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# Report from the fifth international consensus meeting to harmonize core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative)

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## Summary

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The meeting was supported by donations and grants from the University of Nantes and CHU Nantes (SFR Santé François BONAMY and DHU 2020), the Department of Dermatology CHU Nantes and the School of Medicine, University of Nottingham. Two independent charities (Fondation Dermatite Atopique Pierre Fabre and Fondation Bioderm) covered the costs of the two meeting dinners. Delegates were charged a fee as follows: industry, £150; nonindustry, £50; patients, free of charge. All delegates covered their own travel and accommodation expenses, with the exception of patients and representatives from patient groups, whose costs were met either by their national eczema patient association or by a participating HOME member. H.C.W. supported the fees, travel and accommodation costs for M.B. (OMERACT) to attend as the independent moderator.

### Conflicts of interest

The following authors have been involved with the development or validation of scales relevant to the meeting: H.C.W. was involved in the development of POEM; J.F.S., S.B., Å. S. and A.W. were involved in the development of the Patient-Oriented SCORAD.

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This is the report from the fifth meeting of the Harmonising Outcome Measures for Eczema initiative (HOME V). The meeting was held on 12–14 June 2017 in Nantes, France, with 81 participants. The main aims of the meeting were (i) to achieve consensus over the definition of the core domain of long-term control and how to measure it and (ii) to prioritize future areas of research for the measurement of the core domain of quality of life (QoL) in children. Moderated whole-group and small-group consensus discussions were informed by presentations of qualitative studies, systematic reviews and validation studies. Small-group allocations were performed a priori to ensure that each group included different stakeholders from a variety of geographical regions. Anonymous whole-group voting was carried out using handheld electronic voting pads according to predefined consensus rules. It was agreed by consensus that the long-term control domain should include signs, symptoms, quality of life and a patient global instrument. The group agreed that itch intensity should be measured when assessing long-term control of eczema in addition to the frequency of itch captured by the symptoms domain. There was no recommendation of an instrument for the core outcome domain of quality of life in children, but existing instruments were assessed for face validity and feasibility, and future work that will facilitate the recommendation of an instrument was agreed upon.

### What's already known about this topic?

- The Harmonising Outcome Measures for Eczema initiative previously agreed on four essential domains to be included in all atopic eczema/dermatitis trials: clinician-reported signs, patient-reported symptoms, quality of life and long-term control.
- EASI and POEM are the recommended instruments for signs and symptoms, respectively. Instruments for quality of life (in adults and children) and long-term control have yet to be decided upon.
- Long-term control is relevant to trials of at least 3 months' duration.

### What does this study add?

- It was agreed that the core outcome domain of long-term control should include signs, symptoms, quality of life and a patient global instrument.
- For the core outcome set for quality of life in children, no single instrument can currently be recommended, but some instruments have better face validity and feasibility.
- A clear plan was agreed on to identify instruments to measure quality of life in children and long-term control.

The Harmonising Outcome Measures for Eczema (HOME) initiative is an international group working together to develop a core outcome set (COS) for clinical trials in eczema (synonymous with atopic eczema and atopic dermatitis). HOME is coordinated from the Centre of Evidence Based Dermatology, University of Nottingham, U.K. Participation in HOME is open to anyone with an interest in outcomes for eczema. A COS is the agreed upon minimum set of instruments that should be included in all clinical trials for a particular condition.<sup>1</sup> Use of a COS does not preclude using other instruments; other domains and instruments can also be included to meet the specific requirements of individual trials. COS initiatives are active across many fields of medicine and should enable better synthesis of trial data and reduce selective outcome reporting bias.<sup>1,2</sup>

The HOME initiative follows the best current guidance on developing a COS.<sup>2-4</sup> Four core domains have been identified: clinician-reported signs; patient-reported symptoms; quality of life; and long-term control. The core outcome measurement instruments for clinician-reported signs and patient-reported symptoms have been established: the Eczema Area and Severity Index (EASI) for measuring clinician-reported signs was agreed on at the HOME III meeting,<sup>5,6</sup> and the Patient-Oriented Eczema Measure (POEM) was chosen to measure patient-reported symptoms at the HOME IV meeting.<sup>7,8</sup>

This is a report from the fifth consensus meeting of the HOME initiative (HOME V), which was held on 12–14 June 2017 in Nantes, France. The local organizers were Sebastien Barbarot and Jean-Francois Stalder of Nantes University Hospital, France.

## Methods

### Objectives

The purposes of the HOME V meeting were (i) to achieve consensus on the definition of the core domain of long-term control and how to measure it and (ii) to prioritize future areas of research for the measurement of the core domain of quality of life (QoL) in children. Future areas of research for QoL in adults were discussed previously at HOME IV.

### Study design

HOME V was a face-to-face consensus meeting using presentations of up-to-date evidence and a modified nominal group technique including moderated whole- and small-group discussions and anonymous electronic voting. The meeting was held at the CCI Nantes, Nantes, France from 13:00 h, Monday 12 June 2017 to 13:00 h, Wednesday 14 June 2017. A series of planning meetings was held involving the HOME executive group (Table S1; see Supporting Information) and local organizers, and a protocol outlining the aims and methods was prepared prior to the meeting and published on the HOME website.<sup>9</sup> However, there was flexibility in the programme to allow for important issues that arose to be discussed.

The meeting was chaired by Hywel Williams, and Maarten Boers of OMERACT (<http://www.omeract.org>) was the independent moderator. Each session was chaired by the lead for that domain: Kim Thomas for long-term control and Christian Apfelbacher for QoL in children.

### Participants

The meeting was advertised via the HOME website and through mailing lists, including the HOME membership. Patient representatives and pharma representatives were also personally invited by members of the HOME executive group. The meeting was open to anyone with an interest in core outcomes for eczema.

In total, 81 participants from 13 countries attended the meeting. Two nonparticipating observers were also present. The breakdown by stakeholder group is shown in Figure 1.

### Meeting structure and methods

Two optional premeeting refresher/introduction sessions were offered, one for patients, carers and patient representatives and one for other stakeholders. The purpose was to increase knowledge and understanding of those participating in the consensus meeting, in order to ensure meaningful engagement from all stakeholders, regardless of their experience of COS development or attendance at previous HOME meetings. Topics covered included why COSs are important, methods

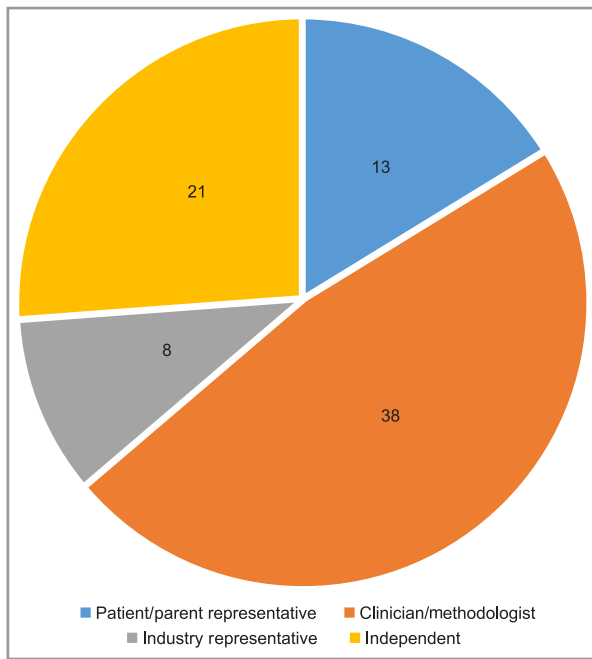


Fig 1. Breakdown of attendees by stakeholder group.

used in COS development, explanations of findings to be presented at the main meeting and what was expected of meeting participants.

Background information and data were presented during the meeting and also provided in handouts. Participants received materials and systematic review summaries prior to the meeting so they were well informed and were required to undertake premeeting tasks to ensure effective small-group discussions.

A modified nominal group technique was used, in which small-group discussions were used to ensure that the opinions of all participants were heard. The aim was to reach consensus within each small group before feeding back to the whole group. Participants were allocated a priori to one of six small groups to ensure a spread of stakeholder groups and geographical coverage in each (Table S2; see Supporting Information). A minimum of two patients were allocated to each small group, although due to an unplanned absence one group included only one patient. A facilitator who remained independent of the discussions and a note taker were nominated beforehand for each small group. After each small group discussion, the results of each small group were collated and presented back to the whole group for discussion and voting. For logistical reasons the small group constitution remained constant throughout the meeting. The materials used can be found on the HOME website.<sup>9</sup>

### Consensus rules and voting

The voting rule to achieve consensus was agreed on at HOME II,<sup>10</sup> and has been used at all subsequent HOME meetings. Consensus is defined as having been reached when < 30% of

voters disagree with the statement. Consensus voting was anonymous using electronic handsets (HM-Pro; Hypermaster, Chennevières-sur-Marne, France) and voting software, with results fed back to the group in real time once each vote was closed. All meeting participants were permitted to vote.

## Results

An overview of why COSs are needed and what HOME has achieved so far was given,<sup>5–8,10,11</sup> and the main aims of the meeting were summarized. The group was reminded of the need to listen to all opinions and be flexible and open minded to achieve consensus.

## Long-term control domain session

### Introduction and background

The overall objectives of this session were to agree by consensus (i) what is long-term control (i.e. its definition) and what is important to measure (i.e. which subdomains and outcomes) and (ii) how the long-term control domain should be measured (i.e. which instruments). Discussions were based on data from international online focus groups with patients and carers, an online survey of HOME clinicians and methodologists and a systematic review showing how long-term control has been measured in published trials.<sup>12</sup>

Each small group decided on the three most important items and factors for defining long-term control and presented their choices to the whole group (Tables S3 and S4; see Supporting Information). It was agreed by voting (Table S5; see Supporting Information) that any items or factors not included in the top three for any of the six groups needed no further consideration in subsequent decisions on face validity of the instruments (i.e. the degree to which an instrument indeed looks to be an adequate reflection of the construct to be measured).<sup>13</sup>

The small groups then decided which (if any) instruments they considered not feasible for inclusion in the COS (i.e. aspects of the outcome measurement instrument that affect the ability to implement it or interpret the results).<sup>12</sup> These choices were presented to the whole group (Table S6; see Supporting Information) and it was agreed that instruments considered not feasible for the COS by more than two small groups would be excluded from further consideration (Table S7 and Fig. S1; see Supporting Information).

These voting results were included in a decision matrix to aid subsequent discussions on which instruments had adequate face validity and were considered feasible (Table 1).

### How should the long-term control domain should be measured?

The purpose of this session was to reduce the long list of candidate instruments for measuring long-term control using the decision matrix (Table 1). The populated decision matrix was

Table 1 Decision matrix showing the face validity and feasibility of different instruments for measuring long-term control

	HOME COS agreed instruments				Other instruments				Flares – cut-off on validated severity scale	Well-controlled weeks (global)
	POEM (repeated measures of patient-reported symptoms)	EASI (repeated measures of clinician-reported signs)	QoL – eczema specific (repeated measures of QoL)	PGA (repeated measures)	PO-SCORAD (repeated measures)	Itch (repeated measures)	Sleep loss (repeated measures)	IGA (repeated measures)		
Items important in long-term control <sup>b</sup>										
Disease severity	+	+	–	+	+	+	+	+	+	+
QoL	–	–	+	–	–	–	–	–	–	–
Flares	–	–	–	–	–	–	–	–	–	–
Acceptable state of eczema to the patient	+	–	+	+	+	±	–	–	–	±
Itch and/or scratching	+	± <sup>d</sup>	–	±	+	+	±	±	±	±
Items and factors to be considered when capturing long-term control <sup>b</sup>										
Can assess the eczema objectively (and probably blinded)	–	+	–	–	–	–	–	–	–	–
Is relevant to most patients with eczema	+	+	+	+	+	+	+	+	±	±
Captures the patient's/parent's perspective on their eczema	+	–	+	+	+	+	–	–	+	+
Captures the clinician's perspective on the patient's eczema	–	+	–	–	–	–	–	–	±	±
Minimal burden on trial participants	± <sup>e</sup>	–	± <sup>f</sup>	+	±	+	+	+	±	±
Easy to understand and results easily interpretable	+	+	+	+	+	+	+	+	±	±
Feasibility <sup>c</sup>	+	±	+	+	+	+	±	±	±	±

The green boxes (+) indicate where the instrument captures that item or factor. The red boxes (–) indicate where the instrument does not capture that item/factor. Orange (±) indicates uncertainty or use depends on how the item is measured. COS, core outcome set; POEM, Patient-Oriented Eczema Measure; EASI, Eczema Area and Severity Index; QoL, quality of life; PGA, Patient's Global Assessment; PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; IGA, Investigator's Global Assessment. <sup>a</sup>The aspects voted as being important to consider when thinking about long-term control. <sup>b</sup>Green (+), all groups considered the method to be feasible for the COS; orange (±), at least four groups considered the method to be feasible for the COS. <sup>c</sup>Measures itch only indirectly (excoriation). <sup>d</sup>If not too frequent. <sup>e</sup>Depending on the instrument.



**Table 2** Summary of discussions on candidate instruments for measuring long-term control

Long-term control is the overall main goal of treatment, so the domain can be viewed differently from signs, symptoms and QoL. Although it was stated as a separate domain in the original HOME eDelphi exercise,<sup>13</sup> and at HOME II,<sup>9</sup> the group should not be constrained by previous statements when deciding how long-term control should be measured.

- The existing core domains of signs, symptoms and QoL are already being measured repeatedly in trials so inclusion in the long-term control domain represents little or no increased burden for patients or researchers. The frequency of data collection needs to be considered and a threshold for repeated measures of existing domains is likely to be required.
- The group needs to consider the added value of including anything over and above repeated measures of the existing core domains.
- The existing three other core domains may be insufficient to capture all aspects of long-term control. The list of agreed items that need to be considered for face validity also suggests that additional items are required to capture long-term control fully.
- Other items considered to add value to the existing COS for measuring long-term control were
  - o Itch intensity: it was agreed at the previous HOME IV meeting that itch is an essential subdomain of symptoms. The core instrument for symptoms (POEM) measures frequency of itch and not intensity. The addition of the intensity of itch is currently being studied by the symptoms group.
  - o A patient-reported holistic global assessment of the eczema that may capture aspects of the disease not well covered by the existing domains. Ideas suggested included
    - i a general question about how has your eczema control been;
    - ii a multiquestion instrument capturing different subdomains of long-term control, as has been developed in urticaria; and
    - iii a global question of well-controlled weeks.
- The COS has to be feasible to enable uptake, and when considering each domain, the burden of the entire COS should be considered.
- It was difficult to discuss the feasibility of QoL specifically, because the instrument has not yet been agreed on. It can be assumed that as part of the selection process, whatever instrument is recommended will be feasible to use.
- Patient-reported outcomes are sensitive enough to pick up changes not detected by clinician-reported outcomes in some instances and can be collected between study visits.

QoL, quality of life; COS, core outcome set; POEM, Patient-Oriented Eczema Measure.

presented and discussed. The rows in the decision matrix comprised the items and factors agreed on earlier as the most important for what to measure (face validity) and the columns comprised only those instruments considered broadly feasible.

**Table 3** Summary of whole-group discussion on validation of the candidate instruments

- Signs-only scores such as EASI do not cover all aspects of the disease.
- Expressing EASI scores as 50/75/90% improvement does not give the full picture of the disease.
- Ensure the core outcome set does not measure the same thing more than once (i.e. be aware of duplication of instruments).
- Possible floor effects of experiencing no well-controlled weeks may become less of an issue as more-effective eczema treatments become available.
- For a binary outcome (e.g. well-controlled weeks), if the baseline state is well controlled, then that patient can only get worse or stay the same. This can impact on trial design and statistical power.

EASI, Eczema Area and Severity Index.

Colour coding (green, orange and red) and symbols (+, – and ±) were used in the matrix to indicate the extent to which each instrument captures each item or factor. Each participant was given a printed copy of this matrix for reference during the whole-group discussion, which is summarized in Table 2.

After examining the decision matrix (Table 1), the group noted that no single method included all of the items or factors previously agreed on as important, no one instrument stood out as meeting significantly more items or factors than another and none could be automatically excluded on the grounds of inadequate face validity. There was general support for the concept of including measurement of the existing core domains as a way of measuring long-term control. However, it was agreed that these alone did not necessarily capture everything deemed to be important for the domain of long-term control and that an additional 'global' measure would also be required.

### Further consideration of candidate instruments

The aim of this session was to consider the validation of candidate instruments in more detail. Presentations on candidate instruments were followed by a whole-group discussion, summarized in Table 3.

In subsequent small-group discussions, four of the six groups considered that the existing core domains (signs, symptoms and QoL) were not sufficient to capture the domain of long-term control. All six groups felt that other aspects were required to capture long-term control fully, including intensity of itch (five of six), eczema being in an acceptable state to the patient (three of six) and flares (two of six), and most felt that an additional instrument would be required to capture potentially missing aspects of long-term control that are currently not in the existing domains (Table S8; see Supporting Information). A subsequent whole-group discussion was held, summarized in Table 4.

The existing core domains of disease severity (incorporating signs and symptoms), QoL and intensity of itch were all voted

**Table 4** Summary of whole-group discussion on capturing long-term control

- Existing domains were sufficient to capture 'flares', but a patient-reported holistic global assessment may also be required to capture fully part of the long-term control domain, which can be hard to define.
- Including some kind of global measure would cover some of the overall impact of eczema.
- Global assessments tend to be sensitive to change.
- PO-SCORAD adds value to the existing core set by adding itch intensity, which is not captured by the existing symptoms-domain instrument POEM. Using PO-SCORAD may reduce the need for an additional instrument to capture itch intensity.
- Including PO-SCORAD in addition to POEM may result in duplication, as the two instruments measure similar aspects of disease symptoms.
- A show of hands indicated that the vast majority considered that intensity of itch should be included in the long-term control domain.

PO-SCORAD, Patient-Oriented Scoring Atopic Dermatitis; POEM, Patient-Oriented Eczema Measure.

as being essential to capture long-term control (Table 5). Flares and 'acceptable state to the patient' were not considered to be essential. Less than half of voters considered that the existing domains were sufficient if used alone to capture long-term control fully, and it was agreed that a patient 'global' assessment was also required (Table 5). The group discussed this final decision against the other considerations for measuring long-term control that had previously been prioritized (Table S9; see Supporting Information).

### Choice of preferred outcome instruments

Because repeated measures of existing domains had formed a significant part of the discussions so far about 'what' to

measure, the existing recommended instruments had already been discussed as part of that decision-making process. Conflicts of interest were declared with regards to instruments under discussion (and can be found in the conflicts of interest section of this report).

There were differing opinions on whether instruments other than those already recommended for the COS should be used to measure signs and symptoms for the long-term control domain. Some felt that the instruments for measuring signs and symptoms had already been decided on, and because they are already included at multiple time points during trials, recommending an additional instrument to measure the same thing would not be appropriate. However, others felt that because long-term control is a separate domain, other instruments should be considered and the COS potentially expanded to include other instruments in addition to EASI<sup>14</sup> and POEM<sup>15</sup> for signs and symptoms. However, there was consensus that no further discussion was required on this issue before the group could continue (Table 5). Therefore, discussions on alternatives to EASI and POEM for measuring signs and symptoms in the long-term control domain will take place subsequently to this meeting. The group then voted and consensus was reached that the existing instruments (EASI and POEM) should be recommended 'for the time being' for measuring long-term control (Table 5). It was not possible to include QoL in this vote as the instrument has not yet been agreed upon.

### Future work

The group agreed with a nonanonymous vote (show of hands) that the following should be the priority and focus for work subsequently to this meeting:

- For the holistic 'patient global' outcome measure: determine what is already available and, if necessary, develop a new instrument. Consider a truly global measurement instrument (single question) vs. a multi-item instrument (such as that developed for urticaria).<sup>16</sup> Set up a dedicated

**Table 5** Voting on the long-term control domain

	Yes	No	Unsure
Is measuring disease severity (signs and symptoms) essential for long-term control?	93%	4%	3%
Is measuring quality of life essential for long-term control?	89%	8%	4%
Is measuring intensity of itch essential for long-term control?	80%	19%	1%
Is measuring flares essential for long-term control?	49%	42%	9%
Is measuring the acceptable state of eczema to the patient essential for long-term control?	53%	40%	7%
Is long-term control sufficiently captured by the domains of signs, symptoms (including intensity of itch) and QoL?	46%	50%	4%
Would a patient-generated global measure help capture what is missing from signs, symptoms (including intensity of itch) and QoL?	82%	10%	7%
Should long-term control (in trials of at least 3 months) be defined by signs, symptoms, QoL and a patient global measure?	91%	4%	4%
Is further discussion required before continuing with the long-term control domain discussion?	49%	49%	3%
Should EASI be recommended 'for the time being' to measure signs in the long-term control domain?	78%	19%	3%
Should POEM be recommended 'for the time being' to measure symptoms in the long-term control domain?	87%	13%	0%

Breakdown of voters by stakeholder group: patients 15%, clinicians 52%, methodologists 9%, pharma industry 25%. QoL, quality of life; EASI, Eczema Area and Severity Index; POEM, Patient-Oriented Eczema Measure.



**Table 6** Overall ranking of each quality-of-life instrument across the six small groups

Rank	Proxy instruments
1	Infant's Dermatitis Quality of Life Index (IDQoL)
2	KINDL-R Neurodermatitis Module
3	DISABKIDS Atopic Dermatitis Module
4	Childhood Atopic Dermatitis Impact Scale (CADIS)
5	Atopic Dermatitis Quality of Life (ADQoL)
6	Childhood Impact of Atopic Dermatitis (CIAD) <sup>a</sup>
Rank	Self-reported instruments
1	Children's Dermatology Life Quality Index (CDLQI)
2	Skindex Teen
3	Children's Dermatology Life Quality Index (CDLQI) cartoon version
4	KINDL-R Neurodermatitis Module
5	DISABKIDS Atopic Dermatitis Module

<sup>a</sup>Although the CIAD was included in the review as validation studies have been published, it was not possible, despite multiple attempts, to obtain a copy. For this reason, it was considered not feasible by all small groups.

working group and draw on how other groups have approached this issue (e.g. OMERACT).

- Continue work already underway by the symptoms group on the value of including intensity of itch.
- Determine thresholds for what could be considered as 'control' on the agreed instruments.
- At the HOME V meeting there was insufficient time to discuss in detail the frequency of measurement. It was recommended to continue work currently underway to determine the optimal frequency or total number of measurements required and to move forward using the e-Delphi technique.

## Quality-of-life domain (in children) session

### Introduction and background

The concept of QoL was introduced as a more complex construct than the other domains, requiring more questionnaire items. More than one instrument is required to cover all age groups, as many are designed for only a restricted age group. A systematic review of the quality of instruments used for measuring QoL in infants, children and adolescents (hereafter referred to as children) with eczema was presented.<sup>17</sup> The aim of the session was to decide where to focus future research efforts based on the face validity and feasibility of the instruments.

### Face validity and feasibility of candidate quality-of-life instruments

Each small group ranked the candidate instruments in order of preference, based on face validity and feasibility for proxy and self-reported instruments (Tables S10 and S11; see Supporting

Information). The overall ranking of instruments based on the small-group results was presented to the whole group (Table 6).

Some of the reasons were discussed among the whole group. There was a general dislike of negatively worded questions and long recall periods (it may be difficult to remember even a week or a month ago). Many felt the family perspective should be captured.

Regarding specific instruments, patients found the use of a dog in the pictures in the Children's Dermatology Life Quality Index (CDLQI) inappropriate. In some cultures, dogs are generally regarded as a negative image, and in other cultures, children are often teased for 'having fleas' due to scratching because of their eczema. Additionally, many children with eczema are allergic to dogs. The name 'DISABKIDS' was generally disliked as children are not disabled because they have eczema. ADQoL (Atopic Dermatitis Quality of Life) was considered to be far too generic, and, despite the name, the questions were not considered to be related to having eczema. The CADIS (Childhood Atopic Dermatitis Impact Scale) was far too lengthy to complete and was perceived as having particularly negative wording. The KINDL-R translation appeared poor and would need improving.

### Discussions

A whole-group discussion initially focused on whether the group of instruments including CDLQI and Infant's Dermatitis Quality of Life Index (IDQoL) (and DLQI for adults) could be recommended. Some meeting participants strongly supported the inclusion of these instruments, but systematic reviews have highlighted some weaknesses and many areas lack validation studies. It was pointed out that legacy instruments would have been developed using standards of the time and so may not meet modern instrument development standards, and part of COS development should be about raising the standards of instruments. If an instrument does not meet content and structural validity then it could be considered to be fundamentally flawed and therefore not recommended.<sup>4</sup> Recommending any instrument for the core set is likely to lead to an increase in the use of that instrument, and recommending flawed instruments could potentially damage the reputation of the HOME initiative. However, the practical aspects of the COS also need to be considered. For instance, where an instrument (or group of instruments such as DLQI, IDQoL and CDLQI) is already embedded in trials, clinical practice, reimbursement and treatment decision making, this could be considered an argument for inclusion in the core set despite possible inadequacies.

While there is no recommended instrument, trialists will continue to measure QoL in many different ways, which is an unsatisfactory situation. A number of potential suggestions were made for future potential ways forward. Short-term solutions could be (i) to accept an instrument rated as poor in the interim because no better option is available, as has been done by OMERACT in some instances, although it was recognized that it can be difficult then to change this recommendation at

a later date and (ii) to recommend a nondermatology-specific instrument in the interim until a good-quality dermatology-specific instrument can be recommended. It was suggested that in the longer term the group should consider developing an entirely new instrument given that validation studies can be lengthy. Also, the use of a family impact instrument, if a suitable instrument can be identified, would be a way to overcome the problem of using different instruments for different ages.

### Future work

It was agreed by voting (Table S12; see Supporting Information) that future research on proxy and self-reported instruments should be prioritized in accordance with Table 6.

## Overall summary and conclusions

For the long-term control domain, the group initially populated a decision matrix with important items and factors considered important (to inform face validity) and instruments that were considered feasible. Inadequate face validity and lack of feasibility are valid reasons for rejection as a candidate instrument for the COS.<sup>4</sup> Although the concepts overlapped at times, they nevertheless provided a useful basis on which to progress the discussions and vote on what was essential to include. The group agreed that signs, symptoms and QoL were essential but alone were not sufficient to capture long-term control fully. Itch intensity should be measured, as well as a patient global measure, which may capture aspects of the disease not well covered by the existing domains. There was clear consensus to use the existing core outcome measurement instruments for signs and symptoms (EASI and POEM) for the time being.

Whether long-term control is a domain in its own right or simply a time function of the other core outcomes was discussed in depth during the small- and whole-group sessions when considering the inclusion of the existing domains. Long-term control was considered to be a time function of other core outcomes, as well as requiring further domains (intensity of itch and the patient global measure), and remains a domain to be measured in the COS for all future eczema trials. However, the nature of the domain inevitably means that other domains (signs, symptoms and QoL) become 'subdomains' when discussed as part of long-term control.

With regards to QoL in children, because there were many gaps in the assessment of the quality of existing QoL instruments for children, the meeting focused on assessing the face validity and feasibility of candidate instruments. Recommending an existing instrument with adequate face validity and feasibility was not supported. The need for different instruments for different age groups further complicates the decision on which instrument to recommend. There was clear steering from the group as to the future priorities for the QoL working group.

Overall, the HOME V meeting has moved the HOME initiative substantially further forward towards a complete COS for

eczema trials. There is still work to be done but the direction and priority areas are agreed on and clear.

## Strengths and weaknesses

There was good stakeholder representation, including patients, with participants from several continents. However, there were no participants from large countries such as India and China. Despite repeated efforts, we were unable to attract regulatory agency representation. Additionally, as the meeting was held during school term time, there were no children present, which was an issue for the discussions around QoL in children. However, some of the younger patient representatives could clearly remember and recount childhood experiences, and we had parents of children with eczema present. Additionally, the premeeting focus groups and survey provided a wider patient input into the meeting. The HOME executive group encouraged scientists from the pharma industry to attend as it is crucial that this stakeholder group is represented, and as a result there were more pharma industry representatives than at previous HOME meetings, although this has potential to affect the outcomes.

There is potential for the HOME executive group to steer the meeting in certain directions. To mitigate this, the meeting chair made it clear that there were no fixed preconceptions to be fulfilled at this meeting. The evidence was presented to facilitate discussions rather than to steer the meeting in any particular direction. The whole-group sessions were facilitated by an independent moderator from OMERACT with extensive experience in COS development, and the small groups were facilitated by either a member of the HOME executive group or an independent moderator from OMERACT.

A small number of participants were unable to be present for the whole meeting, but all were present for the discussions for any session they voted in. Anonymous real-time voting with voting rules agreed on beforehand allowed all participants to vote, and all votes were counted equally. Established consensus methods were used,<sup>4</sup> in which small- and whole-group discussions were held, underpinned by evidence, and there were high levels of consistency between the small-group outputs.

## Acknowledgments

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## References

- 1 Williamson PR, Altman DG, Blazeby JM *et al.* Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; **13**:132.
- 2 Williamson PR, Altman DG, Bagley H *et al.* The COMET Handbook: version 1.0. *Trials* 2017; **18**:280.
- 3 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.

- 4 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.
- 5 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.
- 6 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.
- 7 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.
- 8 Chalmers JR, Simpson E, Apfelbacher CJ *et al.* Report from the fourth international consensus meeting to harmonize core outcome measures for atopic eczema/dermatitis clinical trials (HOME initiative). *Br J Dermatol* 2016; **175**:69–79.
- 9 Harmonizing Outcome Measures for Eczema (HOME). HOME V Meeting, Nantes, France – 2017. Available at: <http://www.homeforeczema.org/meetings-and-events/home-v-meeting-2017.aspx> (last accessed 22 February 2018).
- 10 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**:1111–17.
- 11 Schmitt J, Williams H, HOME Development Group. Report from the First International Consensus Meeting (HOME 1), 24 July 2010, Munich, Germany. *Br J Dermatol* 2010; **163**:1166–8.
- 12 Barbarot S, Rogers NK, Abuabara K *et al.* Strategies used for measuring long-term control in atopic dermatitis trials: a systematic review. *J Am Acad Dermatol* 2016; **75**:1038–44.
- 13 Mokkink LB, Terwee CB, Patrick DL *et al.* The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol* 2010; **63**:737–45.
- 14 Hanifin JM, Thurston M, Omoto M *et al.* The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. *Exp Dermatol* 2001; **10**:11–18.
- 15 Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol* 2004; **140**:1513–19.
- 16 Weller K, Groffik A, Church MK *et al.* Development and validation of the Urticaria Control Test: a patient-reported outcome

instrument for assessing urticaria control. *J Allergy Clin Immunol* 2014; **133**:1365–72.

- 17 Hehl D, Prinsen CAC, Sach T *et al.* Measurement properties of quality-of-life measurement instruments for infants, children and adolescents with eczema: a systematic review. *Br J Dermatol* 2017; **176**:878–89.

## Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

**Fig S1.** Graph of which instruments were not feasible for the long-term control domain.

**Table S1.** HOME executive group composition.

**Table S2.** Composition of small groups.

**Table S3.** Results of small groups: what is long-term control?

**Table S4.** Results of small groups: what items/factors should be considered when measuring long-term control?

**Table S5.** Voting to agree on the proposed list of the most important items and factors for long-term control.

**Table S6.** Results of small groups: instruments considered not feasible for measuring long-term control in the core outcome sets.

**Table S7.** Voting to agree on the proposed list of feasible instruments for measuring long-term control.

**Table S8.** Results of small groups: is long-term control captured by existing domains?

**Table S9.** Summary of discussion and agreement regarding the extent to which the items and factors considered to be important when measuring long-term control are covered by measurement of existing domains (signs, symptoms and quality of life) and a patient global measurement instrument.

**Table S10.** Results of small groups: quality of life in children, proxy instruments.

**Table S11.** Results of small groups: quality of life in children, self-reported instruments.

**Table S12.** Voting on whether the ranked order of quality-of-life instruments should be used to prioritize further research.