists think that the set contains too many outcomes, there will be an open discussion about which items should be dropped, followed by votes. An item will be dropped from the core set if <30% disagree. There will be a vote concerning the remaining set, even if no item was dropped. If 30% or more disagree, possible solutions will be sought through further nominal group exercises.
- If 30% or more panellists think that the set contains too few outcomes, there will be an open discussion about which items should be added, followed by votes. An item will be added to the core set if <30% disagree. There will be a vote concerning the remaining set, even if no item was added. If 30% or more disagree, possible solutions will be sought through further nominal group exercises.
- If 30% or more panellists disagree with the set for other reasons, there will be an open discussion about these reasons. Possible solutions will be sought in plenum or through further nominal group exercises.

All e-Delphi panellists who participated in rounds 2 or 3 will be provided with a summary of this meeting and its results. They will be asked to confirm or reject the consensus as a whole on a 9-point scale ranging for 'strongly disagree' to 'strongly agree'. The CDS is finalized if consensus on all items is reached in the meeting and <30% of the online panellists disagree.

#### Further e-Delphi rounds

- If no consensus was reached concerning certain items, up to three further online Delphi votes will be conducted for these items.
- If consensus was reached in the meeting but disapproved by at least 30% of the online panellists, all items that did not reach consensus during the first three e-Delphi rounds will be included in up to three further e-Delphi rounds concerning single domains followed by one round concerning the set of agreed domains if applicable.
- In case that no consensus can be reached after the additional e-Delphi rounds, the steering committee will develop further steps to reach consensus about the CDS.

#### Ethics and consent

*Systematic review* Not applicable.

*Patient interviews* Participants will be asked for their consent before the interviews, concerning participation itself as well as data analysis and storage. Ethical approval will be sought by the coordinating centre in Dresden and by each centre before recruitment of the first patient. The data protection officer at the coordinating centre has been consulted. The content of the interviews will not be discussed with members of the teams who are treating the respective patients.

*Expert interviews* Participants will be asked for their consent before the interviews, concerning participation itself as well as data analysis and storage. Seeking ethical approval is not planned but may be sought by the groups who work at this project. The data protection officer at each participating centre will be involved.

*E-Delphi* The participating centres consult their responsible ethical boards to ascertain whether ethical approval is required for this consensus study. HECOS is going to seek approval by the data protection officer of the coordinating centre. All personalized data will be available to the study investigators, but data that is shared with panellists or published will be aggregated. All participants need to express their willingness to participate and their consent to this use of their data.

*Face-to-face consensus meeting* The steering committee is going to discuss if ethical approval is required. HECOS is going to seek approval by the data protection officer of the coordinating centre and of the meeting's host. No personalized data will be generated during the meeting. Data that is shared with panellists or published will be anonymized by aggregation. Since no personalized data are gathered, there will be no written or electronic documentation of consent to participate, for the purpose of data minimization.

## Results

#### Systematic review

- Results of the review have already been reported.<sup>12</sup>

#### Qualitative patient interviews

- Participant characteristics will be reported.
- Efficacy/effectiveness domains emerging from the patient interviews will be compared with domains gathered in a previous systematic review of HE trials<sup>12</sup> as described above.

#### Interviews with HE experts

- Participant characteristics will be reported.
- Efficacy/effectiveness outcomes emerging from expert interviews will be listed.
- The experts' opinions concerning consensus criteria will be summarized.

#### Online Delphi study

- Results will be reported according to the checklist recommended by Sinha *et al.* (2017).
- As the main result, we are going to report all domains that reached consensus 'in' or consensus 'out' criteria, respectively.
- Also, mean changes in score between rounds 2 and 3 will be calculated. Mean deviations of more than 1 point could be an indicator of instability for that item. For each item, the

percentage of panellists changing or not changing their vote, respectively, will be reported.

- Bimodality of opinions in each round will be examined by highlighting items that were rated as ‘important/include’ by at least 40% of panellists and at the same time rated ‘not important/do not include’ by another 40% or more.
- As an indicator of agreement, the intraclass correlation coefficient (two-way random effects model) will be calculated for each round.<sup>18</sup>
- Participant characteristics and notable differences between stakeholder preferences will be reported.
- Missing data will not be imputed, but we will address attrition bias by comparing votes from participants who dropped out after round 2 with the remaining participants’ votes.

### Consensus meeting

- We are going to report all domains that reached consensus ‘in’ or consensus ‘out’ criteria, respectively.
- Also, all items that missed consensus will be presented.
- Participant characteristics and notable differences between stakeholder preferences will be reported.
- Results of the online confirmation will be reported.
- If consensus on all items was reached in the meeting and <30% of the online panellists disagree, the final CDS for HE trials will be presented and the domain development will be summarized according to the COS-STAR statement.<sup>9</sup>

### Dissemination and publication

The CDS is going to be presented in publications, on the HECOS website ([www.cs-cousin.org/hecos](http://www.cs-cousin.org/hecos)), at congresses, and to national and international associations of dermatology.

### Future research plan for developing a core set of outcome measurement instruments

To complete the COS, we are going to develop a core set of outcome measurement instruments for the consented CDS. There will be a separate protocol for this step, which will adhere to CS-COUSIN guidelines.

### Acknowledgements

We thank all members of the HECOS initiative for their commitment and valuable contributions. We also thank Jan Kottner from CS-COUSIN for his methodological advice and for reviewing our protocol.

### References

- 1 Coenraads PJ. Hand eczema. *N Engl J Med* 2012; **367**: 1829–1837.
- 2 Thyssen JP, Johansen JD, Linneberg A, Menné T. The epidemiology of hand eczema in the general population—prevalence and main findings. *Contact Dermatitis* 2010; **62**: 75–87.
- 3 Diepgen TL, Agner T, Aberer W *et al.* Management of chronic hand eczema. *Contact Dermatitis* 2007; **57**: 203–210.
- 4 Christoffers WA, Coenraads PJ, Svensson Å, Diepgen TL, Dickinson-Blok JL, Xia J, Williams HC. Interventions for hand eczema. *Cochrane Database Syst Rev* 2019; **4**: CD004055.
- 5 Williamson PR, Altman DG, Bagley H *et al.* The COMET handbook: version 1.0. *Trials* 2017; **18**(Suppl 3): 280.
- 6 CS-COUSIN Methods Group. Guidance on how to develop a core outcome set for skin disease by the CS-COUSIN methods group. [WWW document] 2018. URL [http://cs-cousin.org/wordpress/wp-content/uploads/2018/11/COUSIN\\_guidance\\_version\\_5\\_9\\_2018.pdf](http://cs-cousin.org/wordpress/wp-content/uploads/2018/11/COUSIN_guidance_version_5_9_2018.pdf) (last accessed: 22 July 2019).
- 7 Kirkham JJ, Gorst S, Altman DG *et al.* Core outcome Set-STandardised protocol items: the COS-STAP statement. *Trials* 2019; **20**: 116.
- 8 Kirkham JJ, Davis K, Altman DG *et al.* Core outcome Set-STandards for development: the COS-STAD recommendations. *PLoS Medicine* 2017; **14**: e1002447.
- 9 Kirkham JJ, Gorst S, Altman DG *et al.* Core outcome Set-STandards for reporting: the COS-STAR statement. *PLoS Med* 2016; **13**: e1002148.
- 10 Kottner J, Schmitt J. Core outcome sets in dermatology: next steps. *Br J Dermatol* 2018; **179**: 549–550.
- 11 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; **96**: 84–92.
- 12 Rönsch H, Apfelbacher C, Brans R *et al.* Which outcomes have been measured in hand eczema trials? A systematic review. *Contact Dermatitis* 2019; **80**: 201–207.
- 13 Diepgen TL, Elsner P, Schliemann S *et al.* Deutsche Dermatologische Gesellschaft. Guideline on the management of hand eczema ICD-10 Code: L20. L23. L24. L25. L30. *J Dtsch Dermatol Ges* 2009; **7**(Suppl 3): S1–S16.
- 14 Mollerup A, Johansen JD, Thing LF. Knowledge, attitudes and behaviour in everyday life with chronic hand eczema: a qualitative study. *Br J Dermatol* 2013; **169**: 1056–1065.
- 15 Bruce I, Harman N, Williamson P *et al.* The management of Otitis Media with Effusion in children with cleft palate (mOMent): a feasibility study and economic evaluation. *Health Technol Assess* 2015; **19**: 1–374.
- 16 Brédart A, Marrel A, Abetz-Webb L, Lasch K, Acquadro C. Interviewing to develop Patient-Reported Outcome (PRO) measures for clinical research: eliciting patients’ experience. *Health Qual Life Outcomes* 2014; **12**: 15.
- 17 De Meyer D, Kottner J, Beele H *et al.* Delphi procedure in core outcome set development: rating scale and consensus criteria determined outcome selection. *J Clin Epidemiol* 2019; **111**: 23–31.
- 18 Thorn JC, Brookes ST, Ridyard C *et al.* Core items for a standardized resource use measure: expert delphi consensus survey. *Value Health* 2018; **21**: 640–649.
- 19 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.