Title: Navigating the landscape of core outcome set development in dermatology

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Manuscript word count: 2041 words [excluding capsule summary, abstract, references, figures, tables]

Abstract word count: 182

Capsule summary word count: 28

References: 47

Figures: 2

Tables: 2

IRB approval:

IRB approval is not required.

Funding: None.

Conflicts of interest: All authors are members of the CS-COUSIN initiative.

Abstract (unstructured)

The development of core outcome sets (COS), i.e. a minimum set of 'core outcomes' that should be measured and reported in all trials or clinical practice of a specific condition, in dermatology is gathering pace. A total of 44 dermatology-related COS projects have been registered in the online Core Outcome Measures in Effectiveness Trials (COMET) database (http://www.comet-initiative.org/studies/search), and include studies on 26 different skin diseases. With the increasing number of COS in dermatology, care is needed to ensure the delivery of high quality COS that meet quality standards based on state of the art methodology. In 2015, the Cochrane Skin – Core Outcome Set Initiative (CS-COUSIN) was established. CS-COUSIN is an international, multidisciplinary working group, aiming to improve the development and implementation of COS in dermatology. CS-COUSIN has developed guidance on how to develop high quality COS for skin diseases, and supports dermatology-specific COS initiatives. Currently, 16 COS development groups are affiliated to CS-COUSIN following standardized COS development processes. To ensure successful uptake of COS in dermatology, researchers, clinicians, systematic reviewers, guideline developers and other stakeholders should use existing COS in their work.

Capsule summary

- Core outcome set development must follow state-of-the-art methodology.

- CS-COUSIN provides methodological support for dermatology-specific core outcome set initiatives to ensure high quality across core outcome sets in dermatology.

Key words:
Dermatology, Cochrane Skin, CS-COUSIN, clinical trials, core outcome set, development, implementation

Introduction

For most skin diseases or conditions, it is unclear what aspects need to be measured in clinical trials so that patients, healthcare professionals and commissioners can make fully informed decisions about treatment options. Even when it is clear *what* needs to be measured as a clinical trial outcome, the outcome measurement instruments available may be deficient in terms of validity, reliability and feasibility - or just completely absent. Such a knowledge vacuum results in a chaotic non-uniformity of outcome reporting in dermatology clinical trials, which at best limits, and at worst prevents, meaningful meta-analysis and interpretation of trial evidence. It may lead to selective outcome reporting; hinders comparison of healthcare effects within and across healthcare organisations, and benchmarking of healthcare quality;[1-7] and hampers informed healthcare decision making.[1] Continuation of clinical trials without a focus on their comparability fails to progress evidence-based medicine and is considered a serious waste in research.[8-12] Clinical trials can no longer be thought of as a means to an end as most now typically have a "second life" in the form of systematic reviews that combine all relevant evidence such as those conducted by Cochrane Skin.[13]

Thankfully, a solution has been found in the form of Core Outcome Sets (COS) as a means of standardizing outcome measurement and reporting in clinical trials. A COS is a *minimum* set of the most important outcomes that should be measured and reported in *all* clinical trials for a specific health condition[14], including definitions and the core outcome measurement instruments or methods used to measure the core outcomes. A core outcome does not have to be the primary outcome of a clinical trial and, as such, the COS can be measured in addition to other outcomes of interest. Although the primary emphasis of a COS is for clinical

trials, they can also be used in routine clinical care, for clinical registries, for defining important outcomes in systematic reviews, or for funders of research to ensure that they are funding research that is measuring important aspects of the disease from the perspective of patients and healthcare professionals.

COS hold great potential to improve rigor and relevance of clinical research but to make this potential true, the COS itself need to be developed in a rigorous manner. Reference standards are therefore required for preferred methods of COS development, both across disciplines and within a single discipline to account for subject-specific methodological challenges. The purpose of this article is to navigate through the landscape of COS development in medicine and, more specifically, in the field of dermatology.

Early pioneers of outcome standardization in medicine

One of the first attempts to standardize outcomes in clinical trials was the World Health Organization (WHO)[15] in 1981, when Miller and colleagues published recommendations for standardized approaches to recording data for cancer patients. Since then, interest in standardization of outcomes research has grown and international initiatives on COS development have been launched in many medical disciplines. Since 1992, the Outcome Measures in Rheumatology initiative (OMERACT, http://www.omeract.org) has been the frontrunner in COS development in medicine. The uptake of the COS in rheumatoid arthritis clinical trials increased from 40% in 1995 to 81% in 2016.[16] Furthermore, the rheumatoid arthritis COS is now required by the U.S. Food and Drug Administration (FDA) to be measured in clinical trials in RA.[17] These trials are now more comparable, enabling meta-analysis of clinical trial data and improved health outcomes for patients.[16] The development

of COS in healthcare research has rapidly grown over recent years with 299 published COS up to 2017.[18,19]

Developing standards for Core Outcome Set development

Two main organisations have emerged as leaders in the development of COS globally. The Core Outcome Measures in Effectiveness Trials-Initiative (COMET, http://www.cometinitiative.org) was established in 2010 and is an international umbrella organization that supports the development, dissemination and implementation of COS by establishing agreed COS development methodologies.[20-23] COS development typically implies a range of methodological techniques to identify all possible outcomes by means of systematic reviews and qualitative methods. Subsequently, consensus should be reached on the most important outcome domains and outcome measurement instruments. This may include international e-Delphi consensus studies; face-to-face consensus meetings, including small and large groups discussions; presentations of evidence; and anonymised voting. Furthermore, COMET maintains an international database for existing and ongoing work on COS development in healthcare that helps to reduce duplication of effort.[24] To date, the focus of COMET has been to encourage groups to identify the most important outcome domains for clinical trials. Outcome domains can be thought of as the key aspects of a disease that are needed to evaluate the effectiveness of an intervention.[20] Examples of outcome domains include pain intensity, physical functioning, or fatigue.

By contrast, the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN, www.cosmin.nl) initiative focusses on the selection of outcome measurement instruments to measure the important outcome domains in the COS. To

improve the selection of outcome measurement instruments, COSMIN has developed guidance on how to select instruments for outcomes included in a COS.[20] In four consecutive steps, COS developers are being guided through the process of outcome measurement instrument selection for COS, including finding existing instruments by means of literature searches and/or systematic reviews, and quality assessment of existing instruments (i.e. evaluation of the measurement properties and feasibility aspects). Furthermore, COSMIN has developed guidance on systematic reviews of patient-reported outcome measurement instruments[25], and guidance on the evaluation of the methodological quality of studies on the measurement properties of outcome measurement instruments.[26,27] The COSMIN methodology can be used to inform the selection of the most suitable outcome measurement instruments to measure the core outcome domains.

In addition to COS development, the International Consortium for Health Outcomes Measurement (ICHOM, http://www.ichom.org/), founded in 2012, aims to improve value-based healthcare by developing Standard Sets. Standard Sets are similar to COS but with a clear focus on clinical practice. To date, ICHOM has developed 24 Standard Sets for some of the most prevalent diseases and for vulnerable populations (e.g. cardiovascular, neurological, oncological and musculoskeletal disease areas)[28], but none of these are currently dermatology-specific.

Core outcome set development in dermatology

The longest running COS initiative in dermatology is the Harmonising Outcome Measures for Eczema (HOME) initiative. Founded in 2008, HOME is a global initiative of patients, healthcare professionals, journal editors, regulatory authorities and the pharmaceutical

industry, with a mission to harmonize outcome measurement and reporting in atopic eczema clinical trials and clinical practice. In-depth research on outcomes and measurement instruments, followed by a series of successful consensus meetings, resulted in a recommendation on four core outcome domains to be measured in all atopic eczema clinical trials: signs, symptoms, long-term control, and quality of life[29]. EASI and POEM are the recommended outcome measurement instruments to measures signs and symptoms respectively.[30-32] The HOME group has published a methodological roadmap outlining the essential steps in the development of and implementation of COS in dermatology.[33]

With so many different dermatoses, the need for standardization in outcome reporting in dermatology is imperative.[34] In 2015, the Cochrane Skin – Core Outcome Set Initiative (CS-COUSIN, www.cs-cousin.org) was established. CS-COUSIN is an international, multidisciplinary working group, aiming to improve the development and implementation of COS in dermatology. CS-COUSIN is an umbrella organization to support dermatology-specific initiatives to develop their COS. Recently, the CS-COUSIN methods group has conducted a systematic review to assess the concordance between efficacy outcomes in a random sample of 10 Cochrane Skin systematic reviews and the 220 dermatology clinical trials that are included in these reviews.[35] Results show a low concordance of outcomes between reviews and primary studies, and it was concluded that standardization of outcome reporting could be improved by the development and implementation of COS. Fortunately, and since the inauguration of HOME in 2008, the development of COS in dermatology is gathering pace. A total of 44 dermatology-related COS projects have been registered in the COMET database,[24] and include studies on 26 different skin diseases, such as acne, AE, hidradenitis suppurativa, melanoma, nail psoriasis, rosacea, and vitiligo[24] (Table

1). Most COS are being developed for research and/or clinical practice purposes; two registered COS-related projects are focussing on the development of a "core set of domains and domain items" for registry purposes, i.e. the TREatment of ATopic eczema (TREAT) initiative[36,37] and the European Laser TrEAtment Dermatology (LEAD) Registry.[24]

To achieve a similar level of success in dermatology as OMERACT has achieved in rheumatology[16], care is needed to ensure the delivery of high quality COS that meet quality standards based on state of the art methodology.[20,21,23,25,33,38,39] Based on the HOME roadmap, the CS-COUSIN methods group has developed guidance on how to develop COS for skin disease[40], including a flow diagram for the domain development process and one for the outcome measurement instrument selection/development process (Figures 1 and 2). An important difference between CS-COUSIN and COMET is that CS-COUSIN provides direct methodological support for skin-related COS and is embedded within the international Cochrane Skin group, thus ensuring speedy adoption of COS within high quality systematic reviews that are used by guideline developers.

To date, 16 COS initiatives have been supported by CS-COUSIN.[41] To ensure high quality across COS in dermatology, groups developing COS are supplied with access to protocol templates and recommendations on best practice, and all are assigned a COUSIN Methods Group representative who provides support for the individual groups as a 'critical friend'. In addition, CS-COUSIN organises annual meetings whereby knowledge, ideas, and issues with regard to COS development are exchanged and debated amongst CS-COUSIN members and external experts from COMET, COSMIN and OMERACT.[5,42] An overview of COS projects supported by CS-COUSIN is provided in Table 2, and detailed information about these COS projects can be found on the CS-COUSIN website.[41]

Another initiative in dermatology, although not affiliated within COMET or CS-COUSIN, is the International Dermatology Outcome Measures (IDEOM, http://dermoutcomes.org/). IDEOM seeks to develop and validate dermatology outcome measurement instruments throughout dermatology with an initial focus on psoriatic disease.[43]

[Table 2 about here]

It is important to ensure and to increase international cooperation and collaboration between different COS initiatives in dermatology. It is therefore recommended that present and future COS projects are embedded within CS-COUSIN, to ensure quality standards for COS development. The embedding of COS projects within CS-COUSIN facilitates the exchange of cutting edge knowledge in an international community of COS developers and methodologists that supports COS development and uptake on a global level. CS-COUSIN is open for everyone with an interest in outcomes research and evidence-based dermatology and with enthusiasm to develop and implement COS in dermatology.

CS-COUSIN encourages COS developers to have a clear focus on patient-centeredness and embraces the importance of the involvement of patient research partners in steering committees and throughout the entire course of the COS development process. Standardization of patient-centred outcome reporting allows for synthesizing clinical trial results in a meaningful way. This significantly impacts the patient-value of evidence from research and clinical practice, and allows for delivering value-based health care.[44] Future directions of COS development might include innovative new generic outcome measurement instruments based on Item Response Theory and Computerized Adaptive

Testing (a computer-based test system). These new outcome measurement instruments have recently become available and measure aspects of health more precisely and in a more tailored way than traditional outcome measurement instruments that are based on Classical Test Theory.[45-48] HOME, for example, is currently exploring the possibilities of the implementation of Patient-Reported Outcomes Measurement Information System (PROMIS) instruments in the COS for atopic eczema. In addition to research, the possibility to use COS for the evaluation of dermatological clinical practice should be also developed further.

The challenge to uptake of COS

Global uptake of a COS is crucial to overcome the problem of non-uniformity in outcome reporting. One way of ensuring early adoption into clinical trials is to ensure early engagement with regulatory agencies such as the FDA and European Medicines Agency (EMA). To ensure a successful uptake of the various COS in dermatology, it is important that researchers, clinicians, systematic reviewers and other stakeholders adhere to the COS in their own research work. In doing so, they can be reassured that they are measuring important aspects of the disease in the most reliable, valid and responsive way, and are contributing to a reduction in research waste and improved patient care.

References

1 Tunis SR, Clarke M, Gorst SL *et al.* Improving the relevance and consistency of outcomes in comparative effectiveness research. *J Comp Eff Res* 2016; **5**: 193-205.

2 Hirsch BR, Califf RM, Cheng SK *et al.* Characteristics of oncology clinical trials: insights from a systematic analysis of ClinicalTrials.gov. *JAMA Intern Med* 2013; **173**: 972-9.

3 Miyar J, Adams CE. Content and quality of 10,000 controlled trials in schizophrenia over 60 years. *Schizophr Bull* 2013; **39**: 226-9.

4 Kirkham JJ, Boers M, Tugwell P *et al.* Outcome measures in rheumatoid arthritis randomised trials over the last 50 years. *Trials* 2013; **14**: 324.

5 Schmitt J, Deckert S, Alam M *et al.* Report from the kick-off meeting of the Cochrane Skin Group Core Outcome Set Initiative (CSG-COUSIN). *Br J Dermatol* 2016; **174**: 287-95.

6 Blankers M, Barendrecht, M, Dekker, JJM Meetvariatie als bron van bias bij het benchmarken met verschillende ROM-instrumenten. *Tijdschrift voor Psychiatrie* 2016; **58**: 55-60.

7 de Beurs E, den Hollander-Gijsman ME, van Rood YR *et al.* Routine outcome monitoring in the Netherlands: practical experiences with a web-based strategy for the assessment of treatment outcome in clinical practice. *Clin Psychol Psychother* 2011; **18**: 1-12.

8 Al-Shahi Salman R, Beller E, Kagan J *et al.* Increasing value and reducing waste in biomedical research regulation and management. *Lancet* 2014; **383**: 176-85.

9 Chalmers I, Bracken MB, Djulbegovic B *et al.* How to increase value and reduce waste when research priorities are set. *Lancet* 2014; **383**: 156-65.

10 Chan AW, Song F, Vickers A *et al.* Increasing value and reducing waste: addressing inaccessible research. *Lancet* 2014; **383**: 257-66.

11 Glasziou P, Altman DG, Bossuyt P *et al.* Reducing waste from incomplete or unusable reports of biomedical research. *Lancet* 2014; **383**: 267-76.

12 Ioannidis JP, Greenland S, Hlatky MA *et al.* Increasing value and reducing waste in research design, conduct, and analysis. *Lancet* 2014; **383**: 166-75.

13 Reddi A, Prescott L, Doney E *et al.* The Cochrane Skin Group: a vanguard for developing and promoting evidence-based dermatology. *J Evid Based Med* 2013; **6**: 236-42.

14 Williamson PR, Altman DG, Blazeby JM *et al.* Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; **13**: 132.

15 Miller AB, Hoogstraten B, Staquet M *et al.* Reporting results of cancer treatment. *Cancer* 1981; **47**: 207-14.

16 Kirkham JJ, Clarke M, Williamson PR. A methodological approach for assessing the uptake of core outcome sets using ClinicalTrials.gov: findings from a review of randomised controlled trials of rheumatoid arthritis. *BMJ* 2017; **357**: j2262.

17 Outcome Measures in Rheumatology (OMERACT) Handbook. 2017. https://www.dropbox.com/s/kkph9e3jdwctewi/OMERACT%20Handbook%20Dec%2020%202017.pdf?dl=0. Accessed: 07 January 2018. In.

18 Davis K, Gorst SL, Harman N *et al.* Choosing important health outcomes for comparative effectiveness research: An updated systematic review and involvement of low and middle income countries. *PLoS One* 2018; **13**: e0190695.

19 Dodd S, Clarke M, Becker L *et al.* A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol* 2017.

20 Prinsen CA, Vohra S, Rose MR *et al.* How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. *Trials* 2016; **17**: 449.

21 Williamson PR, Altman DG, Bagley H *et al.* The COMET Handbook: version 1.0. *Trials* 2017; **18**: 280.

22 Kirkham JJ, Davis K, Altman DG *et al.* Core Outcome Set-STAndards for Development: The COS-STAD recommendations. *PLoS Med* 2017; **14**: e1002447.

23 Kirkham JJ, Gorst S, Altman DG *et al.* Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. *PLoS Med* 2016; **13**: e1002148.

24 Core Outcome Measures in Effectiveness Trials (COMET) database. http://www.comet-initiative.org/studies/search. 2017. Accessed: 11 July 2018.

25 Prinsen CAC, Mokkink LB, Bouter LM *et al.* COSMIN guideline for systematic reviews of patient-reported outcome measures. *Qual Life Res* 2018; **27**: 1147-57.

26 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**: 1171-9.

27 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.

28 International Consortium for Health Outcomes Measurement (ICHOM) Medical Conditions. www.ichom.org/medical-conditions. Accessed: 28 December 2017.

29 Schmitt J, Spuls P, Boers M *et al.* Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. *Allergy* 2012; **67**: 1111-7.

30 Chalmers JR, Schmitt J, Apfelbacher C *et al.* Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *Br J Dermatol* 2014; **171**: 1318-25.

31 Schmitt J, Spuls PI, Thomas KS *et al.* The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *J Allergy Clin Immunol* 2014; **134**: 800-7.

32 Spuls PI, Gerbens LAA, Simpson E *et al.* Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: a Harmonising Outcome Measures for Eczema (HOME) statement. *Br J Dermatol* 2017; **176**: 979-84.

33 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**: 24-30.

34 Jochen Schmitt, Toni Lange, Jan Kottner, Cecilia ACPrinsen, Tobias Weberschock, Elisabeth Hahnel, Christian Apfelbacher, Susanne Brandstetter, Andreas Dreher, Giles Stevens, Esther Burden-Teh, Natasha Rogers, Phyllis Spuls, Matthew J Grainge, Hywel Williams, Lena Jacobi, on behalf of the Cochrane Skin Core Outcome Set Initiative (CS-COUSIN). Critical appraisal of the outcomes in Cochrane systematic reviews and corresponding trials. 2018 (manuscript submitted). 2018.

35 Schmitt J, Lange T, Kottner J *et al.* Cochrane reviews and dermatological trials outcome concordance; why Core Outcome Sets could make trial results more usable. *J Invest Dermatol* 2018.

36 Gerbens LAA, Apfelbacher CJ, Irvine AD *et al.* TREatment of ATopic eczema (TREAT) Registry Taskforce: An international Delphi exercise to identify a core set of domains and domain items for national atopic eczema photo- and systemic therapy registries. *Br J Dermatol* 2018.

37 Spuls PI, Gerbens LAA, Apfelbacher CJ *et al.* The International TREatment of ATopic Eczema (TREAT) Registry Taskforce: An Initiative to Harmonize Data Collection across National Atopic Eczema Photo- and Systemic Therapy Registries. *J Invest Dermatol* 2017; **137**: 2014-6.

38 Boers M, Kirwan JR, Wells G *et al.* Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. *J. Clin. Epidemiol* 2014; **67**: 745-53.

39 Kirkham JJ, Gorst S, Altman DG *et al.* COS-STAR: a reporting guideline for studies developing core outcome sets (protocol). *Trials* 2015; **16**: 373.

40 Guidance on how to develop a core outcome set for skin disease by the CS-COUSIN methods group. https://www.uniklinikum-dresden.de/de/das-klinikum/universitaetscentren/zegv/cousin/cousin_guidance_version_2-1.pdf Date accessed: 05-Oct-2018.

41 Cochrane Skin Group Core Outcome Set Initiative (CSG-COUSIN). Project groups. https://www.uniklinikum-dresden.de/de/das-

klinikum/universitaetscentren/zegv/cousin/meet-the-teams/project-groups Accessed: 12 January 2018.

42 Kottner J, Jacobi L, Hahnel E *et al.* Core outcome sets in dermatology: report from the second meeting of the International Cochrane Skin Group Core Outcome Set Initiative. *Br J Dermatol* 2018; **178**: e279-e85.

43 International Dermatology Outcome Measures (IDEOM). http://dermoutcomes.org/ Date accessed: 05-Oct-2018.

44 Porter ME. What is value in health care? *N Engl J Med* 2010; **363**: 2477-81.

45 Cella D, Gershon R, Lai JS *et al.* The future of outcomes measurement: item banking, tailored short-forms, and computerized adaptive assessment. *Qual Life Res* 2007; **16 Suppl 1**: 133-41.

46 Flens G, de Beurs E. [The future of ROM: computerised adaptive testing]. *Tijdschr Psychiatr* 2017; **59**: 767-44.

47 Fries JF, Bruce B, Cella D. The promise of PROMIS: using item response theory to improve assessment of patient-reported outcomes. *Clin Exp Rheumatol* 2005; **23**: S53-7.

48 Patel AA. Patient-Reported Outcome Measures: The Promise of PROMIS. *J Am Acad Orthop Surg* 2016; **24**: 743.

Figure legend

Figure 1. CS-COUSIN flow diagram for the domain development process (with permission)

Figure 2. CS-COUSIN flow diagram for the outcome measurement instrument selection/development process (with permission)

Table legend

Table 1. Overview of COS-related projects in dermatology, registered in the COMET database

Table 2. Overview of COS projects supported by CS-COUSIN

Table 1. Overview of COS-related projects in dermatology, registered in the COMET database[24]

	Skin diseases	Number of projects	COS for clinical research	COS for clinical practice	COS for registry	Other
1	Acne Vulgaris*	1	X			
2	Acne Scarring	1	X	X		
3	Actinic keratosis	1	X	X		
4	Atopic eczema*	11	X	X	X	Systematic reviews, meeting reports, consensus reports, recommendations, guideline
5	Basal Cell Carcinoma*	1	X	X		
6	Congenital melanocytic naevi	1	X	X		
7	Cutaneous leishmaniasis	2	X	X		
8	Epidermolysis bullosa	1	X	X		
9	Facial aging*	1	X	X		
10	Facial Structure and Function Post-Skin Cancer Excision	1	X	X		
11	Hair Loss/non-scarring alopecia	1	X	X		
12	Head and neck lymphatic malformation	1	X			
13	Hidradenitis Suppurativa*	1	X			
14	Hyperhidrosis	1	X	X		
15	Incontinence-associated dermatitis*	1	X			
16	Leprosy	1	-	-		Overview of literature
17	Melanoma*	1	X			
18	Melasma	1	X	X		
19	Nail psoriasis*	2	X			Systematic review, overview of literature
20	Post Inflammatory Hyperpigmentation	1	X	X		
21	Pressure Ulcer*	1	X			
22	Rosacea*	1	X	X		

23	Scarring	1	X	X		
24	Squamous Cell Carcinoma	1	X	X		
25	Vascular Malformations	1	X			Systematic review and consensus report
26	Vasculitis (small-vessel/ ANCA-associated)	1	X			
27	Vitiligo*	4	X			Systematic review, consensus report, recommendations, guideline
28	Vulval skin disorders	1	X	X		Systematic review
29	Medical Indications for Laser Treatments in Dermatology*	1	X	X	X	
TOTAL		44				

* Supported by CS-COUSIN

Table 2. Overview of COS projects supported by CS-COUSIN

	Skin disease	COS initiative	Acronym
1	Acne Vulgaris	Acne Core Outcomes Research Network	ACORN
2	Atopic eczema	Harmonising Outcome Measures for Eczema	HOME
3	Basal Cell Carcinoma (BCC)	Core outcome set for clinical trials in Basal Cell Carcinoma	IMPROVED
4	Chronic spontaneous urticaria (CSU)	Core Outcome Measures in Chronic Spontaneous Urticaria	-
5	Chronic Wounds	Developing a Core Outcome Set for Chronic Wounds	-
6	Facial aging	Core Outcome Set for the Appearance of Facial Aging	IMPROVED
7	Hand eczema	Development of a Hand Eczema Core Outcome Set	HECOS
8	Hidradenitis Suppurativa	Development of a Core Outcome Set in Hidradenitis Suppurativa	HISTORIC
9	Incontinence-Associated Dermatitis	Core Outcome Set in IAD Research project: development of a core set of outcomes and measurement instruments for Incontinence-Associated Dermatitis research	CONSIDER
10	Laser treatment	European Laser TrEAtment Dermatology registry	LEAD
11	Melanoma	Developing a Core Outcome Set for Melanoma trials	-
12	Nail psoriasis	Development of a Core Outcome Set in Nail Psoriasis	-
13	Pressure Ulcer	The Outcomes for Pressure Ulcer Trials project	OUTPUTs
14	Rosacea	Core Outcome Set for Rosacea	IMPROVED
15	Vascular Malformations	Development of a Core Outcome Set for Vascular Malformations	OVAMA
16	Vitiligo	International Initiative for Outcomes (INFO) for vitiligo	INFO vitiligo