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Core outcome set implementation supported by the *BJD*

A core outcome set (COS) is an agreed minimum set of outcomes that should be measured globally in all clinical trials or other specified settings, such as routine clinical practice or quality assurance, for a particular condition.[1] A COS consists primarily of core domains (what to measure) and eventually outcome measurement instruments (how to measure). The universal uptake of a suitable COS is critical to advancing patient-centred care and reducing research waste, through enabling comparative effectiveness research and limiting outcome reporting bias.[2,3] Nonuniformity of outcomes blights the dermatology literature, as demonstrated by studies in eczema, hidradenitis suppurativa, acne, vitiligo, vulval disorders and psoriasis. Moreover, meta-analyses are frequently missing from Cochrane reviews due to incomparable outcomes.[4] This results in obstruction of clear therapeutic recommendations[5] and ultimately suboptimal patient care.

The *BJD* has prioritized the publication of core outcomes research and related papers, recognizing their pivotal role in advancing patient care. However, the clinical trials editorial team have, at times, observed either partial or absent COS utilization and reporting in submitted clinical trial manuscripts, despite the existence of a published COS in that field. This observation is supported by the findings of a recent systematic review examining COS uptake, which demonstrated high variability, ranging from zero uptake in trials for gout to 82% for rheumatoid arthritis, with uptake of a full COS typically found in fewer than 25% of trials.[6]

Gains have been made by the Harmonising Outcome Measures for Eczema (HOME) initiative, with an increase in the use of three of the four published domains (signs, symptoms and quality of life) from 25% of trials in the period 2005–2018, to 33% in 2018.[7] The outcome measure instrument (OMI) for the domain of clinical signs (Eczema Area and Severity Index) has been widely adopted (92% of trials), whereas the OMI for symptoms (Patient-Oriented Eczema Measure, POEM) was used in only 17% of trials;

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consensus for the latter was only reached in 2017.[7] The lack of uptake of POEM was confirmed in a recent living network meta-analysis investigating systemic immunomodulatory therapy for atopic dermatitis.[8]

A COS comprising six domains for psoriasis trials was published in 2018,[9] developed by the International Dermatology Outcome Measure group. The domains 'skin manifestations' and 'investigator global assessment' are routinely reported in primary publications using the instruments Psoriasis Area and Severity Index and Investigator's Global Assessment, and are widely accepted by regulatory bodies such as the US Food and Drug Administration (FDA). However, these do not reflect the patient experience as defined in the full COS. Specifically, patient global assessment, symptoms, health-related quality of life and treatment satisfaction are often omitted. A recent Cochrane network meta-analysis concluded that effective data synthesis was limited by the lack of outcome measure harmonization.[10] Beyond eczema and psoriasis there are nine COSs within dermatology with defined domains, including keratinocyte carcinoma, hidradenitis suppurativa, vascular malformations and vitiligo, all with uncertain levels of uptake.[1]

Broad implementation of a COS is critical, otherwise COS research itself is in danger of being wasteful. This requires multicomponent interventions targeting awareness, acceptance and adherence (Table 1). There are myriad ways to build awareness, from including COS utility in medical curricula to conference programming and editorial decision making. The Core Outcome Measures in Effectiveness Trials (COMET) initiative[1] provides a database of ongoing and completed COSs and promotes COS awareness and engagement through partnering with other agencies such as Cochrane, the National Institute for Health and Care Excellence (NICE) and the National Institute for Health Research (NIHR).

Adherence is facilitated by more stringent funding, regulation and reporting requirements, such as mandating the inclusion (or explanation of exclusion) of a COS in ethics submissions, funding applications, and protocols for clinical trial and systematic review registries. Endorsement from regulatory agencies such as the FDA and European Medicines Agency is essential, and is considered partly responsible for the high rates of adherence in rheumatoid arthritis trials (82%).[11] Progress has been made, as illustrated by the ISRCTN registry and the reporting guideline Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT), which now advise inclusion of a COS, and direct trial designers to COMET for information on an available COS in their

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field.[12] In addition, COSs are also required, where available, for NIHR funding and approval by NICE.

The success of these measures in improving uptake depends entirely on building deeper acceptance within the research community, which in turn requires wide and genuinely representative stakeholder involvement, total transparency and clear demonstration of methodological rigour. There are now numerous resources to facilitate high standards in COS development, namely the HOME roadmap[13] in conjunction with the Cochrane Skin – Core Outcome Set Initiative (CS-COUSIN; http://cs-cousin.org) and COMET. Moreover, Kirkham *et al.* have devised a minimum standard for COS methodology (COS-STAD)[14] with accompanying checklists for protocols (COS-STAP)[15] and reporting (COS-STAR).[16] Journals have an important role to play in both disseminating COS development studies and encouraging COS uptake. The *BJD* has been a frontrunner in showcasing COS and other outcomes research. The next step is to require investigators to report a full COS in clinical trial publications, or to provide an explanation for its absence – for example, if the trial protocol was written before the publication of a COS, or in the absence of a suitable OMI for a specific domain. This will be encouraged for now and will become compulsory for trials published by *BJD* in the medium term.

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Conflicts of interest: E.C.V. has received compensation from the *BJD* as a reviewer. J.R.I. is Editor-in-Chief of the *BJD*. He is a consultant for Novartis, UCB and Boehringer Ingelheim and has participated in advisory boards for Kymera Therapeutics and Viela Bio, all in the field of hidradenitis suppurativa. C.J.A. is a member of the executive committees of the HOME and Hand Eczema Core Outcome Set (HECOS) initiatives, a member of the CS-COUSIN methods group, and *BJD* section editor for Outcomes Research. He has received consultancy fees for advice regarding research on outcomes from the Dr Wolff Group, Sanofi and LEO Pharma. A.M.D. has received compensation from the *BJD* (reviewer and section editor), American Academy of Dermatology (guidelines writer) and National Eczema Association (grant reviewer). He has been a paid consultant for the Canadian Agency for Drugs and Technology in Health. He has received honoraria from CME Outfitters. He is a contributing member to the HOME initiative.

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Table 1 Cited barriers to core outcome set (COS) uptake and proposed measures to address these

Barriers (Hughes *et al.*)[6]	Interventions (HOME Roadmap)[13]
Lack of awareness	Include COSs in research methodology training and prioritize COS research in conference scheduling and publication in high-impact journals. Disseminate COSs and guidance on implementation to industry and
Lack of understanding of the purpose of a COS	

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	regulatory bodies
Perception of inadequate stakeholder involvement	Ensure wide and genuine stakeholder involvement from the outset, including patients, clinicians, industry, regulatory bodies and policymakers
Lack of consensus on validated measures	Use robust and evidence-based methods for attaining consensus (Delphi, nominal group technique)
Lack of clarity	Clearly distinguish and define the components of a COS (domains, OMIs). See www.homeforeczema.org for an example in clarity
Variable reporting quality	Apply standardized reporting using COS-STAR.[16] Peer reviewers should ensure reporting standards are adhered to
Burden to patients and researchers of lengthy questionnaires and cumbersome OMIs	Limit the number of domains and ensure OMIs are developed according to standardized criteria (www.cosmin.nl). Disseminate guidelines on use of OMIs to industry and trial designers
Costs of including a full COS	Provide clear information on related costs and potential savings of using a COS
Inconsistent requirements from regulatory agencies	Improve dissemination of COSs to regulatory agencies with guidance on implementation and benefits

OMI, outcome measure instrument.

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