

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

J.R. Chalmers,¹ E. Simpson,² C.J. Apfelbacher,³ K.S. Thomas,¹ L. von Kobyletzki,^{4,5} J. Schmitt,^{6,7} J.A. Singh,^{8,9} Å. Svensson,¹⁰ H.C. Williams,¹ K. Abuabara,¹¹ V. Aoki,¹² M. Ardeleanu,¹³ M. Awici-Rasmussen,¹⁴ S. Barbarot,¹⁵ T.L. Berents,^{16,17} J. Block,¹⁸ A. Bragg,¹⁹ T. Burton,²⁰ K.K. Bjerring Clemmensen,²¹ A. Creswell-Melville,²² M. Dinesen,²³ A. Drucker,²⁴ L. Eckert,²⁵ C. Flohr,²⁶ M. Garg,²⁷ L.A.A. Gerbens,²⁸ A.L.B. Graff,²⁹ J. Hanifin,² D. Heinel,³ R. Humphreys,²⁹ H.A. Ishii,³⁰ Y. Kataoka,³¹ Y.A. Leshem,² B. Marquort,³² M.-A. Massuel,³³ S. Merhand,³⁴ H. Mizutani,³⁵ H. Murota,³⁶ D.F. Murrell,^{37,38} T. Nakahara,³⁹ I. Nasr,⁴⁰ K. Nograles,⁴¹ Y. Ohya,⁴² I. Osterloh,⁴³ J. Pander,⁴⁴ C. Prinsen,⁴⁵ L. Purkins,⁴⁶ M. Ridd,⁴⁷ T. Sach,⁴⁸ M.-L. A.Schuttelaar,⁴⁹ S. Shindo,³⁶ J. Smirnova,⁵ A. Sulzer,⁵⁰ E. Synnøve Gjerde,¹⁴ R. Takaoka,¹² H. Vestby Talmo,⁵⁰ M. Tauber,⁵¹ F. Torchet,³⁵ A. Volke,⁵² C.-F. Wahlgren,^{53,54} S. Weidinger,⁵⁵ E. Weisshaar,⁵⁶ A. Wollenberg,⁵⁷ K. Yamaga,³⁶ C.Y. Zhao^{37,38} and P.I. Spuls²⁸

¹Centre of Evidence Based Dermatology, University of Nottingham, Nottingham, U.K.

²Department of Dermatology, Oregon Health and Science University, Portland, OR, U.S.A.

³Medical Sociology, Institute of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany

⁴Lund University, Skåne University Hospital, Department of Dermatology, Malmö, Sweden

⁵Department of Public Health Sciences, Karlstad University, Karlstad, Sweden

⁶Centre for Evidence-Based Healthcare, University of Dresden, Dresden, Germany

⁷Department of Occupational and Social Medicine, Technical University Dresden, Dresden, Germany

⁸Medicine Service, Birmingham VA Medical Center, Birmingham, AL, U.S.A.

⁹Department of Medicine, University of Alabama, Birmingham, AL, U.S.A.

¹⁰Department of Dermatology and Venerology, Malmö University Hospital, Malmö, Sweden

¹¹Department of Dermatology, University of California San Francisco, San Francisco, California, CA, U.S.A.

¹²Department of Dermatology, University of São Paulo Medical School, São Paulo, Brazil

¹³Immunology and Inflammation, Regeneron Pharmaceuticals, Inc., New York, NY, U.S.A.

¹⁴Psoriasis and Eczema Association of Norway, Oslo, Norway

¹⁵Department of Dermatology, CHU de Nantes, Nantes, France

¹⁶Institute of Clinical Medicine, University of Oslo, Oslo, Norway

¹⁷Department of Dermatology, Oslo University Hospital, Oslo, Norway

¹⁸National Eczema Organisation, National Eczema Association, San Rafael, CA, U.S.A.

¹⁹Chugai Pharma Europe Ltd., London, U.K.

²⁰No affiliation (patient representative U.K.)

²¹Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark

²²Société Canadienne de l'Eczéma, Keswick, ON, Canada

²³LEO Pharma A/S, Industriparken 55, Ballerup, Denmark

²⁴Division of Dermatology, University Health Network, Toronto, ON, Canada

²⁵Health Economics and Outcomes Research, Sanofi, France

²⁶St John's Institute of Dermatology, Guy's and St Thomas' Hospitals NHS Foundation Trust and King's College London, London, U.K.

²⁷LEO Pharma, Copenhagen, Denmark

²⁸Department of Dermatology, Academic Medical Centre, University of Amsterdam, Amsterdam, the Netherlands

²⁹National Eczema Society, London, U.K.

³⁰Brazilian Atopic Dermatitis Association (AADA), São Paulo, Brazil

³¹Osaka Prefectural Medical Center for Respiratory and Allergic Disease, Osaka, Japan

³²No affiliation (patient representative Sweden)

³³Sanofi-Aventis, Paris, France

³⁴Association Française de l'Eczéma, Redon, France

³⁵Mie University, Graduate School of Medicine and Mie University Hospital Tsu, Mie, Japan

³⁶Department of Dermatology, Osaka University, Osaka, Japan

³⁷Department of Dermatology, St George Hospital, Sydney, Australia

³⁸University of New South Wales, Sydney, Australia

³⁹Department of Dermatology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

⁴⁰Retired, no affiliation

⁴¹Celgene Corporation, Greater New York City Area Pharmaceuticals, New York, NY, U.S.A.

⁴²Division of Allergy, Department of Medical Subspecialties, National Center for Child Health and Development, Tokyo, Japan

⁴³Ostermed Ltd., Kent, U.K.

⁴⁴Celgene BV, Utrecht, the Netherlands

⁴⁵Department of Epidemiology and Biostatistics, EMGO+ Institute for Health and Care Research, VU University Medical Centre, Amsterdam, the Netherlands

⁴⁶Ziarno Pharma Ltd, Kent, U.K.

⁴⁷School of Social & Community Medicine, University of Bristol, Bristol, U.K.

⁴⁸Health Economics Group, University of East Anglia, Norwich, U.K.

⁴⁹Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

⁵⁰Sanofi-Aventis, Montpellier, France

⁵¹Toulouse University, Toulouse, France

⁵²Department of Dermatology, University of Tartu, Tartu, Estonia

⁵³Dermatology Unit, Department of Medicine, Karolinska Institutet, Solna, Sweden

⁵⁴Karolinska University Hospital, Stockholm, Sweden

⁵⁵Department of Dermatology, Venereology and Allergy University Hospital Schleswig-Holstein, Kiel, Germany

⁵⁶Occupational and Environmental Dermatology, Department of Social Medicine, University of Heidelberg, Heidelberg, Germany

⁵⁷Department of Dermatology and Allergy, Ludwig-Maximilian University, Munich, Germany

Summary

Correspondence

Phyllis Spuls.

E-mail: home@nottingham.ac.uk

Accepted for publication

8 March 2016

Funding sources

All delegates covered their own travel and accommodation expenses with the exception of patients and representatives from patient groups. Costs for patients were met by either their national eczema patient association, a participating Harmonising Outcome Measures for Eczema (HOME) member or by a donation from a pharmaceutical company. H.W. supported the travel and accommodation costs for J.A.S. to attend as our independent advisor from the Outcome Measures in Rheumatology (OMERACT) group. The local organizers (Å.S. and L.v.K.) used an unrestricted educational grant from the LEO Foundation, plus contributions from the Swedish Asthma and Allergy Foundation and the County of Skåne, to support the local meeting arrangements. M.R. is funded by a National Institute for Health Research (NIHR) Post Doctoral Fellowship (PDF-2014-07-013) and T.S. is funded by a NIHR Career Development Fellowship (CDF-2014-07-006). The views expressed in this publication are those of the authors and not necessarily those of the National Health Service, the NIHR or the Department of Health.

This article is a report of the fourth meeting of the Harmonising Outcome Measures for Eczema (HOME) initiative held in Malmö, Sweden on 23–24 April 2015 (HOME IV). The aim of the meeting was to achieve consensus over the preferred outcome instruments for measuring patient-reported symptoms and quality of life for the HOME core outcome set for atopic eczema (AE). Following presentations, which included data from systematic reviews, consensus discussions were held in a mixture of whole group and small group discussions. Small groups were allocated a priori to ensure representation of different stakeholders and countries. Decisions were voted on using electronic keypads. For the patient-reported symptoms, the group agreed by vote that itch, sleep loss, dryness, redness/inflamed skin and irritated skin were all considered essential aspects of AE symptoms. Many instruments for capturing patient-reported symptoms were discussed [including the Patient-Oriented SCOring Atopic Dermatitis index, Patient-Oriented Eczema Measure (POEM), Self-Administered Eczema Area and Severity Index, Itch Severity Scale, Atopic Dermatitis Quickscore and the Nottingham Eczema Severity Score] and, by consensus, POEM was selected as the preferred instrument to measure patient-reported symptoms. Further work is needed to determine the reliability and measurement error of POEM. Further work is also required to establish the importance of pain/soreness and the importance of collecting information regarding the intensity of symptoms in addition to their frequency. Much of the discussion on quality of life concerned the Dermatology Life Quality Index and Quality of Life Index for Atopic Dermatitis; however, consensus on a preferred instrument for measuring this domain could not be reached. In summary, POEM is recommended as the HOME core outcome instrument for measuring AE symptoms.

Conflicts of interest

The following authors were involved with the development or validation of scales discussed at the meeting: PO-SCORAD: Sebastien Barbarot, Andreas Wollenberg; BODE: Aaron Drucker; DLQI, CDLQI, DFI, FDLQI, FROM-16, EDI, IDQoL: Andrew Finlay; ADQoL-J (Japan): Yoko Kataoka; Japanese versions of POEM, DLQI, CDLQI, FDI, IDQOL, QPCAD, PQCAD short form: Yukihiro Ohya; Ziarco Itch Diary: Lynn Purkins; VAS: Elke Weisshaar; NESS, POEM: Hywel Williams.

DOI 10.1111/bjd.14773

What's already known about this topic?

- Previous meetings of the Harmonising Outcome Measures for Eczema (HOME) initiative have achieved international consensus that the domains of clinician-reported signs, patient-reported symptoms, quality of life and long-term control should be measured as the core outcomes for atopic eczema clinical trials.
- It has been recommended that clinician-reported signs should be measured using the Eczema Area and Severity Index.

What does this study add?

- During the HOME IV meeting (Spring 2015, Malmö, Sweden), a consensus was achieved that the Patient-Oriented Eczema Measure should be used to capture patient-reported symptoms in future atopic eczema trials.
- The remaining two core outcome domains of quality of life and long-term control require further work to determine the preferred core outcome measurement instruments.

This is a report of the fourth meeting of the Harmonising Outcome Measures for Eczema (HOME) initiative (HOME IV), an initiative to validate and standardize the use of core outcome measurement instruments for atopic eczema (AE) (also known as atopic dermatitis). The main meeting was held in Malmö, Sweden on 23–24 April 2015 with a patient session held prior to the main meeting on the afternoon of the 22 April. The full minutes including details of the discussions and voting results from this meeting can be found at <http://nottingham.ac.uk/homeforeczema/meetings-and-events/home-iv-meeting-2015.aspx>.

The aims of the HOME IV meeting were:

- 1 To discuss systematic review data on the measurement properties of instruments available for measuring patient-reported symptoms and quality of life (QoL) in AE trials.
- 2 To work towards a consensus on which instruments should be recommended for inclusion in the core outcome set for patient-reported symptoms and QoL.
- 3 To determine how best to proceed with the core outcome domain long-term control.

A summary timeline of progress with the HOME core outcome set development process is shown in Table 1. Full details of outputs from previous HOME meetings can be found at <http://nottingham.ac.uk/homeforeczema/meetings-and-events/next-home-meeting.aspx/>.

An invitation to participate in the meeting was sent to all 246 HOME members. Membership of the HOME initiative is open to anyone with an interest in outcome measures for AE. There were a total of 70 participants at the HOME IV meeting from North and South America, Europe, Asia and Australia (Fig. 1). Delegates included patients with AE or patient representatives, clinicians, methodologists and representatives of the pharmaceutical industry (Fig. 2).

Methods

All patients and patient representatives were invited to attend a premeeting session on the afternoon prior to the meeting where the background to the HOME initiative and relevant terminology was explained to enable them to participate fully in the subsequent meetings over the following 2 days.

The HOME meeting structure included a combination of presentations of background information and data from members of the HOME research groups, and nominal group techniques to achieve consensus.¹ For each topic there were large group discussions and small breakout group discussions where participants were allocated *a priori* to a group to ensure representation from the different stakeholder groups and countries. Voting was conducted anonymously using electronic handsets [Interactive Voting System, IVS[®] and RF2 Keypads, Dronten, the Netherlands (<https://www.ivsystem.nl/en/>)] coordinated by Teletech Konference Kommunikation (Herlev, Denmark) (<http://www.teletech.dk>). The results were presented to the group once the voting had closed. Only members who were present for the discussions were permitted to vote and all stakeholder groups participated in the voting. The voting rule agreed at HOME II was used at this meeting, i.e. consensus is reached where less than 30% of voters disagree.²

Results

Session 1: Introduction

Presentation 1-1: Introduction and background

Professor Hywel Williams opened the meeting by describing the many outcome measures for AE currently being used and why this hampers evidence-based practice. He also

Table 1 Timeline for Harmonising Outcome Measures for Eczema (HOME) development of a core outcome set for atopic eczema (AE)

HOME meeting	Key output from the meeting	Work undertaken to inform next meeting (by working groups)
HOME I Munich, Germany (July 2010)	<ul style="list-style-type: none"> Confirmed international enthusiasm for establishing a core outcome set for eczema 	<ul style="list-style-type: none"> International e-Delphi consensus study to inform choice of core outcome domains for trials and clinical practice¹⁰ Link with key groups to inform methodology (OMERACT, COMET, COSMIN)^{11,12} Systematic review of outcome instruments used in eczema trials¹² Validation of AE signs scales¹³
HOME II Amsterdam, the Netherlands (April 2011)	<ul style="list-style-type: none"> Agreed to focus initially on core outcome set for clinical trials Confirmed core outcome domains for clinical trials: <ol style="list-style-type: none"> Signs Symptoms Quality of life Long-term control 	<ul style="list-style-type: none"> HOME Roadmap methodology developed⁵ Systematic review of validation studies for instruments to measure AE signs¹¹
HOME III San Diego, CA, U.S.A. (April 2013)	<ul style="list-style-type: none"> Agreed core instrument for clinician-reported signs is Eczema Area Severity Index (EASI)³ 	<ul style="list-style-type: none"> Systematic review of how symptoms are captured in clinical trials¹⁴ Systematic review of validation studies for instruments to measure AE symptoms¹⁵ Systematic review of how quality of life is captured in clinical trials¹⁶ Systematic review of validation studies for instruments to assess quality of life in patients with AE (adults)⁹ Systematic review of how long-term control is captured in trials¹⁷ International patient survey¹⁸
HOME IV Malmö, Sweden (April 2015)	<ul style="list-style-type: none"> Agreed core instrument for patient-reported symptoms is Patient-Oriented Eczema Measure (POEM)¹⁹ 	<ul style="list-style-type: none"> Surveys, qualitative studies and e-Delphi consensus study to establish what patients and healthcare professionals mean by long-term control Validation studies of different methods of capturing long-term control
HOME V (To be confirmed, 2017)	<ul style="list-style-type: none"> Aim to agree core instrument for quality of life (adults) and long-term control 	

COMET, Core Outcome Measures in Effectiveness Trials; COSMIN, COnsensus-based Standards for the selection of health Measurement INstruments; OMERACT, Outcome Measures in Rheumatology.

summarized the progress made by the HOME initiative to date.²⁻⁴ He encouraged the group to put aside prejudices and allegiances to achieve the greater good for patient care. He concluded by reminding the group of the previously agreed consensus voting rules.²

Presentation 1-2: Reflections from Outcome Measures in Rheumatology (OMERACT)

Dr Jas Singh, attending as an independent advisor from the Outcome Measures in Rheumatology (OMERACT) group

(<http://www.omeract.org>), acted as a group moderator. Dr Singh stated that the purpose of this meeting was to agree on core outcome measurement instruments and emphasized that the patient voice is crucial in determining the patient-reported outcome measures of symptoms and QoL. He encouraged the group to listen to disagreement and to share their views during the meeting rather than afterwards. Dr Singh reminded participants that there is never a perfect instrument and developing a new instrument takes years of work. He urged everyone to ask themselves the question 'Can I live with it?' rather than 'Is this the perfect solution?'.

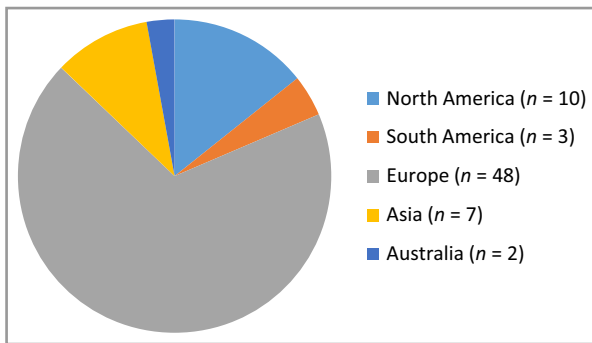


Fig 1. Geographic location of Harmonising Outcome Measures for Eczema IV meeting participants.

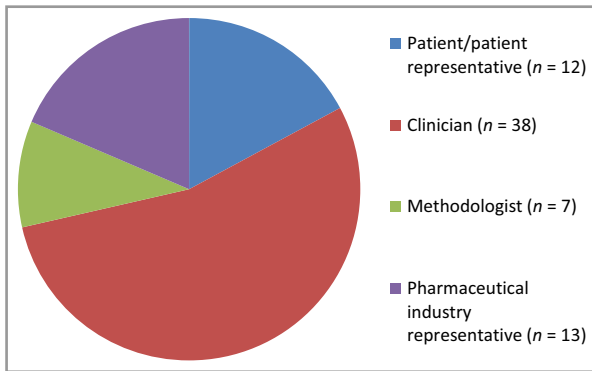


Fig 2. Background of Harmonising Outcome Measures for Eczema IV meeting participants.

Session 2: Symptoms domain (Chair: Eric Simpson and Phyllis Spuls)

Presentation 2-1. Introduction

Professor Phyllis Spuls opened the symptoms session stating that the goal was to agree on a core outcome instrument to measure the symptoms of AE in clinical trials and explained how the systematic reviews conducted by the symptoms working group related to the HOME roadmap.⁵ The group agreed by vote that a patient-reported symptom should be defined as 'departure from normal function, appearance or feeling that is noticed by the patient, indicating the presence of disease or abnormality' (95% agreed, 3% disagreed, 2% unsure).

Professor Spuls then described the individual symptoms that had been identified as being important to measure. These were identified from a global survey of patients (Presentation 2-2), input from patients at the HOME IV meeting and a systematic review of what symptoms are measured and reported in clinical trials (Presentation 2-3).

Presentation 2-2. Atopic eczema symptoms: what is important to patients?

Dr Laura von Kobyletzki presented the results of a global patient survey in which respondents were given a list of AE

symptoms and asked to give each a rating on a 5-point Likert scale ranging from 'very important' to 'not relevant to me' in response to the question 'How important are these features in deciding whether or not a treatment is working?'.

A total of 1104 responses were received from 35 countries, mainly in Europe and North America. A wide range of severity and skin colours were represented. Nine items were rated as being quite or very important by more than 80% of the respondents. These included itch, pain/soreness, skin feels hot or inflamed, bleeding, involvement of visible or sensitive body sites, cracks, sleep difficulties, amount of body affected and weeping. Itch and pain/soreness were the symptoms most frequently rated as very or quite important.

Presentation 2-3. A systematic review of how symptoms are reported in randomized controlled trials of atopic eczema treatments

Dr Louise Gerbens presented data from a systematic review revealing that most of the clinical trials of treatments for AE reported symptoms (78%), with itch and sleep loss being the most commonly reported symptoms (98% and 61%, respectively). Symptoms were often reported as part of a composite instrument and the most commonly used instrument to measure symptoms was the SCORing Atopic Dermatitis (SCORAD) index (49%). However, most trials did not report the symptom score separately, meaning that the treatment effect on symptoms alone was not clear.

Whole group discussion

Patients gave feedback and reflections to the whole group on their opinion regarding the most important symptoms and why they felt that way. It became clear that many symptoms may be related (e.g. sleep loss and soreness may be a direct reflection of the degree of itch being experienced). There was divided opinion on whether pain/soreness was a true symptom of AE or a consequence of other symptoms such as cracking.

Presentation 2-4. The COSMIN checklist

Dr Cecilia A.C. (Sanna) Prinsen presented an overview of the COnsensus-based Standards for the selection of health Measurement INSTRUMENTS (COSMIN) taxonomy and the COSMIN checklist (<http://www.cosmin.nl>), a tool developed to evaluate the methodological quality of validation studies on the measurement properties of health measurement instruments used by the HOME initiative.^{6,7} Further quality criteria to evaluate the quality of the measurement instruments (i.e. measurement properties) were discussed.⁸ There was a discussion about how each instrument is given a quality rating and why COSMIN is used in core outcome instrument selection in HOME.

Presentation 2.5. Systematic review of the measurement properties of instruments designed to capture atopic eczema symptoms

Professor Phyllis Spuls presented the preliminary results of a systematic review completed by the symptoms working group of the measurement properties of instruments designed to measure AE symptoms. Each instrument was rated according to the methodological quality of the validation studies and the quality of the measurement instrument, by using the COSMIN checklist and the quality criteria, respectively. For each reviewed instrument, a standardized recommendation was made based on the quality of validation studies found (Table 2). These ratings helped to prioritize which instruments to focus on in further discussion. Based on the preliminary results of the systematic review, recommendations were made and can be found in Table 3.

Whole group discussion

After whole group discussions, it was agreed that the list of symptoms to be considered by the groups was a comprehensive list that captured all of the important AE symptoms (77%

agreed, 3% disagreed, 20% unsure). Because of the high number of symptoms associated with AE and (with the exception of itch) the huge variation between patients, it was accepted that producing a definitive shortlist of essential symptoms would not be possible. However, the group agreed by voting that itch, sleep loss, dryness, redness/inflamed skin and irritated skin were all considered essential. There was no consensus as to whether pain/soreness should be considered an essential item (31% agreed, 37% disagreed, 32% unsure), but it was agreed by vote that more research was needed to explore the importance of pain/soreness in the assessment of AE.

Breakout group discussions were then held (for groups see Appendix 1). Each group was asked to consider the following in their discussions:

- 1 Which symptoms are considered 'essential' to be included from the long list of all symptoms?
- 2 Which is the preferred measurement instrument(s) taking into account the content (important symptoms) and the validation of instruments?

Each group then presented the results of their discussions to the whole group. All six groups reported that the preferred

Table 2 Definitions used for determining summary quality ratings

Rating	Definition	Recommendation
A	Measurement instrument meets all required quality items	Could be recommended for use
B	Measurement instrument meets two or more required quality items, but performance in all other required quality items is unclear	Has the potential to be recommended in the future depending on the results of further validation studies
C	Measurement instrument has low quality in at least one required quality criterion	Not recommended for use
D	Measurement instrument has very little validation work so the performance in all or most relevant quality items is unclear	Not recommended to be used until further validation has been performed. Future recommendation would depend on the results of further validation studies

Table 3 Rating of outcome instruments used to capture patient-reported symptoms

Rating	Recommendation
A	—
B	ISS, POEM, SA-EASI
C	ADAM, IEQ, LIS, subjective SCORAD, ZRADSQ
D	ADQ, CoIQ, mEASI, method 4, NESS, PO-SCORAD, SDQ

ADAM, Atopic Dermatitis Assessment Measure; ADQ, Atopic Dermatitis Quickscore; CoIQ, web-based Characteristics of Itch questionnaire; IEQ, Eppendorf Itch Questionnaire; LIS, Leuven Itch Scale; mEASI, Modified Eczema Area and Severity Index; NESS, Nottingham Eczema Severity Score; SCORAD, SCORing Atopic Dermatitis index; SDQ, Skin Detective Questionnaire; ZRADSQ, Zheng-Related Atopic Dermatitis Symptom Questionnaire. Following small group and whole group discussions, it was agreed that only Patient-Oriented Eczema Measure (POEM), Patient-Oriented SCORing Atopic Dermatitis index (PO-SCORAD) and Self-Administered Eczema Area and Severity Index (SA-EASI) would be considered in the final vote (67% agreed, 25% disagreed, 8% unsure). Post meeting note: some instruments have subsequently changed category due to updating of the systematic review of validation studies for these instruments.¹⁴

Table 4 Results of final voting to decide core outcome instrument (%): Patient-Oriented Eczema Measure (POEM) confirmed as preferred instrument

	Agreed	Disagreed	Unsure
POEM	87.5	3.0	9.4
PO-SCORAD	15.4	61.5	23.1
SA-EASI	4.7	71.9	23.4

PO-SCORAD, Patient-Oriented SCOring Atopic Dermatitis index; SA-EASI, Self-Administered Eczema Area and Severity Index.

instrument was Patient-Oriented Eczema Measure (POEM), but other instruments were also discussed [Itch Severity Scale, Self-Administered Eczema Area and Severity Index (SA-EASI), Patient-Oriented SCOring Atopic Dermatitis index (PO-SCORAD), Atopic Dermatitis Quickscore, Nottingham Eczema Severity Score]. The meeting then broke for the day.

The following day began with the group voting on instruments that had been determined by the groups as having potential for inclusion in the core set, taking into account the measurement properties and the list of essential symptoms. It was agreed by vote that only POEM, SA-EASI and PO-SCORAD were to be considered for the final vote (67% agreed, 25% disagreed, 8% unsure). Prior to the final vote, anyone with a conflict of interest associated with these instruments declared themselves to the group, but all present at the meeting were included in the voting.

The group voted on each of the three outcome instruments separately to the question 'Is [instrument name] an adequate instrument to measure the domain of patient-reported symptoms?' (Table 4).

Consensus was achieved that POEM is the preferred instrument to measure patient-reported symptoms and that it should be recommended as the HOME core outcome instrument for symptoms.

Remaining validation gaps

Although POEM generally passes the OMERACT filter of truth, discrimination and feasibility, it was agreed that the validation gaps for POEM should be addressed in time as per the HOME roadmap. Uncertainties remain around the structural validity of the POEM scale and its cross-cultural validity. Reliability and measurement error also remain unclear. The importance of the intensity of symptoms (in addition to the frequency of symptoms) requires further study.

The symptoms session was then brought to a close.

Session 3: Quality of life domain (Chair: Hywel Williams and Jas Singh)

Presentation 3.1. Introduction

Dr Christian Apfelbacher opened the session by explaining the difficulties in defining QoL and its multidimensionality. Many

instruments that have been developed are measures of functional limitations. Modern instruments are now usually developed using conceptual models. The group discussed the important role of patients in relation to this topic and accepted that this would be challenging to determine the core outcome measure for this domain.

Presentation 3.2. Systematic review of how quality of life is measured in atopic eczema clinical trials

Daniel Heintz presented a scoping review showing that approximately one in five clinical trials concerning AE report on QoL and 22 different instruments had been used. Most were skin specific with a few generic and AE-specific instruments.

The whole group discussion then focused on adults because the required systematic review on validation of QoL scales for children has not yet been completed. The patients and patient representatives were asked about the aspects of AE that affected their QoL. It was clear that having AE affected both their personal and professional lives.

Presentation 3.3. Systematic review of measurement properties of quality of life instruments in adults

Daniel Heintz summarized the methods used in this review of the measurement properties of QoL instruments in adults and emphasized that only validation or development studies were included in the review, not indirect evidence such as responsiveness collected in trials. Each instrument had been given a rating of A, B, C or D as per the symptoms review (Table 5).⁹

Whole group discussion

The following whole group discussion explained that different language versions are treated separately because the measurement properties relate to the data, rather than the instrument itself, and therefore small nuances of interpretation in different settings may influence the performance of the scale. Ideally, validation studies should be performed in each language. It was generally agreed that the number of questions in the instrument is important for feasibility.

The meeting then split into the same smaller breakout groups as for the symptoms session. Each group was asked to consider what they felt were the essential domains for QoL and to discuss their preferred QoL instruments.

Most groups felt that emotions, treatment burden and personal relationships were essential aspects of QoL. All groups had concerns about some aspects of all currently available instruments, such as acceptability to patients, structural validity, content validity and cross-cultural validity. Three of the six groups preferred the Dermatology Life Quality Index (DLQI), one group preferred Quality of Life Index for Atopic Dermatitis (QoLIAD), and two felt unable to state a preferred instrument based on the available evidence. Other instruments that were rated B or C were also discussed within the groups and comments were presented.

Table 5 Rating of outcome instruments used to capture health-related quality of life

Degree of recommendation	Instrument(s)	Recommendation
A	None	Could be recommended for use
B	English QoLIAD (U.K.)	Has the potential to be recommended in the future depending on the results of further validation studies
	English QoLIAD (U.S.A.)	
	French QoLIAD	
	German QoLIAD	
C	Spanish QoLIAD	Not recommended for use
	English DLQI (U.K.) ISDL	
D	Dutch QoLIAD	Not recommended to be used until further validation has been performed. Future recommendation would depend on the results of further validation studies
	DIELH	
	Danish DLQI	
	German DLQI	
	Spanish DLQI	
	FLQA-c	
	FLQA-d	
Italian QoLIAD		
	German Skindex-29	

DIELH, German Instrument for the Assessment of Quality of Life in Skin Diseases; DLQI, Dermatology Life Quality Index; FLQA, Freiburg Life Quality Assessment; QoLIAD, Quality of Life Index for Atopic Dermatitis; ISDL, The Impact of Chronic Skin Disease on Daily Life; Post meeting note: some instruments have subsequently changed category as a result of updating of the systematic review of validation studies for these instruments (see published review for details).⁹

The whole group discussions that followed focused mainly on the DLQI and QoLIAD, but other instruments including Skindex were also discussed.

The group then voted that psychological functioning, social functioning and physical functioning are all essential subdomains for the construct QoL and that there are no other essential subdomains. Subsequent voting on whether the DLQI, QoLIAD or Skindex could be recommended for the core outcome set failed to reach a consensus approval for any of the three scales (Table 6). As a result, no QoL instrument was recommended for the core outcome set at this meeting.

Table 6 Results of final voting to decide core outcome instrument for health-related quality of life (%): no consensus achieved

	Agreed	Disagreed	Unsure
Dermatology life quality index	45	35	20
Quality of life index for atopic dermatitis	26	59	15
Skindex	2	95	3

The reasons why DLQI was not rated more highly were discussed in detail, as DLQI is the most commonly used QoL scale in dermatology trials.

The issues around the structural validity of DLQI, particularly the redundancy of some items on the scale, lack of cultural validity data and the problem of subquestions within a single item were discussed. The group discussed what changes and further validation studies would be required to enable DLQI to be recommended for the core set and the possibility of a conditional recommendation for DLQI was rejected. It was confirmed that the main areas of concern are content validity and structural validity. In addition, responsiveness has not yet been established in patients with AE. The group also determined that further testing of QoLIAD with respect to measurement error, reliability, cross-cultural validity and responsiveness was required to be able to recommend this instrument and concerns were raised about the acceptability of the scale to patients.

Discussion also covered the need for other factors to be taken into account when selecting a QoL instrument, including the need to compare AE with other skin conditions, the need to compare new studies with older ones, the need for good responsiveness of the instrument and the length of time it takes to develop a new instrument.

The discussion showed a lot of support for DLQI, so the group were asked to decide whether the DLQI should be voted on again (as a preliminary recommendation), but there was insufficient support for this as a way forward (38% agreed, 48% disagreed, 14% unsure). Therefore, consensus on a preferred instrument for QoL in adults was not reached. The session on QoL was then brought to a close. A future research agenda for the QoL working group will be established.

Session 4: Long-term control domain (Chair: Jochen Schmitt)

Presentation 4-1: Introduction to the domain of long-term control

Professor Kim Thomas opened the session by discussing what is meant by the core outcome long-term control and reminded the group that previous agreement had been reached that the long-term control should apply to trials with a duration of 3 months or longer.

Owing to time constraints, meeting participants were asked to complete a questionnaire to elicit opinion for guiding future work in preparation for the HOME V meeting in 2017.

Presentation 4-2: How has long-term control been captured in randomized controlled trials of atopic eczema treatments?

Dr Sebastien Barbarot presented a systematic review showing that most long-term control studies use repeated measurement of disease severity (usually monthly clinician-reported outcomes assessing disease severity). Less than a third used either

flare data or standard medication use to assess long-term control.

Presentation 4.3: Thoughts on long-term control – Is long-term control a separate domain or a function of the other three domains?

Professor Andreas Wollenberg presented thoughts on why the only measure of long-term control that can be considered a truly separate outcome is flares. He proposed a flare definition and proposed a new outcome instrument based on time to first flare presented as a Kaplan–Meier plot.

A brief whole group discussion followed where the group discussed the potential advantages and limitations of a distinct measure of long-term control compared with repeated measurement over time using existing core instruments [e.g. Eczema Area and Severity Index (EASI) or POEM]. Different measures of long-term control could include time to first flare, behavioural changes in response to worsening disease and the use of rescue medicine. The need for a core set to include an outcome instrument for long-term control that would enable treatments for secondary flare prevention to be measured was reiterated.

The group then voted on whether long-term control should be measured as a separate unique construct (e.g. flares) or whether it should be captured using repeated measurement of one or more of the other three core outcomes. No consensus was reached. This issue needs further discussion at HOME V.

The long-term control session was then brought to a close.

Post meeting

The results of the questionnaires ($n = 23$) completed by the group were assessed after the meeting and this resulted in the identification of two pieces of work to be taken forward by the long-term control working group: qualitative work to establish what long-term control means to patients (with reference to the existing qualitative literature) and a consensus study to agree what is meant by the domain of long-term control to inform discussions at the HOME V meeting in 2017.

Meeting close

Participants were made aware of the work to disseminate the outcome of the previous HOME meeting (HOME III) with publications, an EASI training manual, EASI video and EASI app available on the HOME website (www.homeforeczema.org).

Professor Hywel Williams then thanked everyone for coming and for their valued contributions to the meeting. He reflected that much had been achieved in terms of recommending a new core instrument for patient-reported symptoms, but much remains to be done in terms of developing or further testing of instruments for QoL, and more conceptual work is needed on long-term control. He then drew the meeting to a close.

Acknowledgments

The HOME IV meeting was organized and coordinated by the HOME Executive Group [Hywel Williams (U.K.), Jochen Schmitt (Germany), Christian Apfelbacher (Germany), Phyllis Spuls (the Netherlands), Eric Simpson (U.S.A.), Kim Thomas (U.K.) and Joanne Chalmers (U.K.)] and the local organizing team (Åke Svensson and Laura von Kobyletzki in Sweden). Individual HOME Working Groups contributed to the collection and synthesis of evidence for presentation at the meeting in the form of up-to-date systematic reviews. Membership of the individual working groups is listed on the HOME website (www.homeforeczema.org). Assistance in preparing this report for publication was provided by Dr Natasha Rogers.

Further information and resources

Full minutes of the HOME IV meeting are available at www.homeforeczema.org. Details of how to use the POEM and downloadable POEM forms can be found at <http://www.nottingham.ac.uk/homeforeczema/resources.aspx>.

References

- HOME IV Meeting, Malmö, Sweden, 2015. Available at <http://www.nottingham.ac.uk/homeforeczema/meetings-and-events/home-iv-meeting-2015.aspx> (last accessed 21 June 2016).
- 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.
- 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.
- Schmitt J, Williams H. Harmonising Outcome Measures for Eczema (HOME), Report from the First International Consensus Meeting (HOME 1), 24 July 2010, Munich, Germany. *Br J Dermatol* 2010; **163**:1166–8.
- 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.
- 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.
- Mokkink LB, Terwee CB, Patrick DL *et al.* The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res* 2010; **19**:539–49.
- Terwee CB, Bot SD, de Boer MR *et al.* Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol* 2007; **60**:34–42.
- Heinl D, Prinsen CA, Deckert S *et al.* Measurement properties of adult quality-of-life measurement instruments for eczema: a systematic review. *Allergy* 2016; **71**:358–70.
- Schmitt J, Langan S, Stamm T, Williams HC. Harmonizing Outcome Measurements in Eczema (HOME) Delphi panel. Core outcome domains for controlled trials and clinical recordkeeping in eczema: international multiperspective Delphi consensus process. *J Invest Dermatol* 2011; **131**:623–30.

10 Meeting report: HOME IV, Sweden, J.R. Chalmers *et al.*

- 11 Schmitt J, Langan S, Deckert S *et al.* Assessment of clinical signs of atopic dermatitis: a systematic review and recommendation. *J Allergy Clin Immunol* 2013; **132**:1337–47.
- 12 Schmitt J, Langan S, Williams HC; European Dermato-Epidemiology Network. What are the best outcome measurements for atopic eczema? A systematic review. *J Allergy Clin Immunol* 2007; **120**:1389–98.
- 13 Schram ME, Spuls PI, Leeftang MM *et al.* EASI, (objective) SCORAD and POEM for atopic eczema: responsiveness and minimal clinically important difference. *Allergy* 2012; **67**:99–106.
- 14 Gerbens LAA, Chalmers JR, Rogers NK *et al.* Reporting of symptoms in randomised controlled trials of atopic eczema treatments: a systematic review. *Br J Dermatol* 2016; doi: 10.1111/bjd.14588. [Epub ahead of print].
- 15 Gerbens LAA, Prinsen AC, Chalmers JR *et al.* Evaluation of the measurement properties of symptom measurement instruments for atopic eczema: a systematic review. *Allergy* 2016. doi: 10.1111/all.12959. [Epub ahead of print].
- 16 Heintz D, Chalmers J, Nankervis H, Apfelbacher CJ. Eczema trials: quality of life instruments used and their relation to patient-reported outcomes. A systematic review. *Acta Derm Venereol* 2016; **96**:596–601.
- 17 Barbarot S, Rogers NK, Abuabara K *et al.* Strategies for measuring long-term control in atopic dermatitis trials: a systematic review. *J Am Acad Dermatol* 2016. (in press).
- 18 von Kobyletzki LB, Thomas KS, Schmitt J *et al.* What Factors are Important to Patients when Assessing Treatment Response: An International Cross-sectional Survey. *Acta Derm Venereol* 2016. doi: 10.2340/00015555-2480. [Epub ahead of print].
- 19 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.

Appendix

Harmonising Outcome Measures for Eczema (HOME) IV breakout groups

Name	Stakeholder Group	Country
Group 1		
Hywel Williams (facilitator for quality of life discussion)	Clinician – Dermatology	U.K.
Dedee Murrell (facilitator for symptoms discussion owing to the conflict of interest for Hywel Williams)	Clinician – Dermatology	Australia
Valeria Aoki	Clinician – Dermatology	Brazil
Julie Block	Patient/Carer/Patient Representative	U.S.A.
Lykke Bjerglund Graff	Pharmaceutical Industry Representative	Denmark
Burchard Marquort	Patient/Carer/Patient Representative	Sweden
Kristine Nograles	Pharmaceutical Industry Representative	
Yukihiro Ohya	Clinician – Paediatrician	Japan
Jasvinder Singh	Methodologist	U.S.A.
Anne Sulzer	Pharmaceutical Industry Representative	France
Helle Vestby Talmo	Patient/Carer/Patient Representative	Norway
Elke Weisshaar	Clinician – Dermatology	Germany
Group 2		
Christian Apfelbacher (facilitator)	Methodologist	Germany
Katrina Abuabara	Clinician – Dermatology/Methodologist	U.S.A.
Marius Ardeleanu	Pharmaceutical Industry Representative	U.S.A.
Tim Burton	Patient/Carer/Patient Representative	U.K.
Amanda Creswell-Melville	Patient/Carer/Patient Representative	Canada
Laurent Eckart	Pharmaceutical Industry Representative	France
Takeshi Nakahara	Clinician – Dermatology	Japan
Ibrahim Nasr	Clinician – Dermatology	
Marie-Louise Schuttelaar	Clinician – Dermatology	The Netherlands
Tracey Sach	Methodologist (Health Economist)	U.K.
Annika Volke	Clinician – Dermatology	Estonia
Carl-Fredrik Wahlgren	Clinician – Dermatology	Sweden
Stephan Weidinger	Clinician – Dermatology/Molecular Epidemiology	Germany
Group 3		
Kim Thomas (facilitator)	Methodologist	U.K.
Maren Awici-Rasmussen	Patient/Carer/Patient Representative	Norway
Sebastien Barbarot	Clinician – Dermatology	France
Linda Beckman	Other – Researcher	Sweden
Anthony Bragg	Pharmaceutical Industry Representative	U.K.
Rosemary Humphreys	Patient/Carer/Patient Representative	U.K.
Yoko Kataoka	Clinician – Dermatology	Japan

(continued)

Appendix (continued)

Name	Stakeholder Group	Country
Yael Leshem	Clinician – Dermatology	U.S.A.
Bronwyn Lund	Pharmaceutical Industry Representative	Denmark
Hiroyuki Murota	Clinician – Dermatology	Japan
Florent Torchet	Patient/Carer/Patient Representative	France
Laura von Kobyletzki	Clinician – General practitioner	Sweden
Andreas Wollenberg	Clinician – Dermatology	Germany
Group 4		
Phyllis Spuls (facilitator)	Clinician – Dermatology	The Netherlands
Maj Dinesen	Pharmaceutical Industry Representative	Denmark
Aaron Drucker	Clinician – Dermatology	Canada
Andrew Finlay	Clinician – Dermatology	U.K.
Louise Gerbens	Clinical – Other MD PhD Student – Dermatology	The Netherlands
Daniel Heintl	Student of Medicine	Germany
Marie-Anne Massuel	Pharmaceutical Industry Representative	France
Stephanie Merhand	Patient/Carer/Patient Representative	France
Jevgenija Smirnova	Clinician – Junior Doctor	Sweden
Åke Svensson	Clinician – Dermatology	Sweden
Group 5		
Eric Simpson (facilitator)	Clinician – Dermatology	U.S.A.
Carsten Flohr	Clinician – Paediatric Dermatology	U.K.
Henrique Akira Ishii	Patient/Carer/Patient Representative	Brazil
Teresa Løvold Berents	Clinician – Dermatology	Norway
Ian Osterloh	Pharmaceutical Industry Representative	U.K.
Cecilia (Sanna) Prinsen	Clinical Epidemiologist, Methodologist	The Netherlands
Lynn Purkins	Pharmaceutical Industry Representative	U.K.
Shoko Shindo	Clinician – Dermatology	Japan
Eli Synnøve Gjerde	Patient/Carer/Patient Representative	Norway
Roberto Takaoka	Clinician – Dermatology	Brazil
Cathy Zhao	Clinician – Dermatology	Australia
Jan Pander	Pharmaceutical Industry Representative	The Netherlands
Group 6		
Jochen Schmitt (facilitator)	Clinician – Dermatology	Germany
Madhur Garg	Pharmaceutical Industry Representative	Denmark
Jon Hanifin	Clinician – Dermatology	U.S.A.
Hitoshi Mizutani	Clinician – Dermatology	Japan
Matthew Ridd	Clinical – General Practitioner/Academic Researcher	U.K.
Marie Tauber	Clinician – Dermatology	France
Willem Kouwenhoven	Patient/Patient Representative	The Netherlands
Kosuke Yamaga	Clinician – Dermatology	Japan
Kim Katrine Clemmensen	Clinician – Dermatology	Denmark

One delegate (J.C.) acted as facilitator for the groups and did not participate in the small group discussions.