Harmonizing Outcome Measures for Eczema

HOME X Meeting

15-16th October 2022

Montreal, Canada

Meeting Report

List of Attendees

	Name	Stakeholder group	Country
1	Roselie Achten	Clinician	The Netherlands
2	Safin Aly	Researcher/methodologist	Canada
3	Petra Arlert	Industry representative	Sweden
4	Christian Apfelbacher	Researcher/methodologist	Germany
5	Andrea Cohee	Industry representative	United States of America
6	Marjolein de Bruin-Weller	Clinician	The Netherlands
7	Marlies de Graaf	Clinician	The Netherlands
8	Lawrence Eichenfield	Clinician	United States of America
9	Claire Feeney	Industry representative	UK
10	Allison FitzGerald	Patient advocate	Canada
11	Michaela Gabes	Researcher/methodologist	Germany
12	Louise Gerbens	Clinician	The Netherlands
13	Michael Haft	Researcher/methodologist	United States of America
14	Henrique Ishii	Patient/Patient advocate	Brazil
15	Carolyn Jack	Clinician	Canada
16	Michael Jacobson	Researcher/methodologist	United States of America
17	Maxine Joly-Chevrier	Researcher/methodologist	Canada
18	Mike Lanigan	Patient/Patient advocate	Canada
19	Wan-Ju Lee	Industry representative	United States of America
20	Sonia Montmayeur	Industry representative	Canada
21	Amy Paller	Clinician	United States of America
22	Catalina Rincon-Perez	Clinician	Mexico
23	William Romero Gallardo	Industry representative	Chili
24	Ana B Rossi	Industry representative	Brazil/France
25	Tammi Shipowick	Patient advocate	Canada
26	Eric Simpson	Clinician	United States of America
27	Wendy Smith Begolka	Patient advocate	United States of America

28	Phyllis Spuls	Clinician	The Netherlands
29	Jean-francois Stalder	Clinician	France
30	Louise Abildgaard Steffensen	Industry representative	Denmark
31	Isabelle Thibau	Researcher/methodologist	United States of America
32	Lisa van der Rijst	Clinician	The Netherlands
33	Annika Volke	Clinician	Estonia
34	Andreas Wollenberg	Clinician	Germany
35	Baki Emre Çetindağ	Patient/Patient Caregiver	Turkey
36	Piere Ahad	Researcher/methodologist	Canada
37	Yael Leshem	Clinician	Israel
38	Charlie Bouchard	Patient advocate	Canada
39	Darryl	Patient	Canada
40	Joanne Ramos	Patient/Patient Caregiver	Canada/Philippines
41	Julianne Denault	Patient/Patient Caregiver	Canada
42	Danielle Marcoux	Clinician	Canada

Saturday 15th October 2022 (13:00 – 17:00)

Aims of the HOME X meeting

- **Day 1**: Focus on implementation of the HOME core outcome set (COS): to develop implementation projects and advance the 3 newly formed working groups, each corresponding to an implementation theme.
- **Day 2**: To reach consensus on recommended **clinical signs** instrument(s) for clinical practice.

Participants

- **Day 1**: The meeting was attended by 33 delegates from 13 different countries. 9 (27%) were patients, patient caregivers or patient representatives, 7 (21%) were healthcare professionals, 8 (24%) were from the pharmaceutical industry and 9 (27%) were researchers.
- **Day 2**: The meeting was attended by 34 delegates from 13 different countries. 7 (21%) were patients, patient caregivers or patient representatives, 16 (47%) were healthcare professionals, 7 (21%) were from the pharmaceutical industry and 4 (11%) were researchers.

HOME X – Day 1: Implementation

The meeting was structured into four sessions.

SESSION 1: INTRODUCTION TO HOME

This session introduced the HOME initiative and outlined the key activities (including outcomes of the HOME IX meeting) and aims of the upcoming meeting.

SESSION 2: INTRODUCTION TO IMPLEMENTATION

The concept and importance of implementation of the completed HOME COS was highlighted. The uptake of the COS shows increase, but there are still significant gaps in implementation of the entire HOME COS. Only if the COS is utilized by stakeholders, the goals of research harmonization and ultimate patient benefit will be realized. If we do not use them this is another source of research waste.

Therefore, the HOME implementation roadmap was developed (link). It is an extension of the original HOME roadmap for COS development and provides a pragmatic framework to develop COS implementation strategies. Its content was explained and discussed.

Discussion points:

- Regulatory agencies are missing in HOME meetings.

- Difficulty of gaining FDA support of HOME instruments.

Next, the implementation working groups were introduced, based on HOME IX meeting (virtual, September 2021) and a pre-meeting survey.

1) Stakeholder engagement: Yael Leshem and Hywel Williams
2) Universal applicability: Laura Howells and Kim Thomas
3) Ease of use: Louise Gerbens and Phyllis Spuls

Participants were divided into small groups to think out-of-the-box on implementation projects for each working group; ideally projects that can be performed in 2 years.

SESSION 3: SMALL GROUPS FOR EACH IMPLEMENTATION WORKING GROUP

Projects for each working group were fed back to the group. Feedback was provided and in the end projects were prioritized for each group.

WG 1: Stakeholder engagement

Aim of WG1:

- To promote **adoption** of the HOME COS to multiple stakeholders in order to facilitate **uptake**.

- Project 1: FDA guidance document (*why to use the COS*). Big project, long-term goal. The FDA can give an unofficial seal of approval. There's similar one published for pediatrics trials. The involvement of patients, clinicians, major derm and allergy associations, industry: groups that endorse this to be implemented in AD clinical trials to lead political pressure to use it.
  Leaders: Andreas Wollenberg, Christian Apfelbacher, Thomas Bieber, Jochen Schmitt, Catalina Rincon-Perez, William Romero.
- Project 2: Dissemination and communication strategy for patient organizations like Global Skin and "skinfluencers" so they can influence organizations like FDA. Very powerful resource if it comes from patients, because treatments need to be useful for patients.
  Leaders: Tammi Shipowick (representative Global Skin) and Charlie Bouchard (patient and patient advocate (Eczema Quebec), Joanne Ramos, Andrea Cohee, Wan-Ju Lee.
- Project 3: Social media representatives (LinkedIn, Twitter, TikTok) who prepare messages for all social media channels and make social media dissemination packages that can be used across different platforms (incl. infographic).
  Leaders: same as project 2.
- Project 4: Inventory of regulators. Agreement of HOME membership of what the 'ask' is, mapping out the needs. Influencers within countries.
  Leaders: same as project 1.
- Project 5: Clarity on the process of how regulators endorse the COS.
  Leaders: same as project 1.

WG 2

Aim of WG2:

- To promote and support implementation of the COS in **different languages, cultures, and groups**.

- The purpose of this working group is **to share information** that helps core outcome set users to understand how to use the HOME Core Outcome Set in different settings and participant groups.

- Project 1: Identify if the 6 core outcome instruments have translations (first in French) and if their quality is okay. Develop methodology for identifying translations and evaluating their translation qualities. Start with French as a pilot and move to other languages. Translations need to be freely available. Should be accomplished in 6 months by students.
  Leaders: Christian Apfelbacher (mentor), Annika Volke, Maxine Joly Chevrier, Safin Aly (all students).
- Project 2 (side project): Accessibility of COS instruments across different ability levels. Video explaining patients the COS, to understand how to fill in the questionnaires (incl. understanding grading). Also, for patients with reading problems (questionnaires can induce injustice). Photos of AD across skin colors/ages, build a repository. Visual guide AD across skin types from National Eczema Society is available, opportunity of existing repository to build on.

WG 3: Ease of use

Aim of WG3:

- To minimise the **burden** (**time** and **effort**) and optimise the use of the COS.
- The purpose of this working group is **to provide guidance** how to best access, collect, analyse and interpret the COS, and to reduce overlap between core instruments for atopic dermatitis clinical trials.

- Project 1: Is the COS really easy to use? Analyzing time to complete (pre- and post-education, in different centers, if possible industry versus investigator-led studies, digital versus paper). Feasibility study.
  Leaders: Phyllis Spuls and Louise Gerbens.
- Project 2: How frequent should measures be done, what is the duration (and order)? Consensus meeting necessary after input from study by Beth Stuart, TREAT Registry Taskforce and maybe others. Also, when do we measure long-term control and how often?
- Project 3: Product (=COS) advertising. Access, copyrights, approval. Email and social media campaign. Movie by Mike Lanigan (patient, CEO Canada patient society) → combine with workgroup 1 project 2 and 3.
- Project 4: Make it easy to use. Education video for patients (why patients need to fill in the questionnaires; education about PP-NRS and long-term control (difficult for patients to understand)). Webinar.
- Project 5: National Eczema Association has an application ('Eczema Wise'; for symptoms and flares (pain, NRS itch peak 24h, stress)) with some HOME instruments. Can we adapt these to RCTs? Can we develop a universal code for open access and put it into apps/databases? More difficult because IT specialist(s) is (are) necessary. Inventory of existing apps should be a project, >30 are available. What is the experience with these apps, are they feasible?
- Project 6 (already ongoing): 'How to use the HOME COS' guide, led by Kim Thomas.

PRIORITIZED PROJECTS

- WG 1 Stakeholder engagement: project 2 (“Dissemination and communication strategy”) and project 3 from WG3 (“Product (=COS) advertising”)
- WG 2 Universal applicability: project 1 (“Develop methodology for identification and evaluation of translations” + “Translate 6 COS instruments to French if not available and evaluate their quality”)
- WG 3 Ease of use: project 1 (“Time to complete COS”)

SESSION 4: HOME: CHORD-COUSIN COLLABORATION (C3) AND BEYOND

The umbrella organization for Dermatology and related areas (e.g. plastic surgery, pediatrics) concerning COS was presented. C3 can be of help for different COS groups, not only for methodology but also for funding advice.

Sunday 16th October 2022 (10:00 – 17:00)

HOME X – Day 2: HOME Clinical Practice Set (HOME-CPS) – Clinical signs

The meeting was structured into four sessions.

SESSION 1: INTRODUCTION TO HOME CLINICAL PRACTICE SET (HOME-CPS)

Day 2 focused on the HOME-CPS. The HOME-CPS aims to provide patients, health care professionals, health systems and other stakeholders with a vetted list ("*pick and choose*") of valid and easy-to-use instruments to measure domains of health in patients with AD in the clinical practice setting. Feasibility is of main importance (time, access, costs).

Such instruments are beneficial on individual level (for severity assessment, shared decision making, and patient monitoring) and aggregated level (e.g. drug safety analysis, comparative effectiveness studies, informing clinical trials design). Different from the HOME COS in clinical trials, the HOME-CPS is not a mandatory core set of instruments, and neither the number of domains nor the number of instruments are limited.

Prior work identified symptoms (including itch intensity), eczema control, patient global assessment, clinician reported signs and eczema specific quality of life as the most important domains to measure in clinical practice. Previous consensus exercises recommended instruments for symptoms, itch intensity and eczema control. Today we focus on instruments that measure clinical signs of atopic dermatitis.

Summary of prior HOME-CPS work

1. **Prioritizing domains to guide the work of HOME-CPS (HOME online survey, May 2017)**
   The top prioritized domains of health to measure in patients with AD in clinical practice were: symptoms, long-term/eczema control, patient global assessment (PtGA), clinician reported signs and atopic eczema specific quality of life.
2. **Consensus on the recommended instruments to measure symptoms (HOME VI, Utrecht, 2018 & HOME VIII, 2020, virtual)**
   - The Patient-Oriented Eczema Measure (**POEM**)
   - The Patient-Oriented SCORing Atopic Dermatitis index (**PO-SCORAD**)
   - Numerical Rating Scales for itch intensity (**NRS-itch intensity**):
     a. A 24-hour peak itch NRS
     b. A 1-week peak itch NRS (PROMIS instrument)
     c. A 1-week average itch NRS (PROMIS instrument)
3. **Consensus on the recommended instruments to measure long-term control (HOME VIII, 2020, virtual)**

- **RECAP** (Recap of atopic eczema)
- **ADCT** (Atopic Dermatitis Control Tool)

SESSION 1: BACKGROUND AND CONCEPT OF CLINICAL SIGNS

The definition of a 'sign' was explained; a sign should be measured by a clinician. Further, the philosophy of HOME and its methodology was outlined.

A decision regarding an instrument should be based on validation information, feasibility characteristics and other factors (e.g., do you want to use it in your practice?). For HOME X, the systematic review of clinical signs by Schmitt et al. has been updated, following the HOME roadmap.

All aspects of validity were discussed. Content validity for a clinical signs instrument should include both intensity and extent, and should include the signs erythema, excoriation, oedema/papulation and lichenification as a minimum to achieve content validity (based on consensus at HOME III).

Next, all clinical signs instruments were presented.

Some important comments were made:

- In some countries there is a mandate for the use of EASI before start of new drug therapies (reimbursement). This may be an argument to include such instruments in the CPS.
- Feasibility for primary care should be kept in mind, because in many countries the patients are seen in primary care.

SESSION 1: SIGNS SYSTEMATIC REVIEW UPDATE AND NEW INSTRUMENTS

The updated systematic review of clinical signs was presented. 24 studies were included, COSMIN methodology adapted for ClinROMs (clinician-reported outcomes) was followed. Recommended instruments based on the results are shown in Figure 1.

Table 1. Clinical sign instrument recommendations. Instruments denoted in blue are composite instruments.

Recommended	**EASI, *mEASI*, oSCORAD, *SCORAD*, SGA x BSA**
Promising	**ADAS, ADSI, BSA, *CAPS*, SASSAD, vIGA-AD, vIGA-AD x BSA, ISGA, SGA, IGA x BSA**
Insufficient	***Rajka-Langeland*, TISS**

SESSION 2: SMALL GROUPS CP-CLINICAL SIGNS

Purpose of small groups:

- List top 3 instruments and why. Discuss bare minimum documentation for signs in clinical practice.

Before the start of the small groups a discussion was held concerning whether or not to include composite measures for the clinical signs practice set. Some participants thought it would be quick and easy: you can kill two birds with one stone. Others thought we already have recommendations for symptoms in clinical practice, and in the past HOME decided to distinguish patients- versus physician-reported signs. A vote was held. There was no consensus (56% of participants disagreed), and thus all instruments were taken to the small group discussions.

Small Group Reports – top 3 instruments

roup	No 1	No 2	No 3	Comments
1	SGA x BSA	EASI	oSCORAD	- SGA x BSA: broadly applicable, but SGA requires more work to define what it really represents. Should it be static, should it be the mean or a representative lesion. Which global measure should be included (SGA, IGA, vIGA-AD)? - EASI: already used, tools available, data can be used in clinical research.
2	SCORAD	IGA x BSA	EASI	- SCORAD: good content validity and PROs included, quick and easy to score, assesses extent and intensity, good with PO-SCORAD; limitation that it is not included in COS for trials. - EASI: part of HOME COS for trials, easy to compare with registries, feasible because many people use it but not always for everybody (in the right hands it's pretty quick)).
3	vIGA-AD	vIGA-AD x BSA	EASI	- vIGA-AD: includes extent when patients have severe AD, very feasible, easy to translate to patients (interpretability for patients)). - vIGA-AD x BSA: instead of SGA because validated in AD, combination of concepts but BSA may be a heavier factor. Combining the two in a way that's the intensity less "secondary" to the whole score would be better than the product. BSA alone does not reflect the disease. - EASI: easy to use when experienced, but not for everyone; easier to combine and pool; validating clinical practice versus clinical trials; in moderate-to-severe patients a score may help to patient to be felt taken seriously.
4	SGA x BSA	SCORAD	EASI	- SGA x BSA: global scales are quick, but they're not specific enough. Having the physician take the time for completing the

				EASI/SCORAD – will gain confidence and trust. - SCORAD: composite (win-win), patients feel being heard by asking itch and sleep, accurate picture if you take time for an evaluation instead of a very quick measure.
5	EASI	vIGA-AD	BSA x or alongside IGA	- EASI: for dermatologists with good resources/tertiary care, already used in registries and trials, and acknowledged by regulatory bodies. - vIGA-AD: for primary care physicians, global uptake and trainings available, used in studies, can help with referrals. - BSA x or alongside IGA: type to discussed; for secondary care dermatologists, both intensity and extent.

SESSION 3: CP-CLINCAL SIGNS FACILITATED DISCUSSION

A discussion was held to make clear what the group was voting on:

- Can we vote on instruments for all settings, or should we select tools for primary, secondary and/or tertiary care?
  There were no GPs in the room, a drawback. Participants wondered if the decision should be taken back to the larger community. Others felt it is not a mandated set, we are providing options/recommendations for tools to use which can be tools for different settings. Further, in earlier CPS meetings, the setting was not determinative.
- Are we talking about instruments to allow monitoring over time? Or to facilitate patient-doctor interaction? Or for reimbursement issues and referral decisions? Or to capture data in clinical practice to use for real world observations and registries?
  In some countries real world and research are close, and therefore they like to use the same instruments (e.g. Denmark, the Netherlands); versus in other countries, like the UK where primary care handles most of eczema cases, they need instruments for referral decisions.
  A comment was made that we do not need a core set unless we use it for research. Instruments are only useful in big populations. Measurement properties are designed for populations, not for individuals. “Research meets practice at measurement.”

This discussion was followed by two voting questions:

1. Are we excluding primary care as a setting in the vote of signs instruments by physicians for clinical practice? 21 **no**, unsure 4, yes 4.
2. Should we restrict voting to only the instruments identified by the three small groups? 30 **yes**, 1 no.

SESSION 3: CP-CLINICAL SIGNS VOTING

Voting on all top 3 instruments followed, see Table 1. 33 people were in the room.

Before voting, the global + (alongside) / x (product) BSA was discussed. The group decided to vote on the concept of "global x BSA", and at a later stage the executives should come back to the group with details on which global to use.

Table 1. Consensus voting results for instruments under consideration after small group recommendations

Instrument	Yes	No	Unsure	Abstentions (COI)
IGA x BSA (n=31)	**20 (**64.5**%)**	**7** (22.6%)	**4** (12.9%)	**2**
EASI (n=28)	**26** (92.9%)	**1** (3.6%)	**1** (3.6%)	**4**
oSCORAD (n=32)	**11** (34.4%)	**19** (59.4%)	**2** (6.5%)	**1**
SCORAD (n=32)	**13** (40.6%)	**18** (56.3%)	**1** (3.1%)	**1**
vIGA-AD (n=29)	**22** (75.9%)	**5** (17.2%)	**2** (6.9%)	**3**
IGA alongside BSA (n=33)	**24** (72.7%)	**5** (15.2%)	**4** (12.1%)	**0**

Limitations and dissenting voices regarding votes

- The voting questions were not on the screen before voting.
- mEASI was not on the tables.
- Group size of 33 people: is it sufficient for voting? The credibility may be affected. The number of participants also depends on the location of the meeting (different instruments used in different countries may affect the vote). However, the small group size allowed for people at the meeting to be very engaged. It was discussed if a Delphi exercise with the whole HOME community would be good after the meeting to ratify the consensus. However, limitations to this approach are: online exercise does not have the same deep understanding of the material; less engagement; no multistakeholder interaction; limited technical support and finance available. Thus, it was decided not to hold a Delphi exercise.
- The content of oSCORAD was not clear in all groups.
- The order of the voting and the advice to "restrain" voting (to minimize instrument number) led some people to vote the oSCORAD out, but as the SCORAD was also left out – they felt they would have changed their initial response 'had they known'. Others mentioned this dilemma comes from the methodology of voting instrument after instrument, and that others in the group faced the same concerns with other similar situations (e.g BSA/IGA). Did it fall out because people were selective? However, the votes were performed independently on each instrument.
- SCORAD is used in the EDF guideline and for potential payer issues. It could be a problem that HOME does not include it. The important comment was made that although SCORAD is not included, it has a place historically and it can still be used. Further, HOME is an evidence-based initiative and consensus driven to recommend instruments, not guidelines.
- Based on the (o)SCORAD discussion, a vote on whether to revote on SCORAD and oSCORAD was held (although not according to HOME methodology): "vote to revote" - Yes 17, **No** 13, Unsure 3 (denominator 33). This means a negative vote per HOME consensus criteria.