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Appendix SI. Instructions for clinical and photographic raters.

Hand Eczema Severity Index (HECSI)[1,2]

Hand eczema severity index (HECSI) ranges from 0-360 points and incorporates both the extent and severity of hand eczema. According to the scale, the hands are divided into five regions: fingertips (corresponding to the distal phalanges), fingers (excl. fingertips), palm of hands, back of hands and wrists. Be aware that the fingertips should not be taken into account when assessing the fingers. The clinical signs considered are erythema, infiltration/papulation, vesicles, fissures, scaling and oedema.

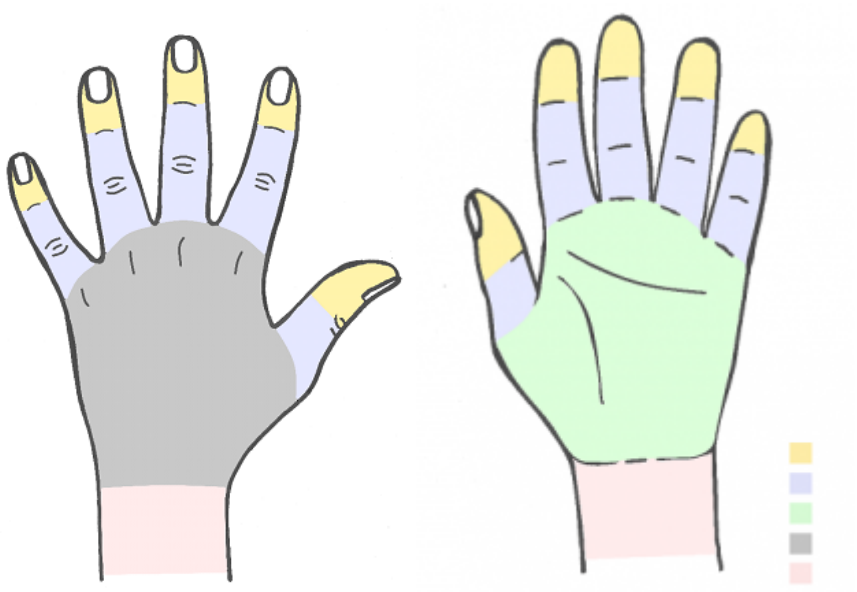


Figure 1: Regions of the hands

How to assess hand eczema severity with HECSI

The first step is to assess the extent of eczema for a given region e.g. fingertips on both hands with an area score (Table 1). The second step is to assess the average severity (none, mild, moderate or severe) of the six clinical signs at each given region. To calculate the total HECSI, repeat the process for all five regions.

Area / extent

The five different area scores are given in Table 1. The area score is given collectively for both hands. For example, if only one palm of the hands is completely covered by eczema, the area score will be 50% (score of 2).

Table 1: Area score scale

Area score scale (based on the area of BOTH hands)	
0	0% affected area
1	1–25% affected area
2	26–50% affected area
3	51–75% affected area
4	76–100% affected area

Severity of symptoms

If there are areas with mild and severe symptoms close to equal in size, a score of 2 (moderate) would be the most appropriate. If the majority of the involved areas correspond to a score 1 (mild), a score of 1 is more appropriate. Be careful not to score the highest severity in a region but the average one.

The severity of vesicles is not only based on the size of the vesicles but also the density. Thus, severe vesicles (score of 3) can comprise very large vesicles or a high density of several small vesicles in a region.

For assessment of oedema, please compare the area with eczema with the corresponding clear area. If for example all fingers are covered with eczema and there are no corresponding areas to compare with, please give an approximate score for the oedema.

Keep in mind that hyper or hypopigmentation are not considered as clinical symptoms when using the HECSI. Erythema should only be taken into account in the case of active hand eczema.

Interpretation of the final HECSI score

According to the literature, a HECSI score of 1-16 corresponds to mild hand eczema, 17-37 to moderate, 38-116 to severe and >116 to very severe.[3,4]

HECSI scoring form

	Fingertips	Fingers	Palm of hands	Back of hands	Wrists
Erythema					
Papulation/induration					
Vesicles					
Fissures					
Scaling					
Oedema					
Affected area					

Severity: 0 = none 1 = mild 2 = moderate 3 = severe

Affected area: 0 = 0% 1 = 1-25% 2 = 26-50% 3 = 51-75% 4 = 76-100%

Appendix SII. Instruction guide for patient-provided photographs (translated from Dutch).

Take **4** photos of the hands:

1. Photo 1: Left dorsum of the hand
2. Photo 2: Left palm of the hand
3. Photo 3: Right dorsum of the hand
4. Photo 4: Right palm of the hand

Example:

Photo 1: left dorsum of the hand

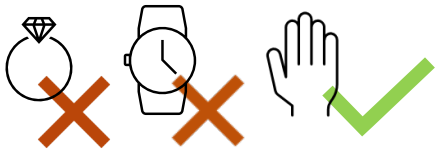
Photo 2: left palm of the hand

Photo 3: right dorsum of the hand

Photo 4: right palm of the hand

Step-by-step plan:

1. Remove jewellery/watches.



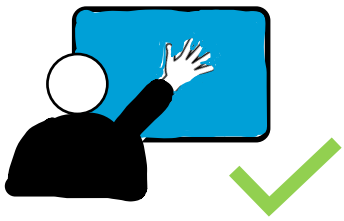
2. Roll up sleeves.

3. Use the smartphone.

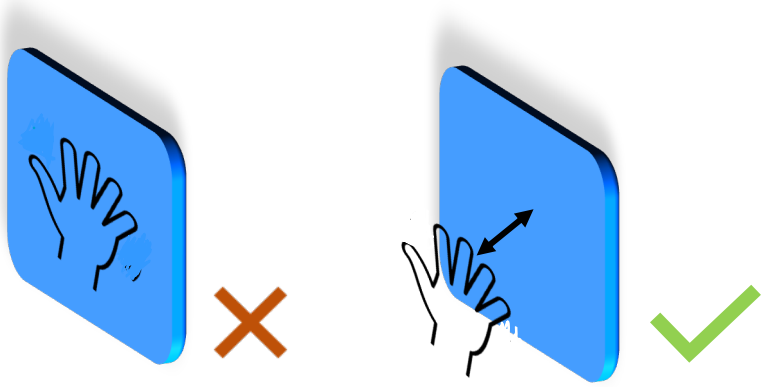
4. Turn off the flash

5. Do not zoom in or out.

6. Take the photos against the blue paper on the wall.

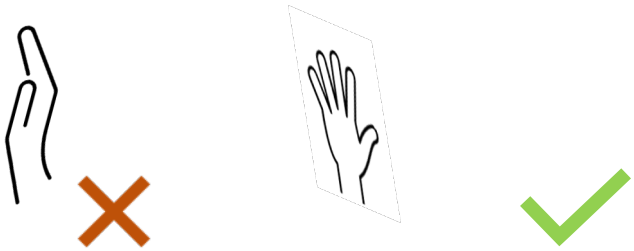


7. Hold the hand directly in front of the blue paper. The hand should not touch the paper!



8. Spread the fingers.

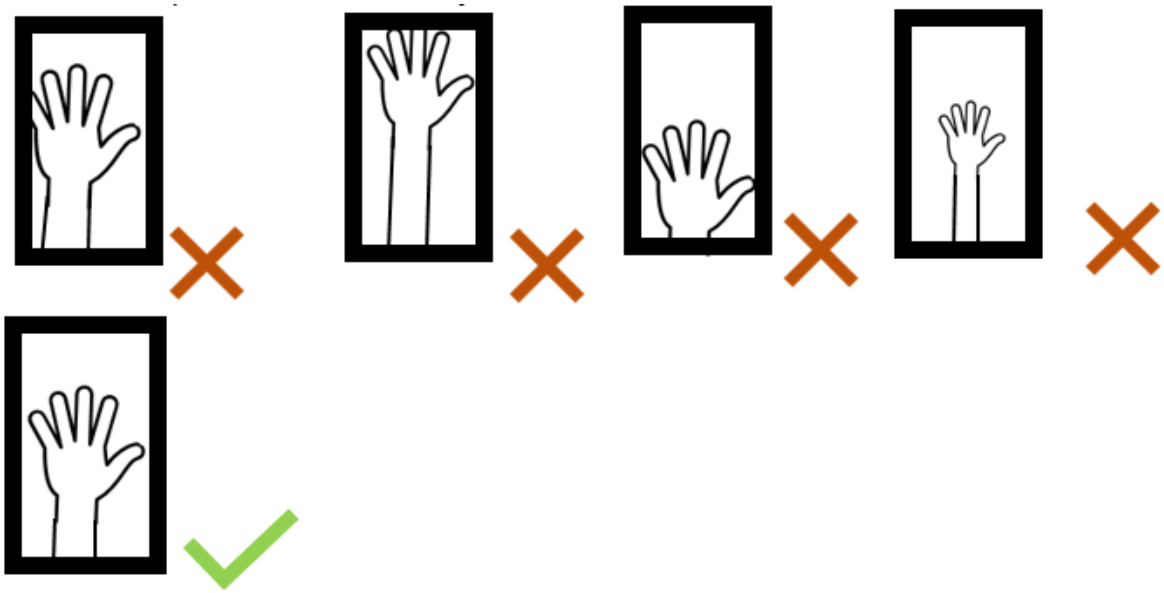
9. Stretch the fingers/wrist.



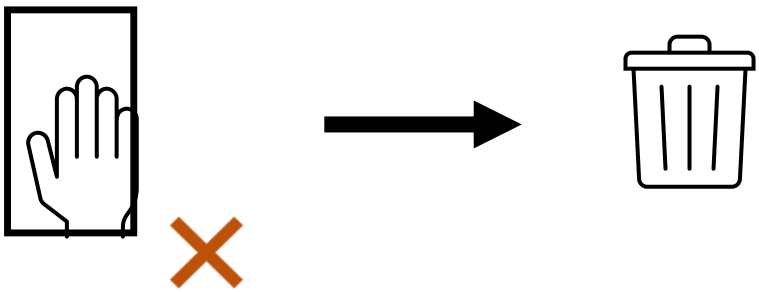
10. Hold the phone in upright position.

11. Keep the hand directly in front of the camera.

12. The entire hand and wrist should be in frame. Also, avoid leaving too much space around the edges.



13. Delete the photos that do not meet the requirements. Keep 4 photos.
    1. Photo 1: Left dorsum of the hand
    2. Photo 2: Left palm of the hand
    3. Photo 3: Right dorsum of the hand
    4. Photo 4: Right palm of the hand



Appendix SIII. Sample size calculations.

PASS power analysis & sample size software was used to calculate the required sample size for the current study, with assistance of a statistician experienced in the use of this software.[5] Based on the study by O'Connor et al., in which an overall concordance between photograph-based vs clinical diagnosis of different skin diseases, for example eczema, of 83% was found[6], the sensitivity and specificity of participant-provided photographs to diagnose hand eczema is assumed to be at least 80%. However, as in the study of O'Connor et al. also other skin diseases were included, and the hands are a very well-defined area of the body, which makes it easy to take pictures of by the participant him or herself, the true sensitivity and specificity could be even higher. Based on this assumption, a one-sample sensitivity and specificity power analysis was performed[7-10]: a total sample size of 40 participants, including 20 participants with and 20 participants without hand eczema, achieves 80% power to detect a change from sensitivity and specificity from 0,50 to 0,80, with a target alpha value of 0,05. A null-hypothesis of a sensitivity and specificity of 0,50 was chosen, as a value of below 0,50 would not be of clinical importance. A lower sample size would be required in case of a true sensitivity and specificity higher than 80%.

Assessment and accurate classification of the severity of hand eczema is essential, for example to evaluate the effectiveness of treatment. Several tools to measure the severity of hand eczema are available, of which the HECSI is the most frequently used tool in clinical trials, as well as in clinical daily practice.[11] By using the HECSI, both the extent and the intensity of hand eczema symptoms could be assessed.[2] Five different areas of the hand, including the fingertips, fingers, palms, back of the hands and the wrists are scored for six clinical signs: erythema, induration/papulation, vesicles, fissuring, scaling oedema.[2] The total HECSI score is a multiplication of the total sum of the intensity of each clinical feature, and ranges from 0-360 points. It has been shown that the HECSI is a valid tool and has good reliability and responsiveness, with an intra-classification coefficient (ICC) for inter and intra-rater reliability of approximately 0,80 and 0,90, respectively.[2,4] In a study of Baumeister et al, ICC's for intra and inter-rater reliability of using the HECSI when assessing the severity of hand eczema based on professional photographs were approximately 0,60.[12] However, in the study of Baumeister et al, no patients with severe hand eczema were included. Possibly, different values of intra-rater reliability would have been found when patients with severe hand eczema were included as well.

A sample size of 63 participants with hand eczema achieves 80% power to detect an ICC of 0,70 under the alternative hypothesis when the ICC under the null hypothesis is 0,50, with a significance level of 0,05, using the intraclass correlation power analysis,[13,14] also available in PASS power analysis & sample size software. A null-hypothesis of an ICC of 0,50 was chosen, as an ICC of ≥0,50 is considered as moderate, and therefore the minimum ICC for clinical importance. In case the ICC under the alternative hypothesis would be higher than

0,70 (which could be assumed based on the assumption that most photographs will be on sufficient quality, due to the instructions that are given to the participants beforehand), the required sample size would be lower than 63 participants.

As it would be interesting to assess criterion validity all different categories of severity of hand eczema (almost clear, moderate and severe-to-very severe), the sample size of all individual severity categories of hand eczema need to be of adequate size. For example, it could be more difficult to assess the severity for almost clear cases of hand eczema, when compared to cases with very severe hand eczema. Based on photographs, clinical signs of cases with severe hand eczema may hypothetically be better visible when compared to cases with only mild clinical signs. Therefore, a kappa test for agreement was performed in PASS power analysis & sample size. A sample size of 76 participants, including 19 participants with almost clear, 19 participants with moderate, 19 participants with severe-to-very severe HE, achieves 80% power to detect a true kappa value of 0,70 in a test of H0: Kappa = 0,50 vs H1: Kappa ≠ 0,50, based on a significance level of 0,05. Again, the sample size would be lower in case of a higher true kappa value of 0,70 (which is assumed to be the case, as participants are provided with instructions beforehand).

Besides abovementioned calculations on the required sample size to answer the questions on criterion validity, an intraclass correlation power analysis[13,14] was performed to calculate the required sample size to answer the research questions regarding intra- and inter-rater agreement. A sample size of 32 participants with hand eczema with four observations per subject achieves 80% power to detect an ICC of 0,70 under the alternative hypothesis when the ICC under the null hypothesis is 0,50. A null-hypothesis of an ICC of 0,50 was chosen, as an ICC of ≥0,50 is considered as moderate, and therefore the minimum ICC for clinical importance. In practice, the alternative hypothesis might be even higher, which requires a lower sample size.

All in all, based on the assumptions and sample size calculations as described above, a total sample size including 19 participants with almost clear, 19 participants with moderate, 19 participants with severe and 19 patients with very severe hand eczema, and an additional 20 participants without hand eczema would be required to answer the research questions of the current study. Due to the scarcity of patients with very severe hand eczema visiting the outpatient clinic of our site during the study period, it was decided to combine the categories severe and very severe hand eczema to one category. Based on the assumption of approximately 20-30% drop out, for example due to blurry images, we aimed for a sample size of at least 93 patients, including 24 participants without hand eczema and 69 patients with hand eczema, evenly distributed among the different severity categories (almost clear: 23; moderate: 23; severe-to-very severe: 23).

References

1 Yüksel YT, Nørreslet LB, Agner T. Training module HECSI 2024. Available at: https://hecsiscore.com/training-module/. Accessed: 7 november 2024.

2 Held E, Skoet R, Johansen JD *et al.* The hand eczema severity index (HECSI): A scoring system for clinical assessment of hand eczema. A study of inter- and intraobserver reliability. *Br J Dermatol* 2005; **152**: 302-7.

3 Yüksel YT, Agner T, Ofenloch R. New evidence on the minimal important change (MIC) for the Hand Eczema Severity Index (HECSI). *Contact Dermatitis* 2021; **85**: 164-70.

4 Oosterhaven JAF, Schuttelaar MLA. Responsiveness and interpretability of the Hand Eczema Severity Index. *British Journal of Dermatology* 2020; **182**: 932-9.

5 NCSS Statistical Software. Webpage PASS: Power Analysis & Sample Size 2024. Available at: https://www.ncss.com/software/pass/. Accessed: 6 November 2024.

6 O'Connor DM, Jew OS, Perman MJ *et al.* Diagnostic accuracy of pediatric teledermatology using parent-submitted photographs a randomized clinical trial. *JAMA Dermatol* 2017; **153**: 1243-8.

7 Zhou X-H, Obuchowski NA, McClish DK. *Statistical Methods in Diagnostic Medicine*. New York: Wiley-Interscience; 2002. 193-229.

8 Machin D, Campbell MJ, Tan SB *et al. Sample Size Tables for Clinical Studies*, Third edn. Chichester: Wiley-Blackwell; 2008.

9 Obuchowski NA, Zhou X-H. *Prospective studies of diagnostic test accuracy when disease prevalence is low*; 2002.

10 Li J, Fine J. On sample size for sensitivity and specificity in prospective diagnostic accuracy studies. *Statistics in medicine* 2004; **23**: 2537-50.

11 Rönsch H, Apfelbacher C, Brans R *et al.* Which outcomes have been measured in hand eczema trials? A systematic review. *Contact Dermatitis* 2019; **80**: 201-7.

12 Baumeister T, Weistenhöfer W, Weistenhöfer W *et al.* Spoilt for choice-evaluation of two different scoring systems for early hand eczema in teledermatological examinations. *Contact Dermatitis* 2010; **62(4)**: 241-7.

13 Winter BJ. *Statistical Principles in Experimental Design*, Third edn. New York: McGraw-Hill; 1991.

14 Walter SD, Eliaszi M, Donner A. Sample size and optimal designs for reliability studies. *Statistics in Medicine* 1998; **17**: 101-10.