Tremfya® ▼ (guselkumab)

Demonstrated sustained relief in Psoriasis at 5 years and in Psoriatic Arthritis at 2 years*[1,2]

COMPLETE SKIN CLEARANCE

- **At Week 16:** PASI 100 achieved in more than 1/3 of PsO patients treated with TREMFYA®.†[3]
- **Long term:** PASI 100 response rate of over 50% at Week 52 sustained at 5 years in PsO patients treated with TREMFYA®.†[1]

RAPID JOINT EFFICACY

- **At Week 4:** ACR20 achieved in 20% of PsA patients treated with TREMFYA®.[2]
- **Long term:** 74% ACR20 response rate seen at 1 year and sustained at 2 years in PsA patients treated with TREMFYA®.¶[2,4]

PROVEN DURABILITY

- Most patients who started on TREMFYA®, stayed on TREMFYA® long-term.[2,5]

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*Sustained improvements in psoriasis disease severity (as measured by PASI 90 and PASI 100 scores) and sustained improvements in psoriatic arthritis disease severity (as measured by ACR scores, HAQ-DI scores and resolution of enthesitis and dactylitis).[1,2] †PASI 100 analysis not part of the statistical analysis plan. 37.4% of patients treated with TREMFYA® achieved PASI 100 at Week 16 (n=329) vs 0.6% of patients treated with placebo (n=174; p<0.001; Non-responder imputation [NRI]).[3] ‡Patients achieving PASI 100 at Week 52: 50.5% (Treatment failure rules [TFR]), 51.3% (As observed), and 47.1% (NRI). In patients randomised to TREMFYA® at baseline. Patients achieving PASI 100 at Week 252: 51% (TFR), 52.8% (As observed) and 39.5% (NRI).[1] ¶In patients treated with TREMFYA® q8w. 74.6% (n=248) of TREMFYA® q8w patients achieved ACR20 at 1 year, and 74% (n=248) of TREMFYA® q8w patients achieved ACR20 at 2 years (NRI).[2,4] Complete skin clearance: Psoriasis Area and Severity Index [PASI] 100.[6] ACR20 – 20% improvement in a set of core measures: tender joint count, swollen joint count, patient's assessment of pain, patient's global assessment of disease activity, physician's assessment of physical function, patient's assessment of physical function and acute-phase reactant value.[7] Durability, also known as patient retention or drug survival, is a combination of efficacy, safety, tolerability and patient satisfaction or preference.[8] VOYAGE 1 was a Phase 3, double-blind, placebo- and active comparator-controlled clinical trial that evaluated the efficacy and safety of TREMFYA® in patients with moderate-to-severe plaque psoriasis.[1] DISCOVER-2 was a Phase 3, double-blind, multi-centre, placebo-controlled clinical trial that evaluated the efficacy and safety of TREMFYA® in bio-naïve patients with active PsA.[9] TREMFYA® is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy.[10] TREMFYA®, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.[10]

References: 1. Griffiths CEM, et al. Maintenance of Response Through 5 Years of Continuous Guselkumab Treatment: Results From the Phase 3 VOYAGE 1 Trial. Presented at the 16th Annual Coastal Dermatology Symposium. October 15-16, 2020. **2.** McInnes IB, et al. Arthritis Rheumatol. 2021 Nov 1. doi: 10.1002/art.42010. **3.** Blauvelt A, et al. J Am Acad Dermatol 2017;76:405-417. **4.** McInnes IB, et al. Arthritis Rheumatol. 2021;73:604-616. **5.** Blauvelt A, et al. J Am Acad Dermatol 2021;S0190-9622:02816-4. **6.** Strober B, et al. J Am Acad Dermatol 2016;75:77-82.e7. **7.** Felson DT, LaValley MP. Arthritis Res Ther 2014;16:101. **8.** Geale K, et al. Rheumatol Adv Pract 2020;4:rkaa070. **9.** Mease PJ, et al. Lancet 2020;395:1126-1136 (Including supplementary appendix). **10.** TREMFYA® (guselkumab) 100 mg Summary of Product Characteristics.

ACR, American College of Rheumatology; **HAQ-DI**, Health Assessment Questionnaire - Disability Index; **PASI**, Psoriasis Area and Severity Index; **PsA**, psoriatic arthritis; **PsO**, psoriasis; **q8w**, every 8 weeks.

Tremfya▼ 100 mg solution for injection in pre-filled pen
PRESCRIBING INFORMATION
ACTIVE INGREDIENT(S): Guselkumab
Please refer to Summary of Product Characteristics (SmPC) before prescribing. **INDICATION(S):** Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Treatment of active psoriatic arthritis in adult patients, alone or in combination with methotrexate, who have had an inadequate response or have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy. **DOSAGE & ADMINISTRATION:** For use under guidance/supervision of physician experienced in diagnosis and treatment of conditions for which Tremfya is indicated. Subcutaneous injection. Avoid areas showing psoriasis. **Adults:** For both indications, 100 mg at weeks 0 and 4, followed by maintenance dose every 8 weeks. In the case of psoriatic arthritis, for patients at high risk for joint damage according to clinical judgement, consider a dose of 100 mg every 4 weeks. Consider discontinuation if no response after 16 weeks of treatment for plaque psoriasis and after 24 weeks for psoriatic arthritis. **Children:** No data available in children/adolescents <18 years. **Elderly:** No dose adjustment required, limited information in subjects aged ≥ 65 years, very limited information > 75 years. **Renal & Hepatic impairment:** Not studied. **CONTRAINDICATIONS:** Serious hypersensitivity to active substance or excipients; clinically important, active infection. **Refer to SmPC for full list of excipients. SPECIAL WARNINGS & PRECAUTIONS:** *Infections:* Potential to increase risk. If signs/symptoms of clinically important chronic/acute infection occur, monitor closely and discontinue Tremfya until resolved. *Tuberculosis:* Evaluate patients for TB pre-treatment; monitor for signs/symptoms of active TB during and after treatment. Consider anti-TB therapy prior to Tremfya if past history of latent/active TB and adequate treatment course not confirmed. *Serious hypersensitivity reaction:* Includes anaphylaxis. Some serious hypersensitivity reactions occurred several days after treatment and included urticaria and dyspnoea. If occurs, discontinue Tremfya immediately and initiate appropriate therapy. *Hepatic Transaminase Elevations:* An increased incidence of liver enzyme elevations has been observed in patients treated with Tremfya q4w compared to patients treated with Tremfya q8w or placebo. When prescribing Tremfya q4w in psoriatic arthritis, consider evaluating liver enzymes at baseline and thereafter according to routine patient management. If increases in ALT or AST are observed and drug-induced liver injury is suspected, Tremfya should be temporarily interrupted until this diagnosis is excluded. *Immunisations:* Consider completing all appropriate immunisations prior to Tremfya. Do not use live vaccines concurrently with Tremfya; no data available; before live vaccination, withhold Tremfya for at least 12 weeks and resume at least 2 weeks after vaccination. **SIDE EFFECTS: Very common:** Respiratory tract infection. **Common:** headache, diarrhoea, arthralgia, injection site reactions, transaminases increased. **Other side effects:** hypersensitivity, anaphylaxis, rash, gastroenteritis, herpes simplex infections, tinea infections, neutrophil count decreased, urticaria. **Refer to SmPC for more detail on side effects. PREGNANCY:** Avoid use of Tremfya; no data. Women of childbearing potential should use effective contraception during and for at least 12 weeks after treatment. **LACTATION:** It is unknown whether guselkumab is excreted in human milk. A decision should be made to discontinue, or abstain from initiating treatment with Tremfya taking into account the benefit of breast-feeding to the child and the benefit of Tremfya therapy to the woman. **INTERACTIONS:** No dose adjustment when co-administering with CYP450 substrates. Concomitant immunosuppressive therapy or phototherapy not evaluated. **Refer to SmPC for full details of interactions. LEGAL CATEGORY:** Prescription Only Medicine (POM) **PRESENTATIONS, PACK SIZES, MARKETING AUTHORISATION NUMBER(S) & BASIC NHS COSTS**

PRESENTATIONS	PACK SIZES	MARKETING AUTHORISATION NUMBER(S)	BASIC NHS COSTS
Pre-filled pen (100mg)	X 1	NI: EU/1/17/1234/002 GB: PLGB 00242/0665	£2250

MARKETING AUTHORISATION HOLDER: Northern Ireland: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium. Great Britain: Janssen-Cilag Limited, 50-100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4EG, UK **FURTHER INFORMATION IS AVAILABLE FROM:** Janssen-Cilag Limited, 50-100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4EG, UK. Prescribing information last revised: June 2021

Adverse events should be reported. ▼This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited on 01494 567447 or at dsafety@its.jnj.com.

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Content validity of the Recap of atopic eczema (RECAP) instrument in Dutch, English and German to measure eczema control in young people with atopic eczema: a cognitive interview study

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Data availability: Data are available upon request from the corresponding author.

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Ethics statement: The ethic committees of all participating institutions approved this project.

What's already known about this topic?

At this moment, Recap of atopic eczema (RECAP) is a Harmonising Outcome Measures for Eczema (HOME) initiative recommended instrument as for the core outcome domain of atopic eczema long-term control. Content validity of RECAP for self-completion by adults and of the proxy-version has been assessed.

What does this study add?

In this study, content validity (comprehensibility, relevance, and comprehensiveness) of the self-reported version of RECAP among young people (aged 8-16 years) with atopic eczema across the United Kingdom, Germany and the Netherlands is assessed. Based on these findings, key recommendations on how to measure eczema control in young people with atopic eczema are formulated.

What are the clinical implications of this work?

The Dutch, English and German self-completion versions of RECAP are recommended for use in adolescents from the age of twelve. The proxy-version could be used in children younger than twelve years or when children are cognitively or physically incapable of reporting their experience of eczema control. Caregivers should be encouraged to complete RECAP together with their child where possible.

Abstract

Background Recap of atopic eczema (RECAP) is a patient-reported outcome measure (PROM) assessing eczema control. This instrument has been developed and validated in the UK. There is a self-reported and a proxy-reported version in English, Dutch and German. However, it is unclear whether the self-reported version shows adequate content validity when completed by young people (8-16 years) in these languages.

Objectives To assess the content validity (comprehensibility, relevance and comprehensiveness) of the English, German and Dutch versions of the self-reported RECAP in young people with atopic eczema and to identify the most appropriate age cut-off for self-completion.

Methods We conducted 23 semi-structured cognitive interviews with young people from 8 to 16 years, using the "think-aloud" method. In Germany and the Netherlands, participants were recruited in dermatology clinics and in the UK through social media and existing mailing lists. Interviews were audio recorded, transcribed verbatim and analysed in the three languages, using a problem-focused coding manual. Transcripts were coded by two independent reviewers in each country. Themes were translated into English and compared across the three countries.

Results Significant age-related comprehensibility issues with the last three items of the questionnaire occurred with young people aged 8 to 11 years, causing difficulties completing RECAP without help. However, older children had only minor problems and were able to complete the questionnaire by themselves. The self-reported version of RECAP has sufficient content validity for self-completion in young people aged 12 years and above. However, the German version with some translational adaptations may be appropriate for children from the age of 8 years. There may be some situations, where the proxy-version is needed for older children too.

Conclusions: The self-reported version of RECAP is appropriate for use from the age of 12 years. The proxy-version can be used in children younger than 12 years. Other measurement properties should be further investigated.

Introduction

Atopic eczema (AE) is a common, inflammatory skin disease affecting both children and adults.[1] A lifetime prevalence of 15-30% is reported for children and 2-10% for adults.[2] The incidence of AE has increased over the past decades in industrial countries.[3,4] ENREF 2 AE is a chronic relapsing condition, typically characterised by period of flare and remission. In terms of AE, we talk about flares that are periods of high disease activity. These 'uncontrolled periods' are associated with higher disease burden.[5] In addition to lowering AE-related symptoms, treatment aims to reduce the intensity and quantity of flares. Assessing how well the eczema is controlled is therefore an important outcome when evaluating the efficacy of treatments.[6] The patient's perspective can be captured using patient-reported outcome measures (PROMs).[7] For the assessment of the experience of eczema control, a new PROM called RECAP has been recently developed and validated in the UK.[8] RECAP is recommended by Harmonising Outcome Measures for Eczema (HOME) initiative as part of the core outcome set for AE.[9] The questionnaire consists of seven questions with five response options each. Currently a self-completion and proxy-reported version are available validated, using adults and parents of affected children.[10-13] However, discrepancies between proxy- and self-reported PROMs in young people has been described in other clinical areas.[14,15] In addition, self-reporting could improve engagement and treatment adherence in young people as they become partners in their treatment.[16,17] Therefore, self-completion of RECAP is preferred. However, it is unclear whether the self-reported version shows adequate content validity when it is completed by young people with AE.

With this study, we aim to fill the content validation gap (comprehensibility, relevance, and comprehensiveness) of the English, German and Dutch version of self-reported RECAP in young people with atopic eczema. Specific objectives of this study were:

- To assess content validity (comprehensibility, relevance, and comprehensiveness) of the English, German and Dutch versions of the self-completed RECAP instrument when completed by young people
- Identify the most appropriate age cut-off for self-completion of the self-reported RECAP to ensure comprehensibility of the instrument.

Patients and methods

Participants and study design

We aimed to recruit at least five young people (8 – 16 years affected by atopic eczema) per language (English, German, Dutch) for a qualitative study using semi-structured cognitive interviews. Most of the children aged 8 and over have the ability to read. In agreement with this, the self-complete version of the widely used EQ-5D-Y health status instrument is appropriate for those aged 8-15 years while for children aged 4-7, the proxy version can be used.[18] Written informed consent was given online by the parents or primary caregivers of the participating young people. Interviews were conducted by telephone

or video call. One parent or caregiver was required to be present during the interview. He or she was just sitting next to the child and was instructed to be quiet. The background of the study was explained to the participants. Questions could be asked by the participants at any time during the interview. The interviews were audio recorded and transcribed verbatim.

Participants were asked to complete the questionnaire whilst reading out loud and saying what they were thinking about when trying to answer the questions. This 'think aloud-method' is a qualitative technique that provides insights into cognitive processes.[19] An interview guide including probing techniques was used to structure the interview (see Appendix A). Aspects of comprehensibility, relevance, and comprehensiveness (regarding the instructions, items, response options and recall period) to young people and were assessed separately for each language.[20] Since the originally developed English version of the RECAP instrument is already finalised and in use, changes to the items included in the questionnaire were only considered if the problem was deemed to be significant and reoccurred across the interviews.[20] The duration of the interviews was approximately 20 – 30 minutes. A voucher of 10€ (or £10) was sent as an inconvenience allowance to the participants.

In Germany and in the Netherlands, parents and primary caregivers of young people with atopic eczema were recruited in dermatology clinics. In the UK, participants were recruited through existing mailing lists with consent to contact and through social media. If recruited through social media self-report of a doctor's diagnosis of atopic eczema was used to confirm eligibility. Purposive sampling was used to ensure a range of different ages of young people were recruited. All participants (except for one German girl) were native speakers.

Ethical approval to conduct this study in each country was obtained from the ethics committees of the participating institutions (Netherlands: MEC-2020-0417; Germany: 19-1521-101; UK: FMHS 18-1805).

RECAP questionnaire

RECAP is a 7-item questionnaire including overall eczema control, itch frequency, itch intensity, impact on sleep etc. with five response options. It is currently available in several different languages, however, it has not been validated in every language so far (see https://www.nottingham.ac.uk/research/groups/cebd/resources/recap.aspx). The German adult and proxy RECAP versions were obtained by translating the original RECAP using forward and backward translation for linguistic validation with a subsequent cognitive debriefing to ensure content validity.[12] The same was applied for the Dutch version. Due to the fact that in German and Dutch children and young people are addressed differently from adults than in English, an 'informal' version of RECAP in German and Dutch has been created by replacing the formal pronoun with its informal equivalent. This replacement is not expected to alter the main content of the instrument in any way. This is only to make

the instrument more suitable for the target population. One question of each language can be found in Appendix B (see Appendix B).

Analysis

Transcripts were analysed using a problem-focused coding manual (see Appendix C). ATLAS.ti, NVivo and/or excel sheets were used to code the transcripts and summarise the results. After the transcripts were coded by two independent reviewers in each country, the data was analysed by six researchers (AB, LH, GK, MG, AR, JO) experienced in qualitative research. The analysis of the data was conducted in the same language as the interview took place. Themes were translated and compared across the three countries. The comments of the young people on the individual items of RECAP were evaluated and based on these findings the items were assessed in relation to comprehensibility, comprehensiveness and relevance. If an issue with an item occurred, the reviewers classified it either as a minor or a major problem. When young people stated having problems with understanding specific words but were able to complete the question by themselves it was rated as a minor problem since this issue was rather negligible. Issues with the items were only rated as a major problem if explicit comments about rewording were made and/or if the young people had difficulty with answering the question on their own. Additionally, the reviewers rated an issue as major when they wanted to discuss a question considering this item with the research team. In general, all results were discussed within the research team.

Results

Demographics

In total we recruited 23 young people from three countries. We conducted seven, seven and nine interviews in the UK, the Netherlands and Germany, respectively (see Table 1). Overall, the mean age of the young people was 10.70 years ($SD = 2.65$) with a range from 8 to 16 years. Ten of the 23 participants were female (43.48 %).

Table 1 Demographic characteristics of Study Participants ($N = 23$)

Relevance

All items on the RECAP questionnaire were considered to be relevant by the participants. In the UK, the response options were difficult for three young people because there were either too few options to choose from or they had problems to decide what to answer. For item 5 ("Over the last week, how much has your eczema been getting in the way of day to day activities?"), item 6 ("Over the last week, on how many days has your eczema affected how you have been feeling?"), and item 7 ("Over the last week, how acceptable has your eczema been to you?") there were minor problems stated by three young people, because they considered the items as overlapping or not related to eczema. In the Netherlands, only one child stated that item 7 was not considered relevant, because this skin disease was not

acceptable to anyone. In Germany, no problems regarding relevance were observed. Since all of these stated problems were minor and only occurred with a few young people, the reviewers reached a consensus to not recommend the removal or changing of these items.

Comprehensiveness

Regarding comprehensiveness only one minor problem occurred. In the UK, one child suggested to include an additional question about 'skin picking', a disorder characterized by repetitive and compulsive scratching or picking at the skin, to which dermatologic conditions such as atopic eczema may contribute.[21] In the Netherlands and Germany, no mentionable problems emerged for the comprehensiveness of RECAP. Since only one child wanted to add a question, the research team agreed that no further changes should be recommended.

Recall period

A recall period of one week was considered to be appropriate by all participants. Furthermore, there were no issues during the think-aloud process regarding the recall period. This means that the young people were able to accurately recall one week when answering the question.

Comprehensibility

In the UK, the interviews did not identify any issues that appeared to warrant recommending a change to the original scale, however, the study did identify issues around comprehensibility that appeared to be age-related. Minor and major problems for the young people occurred with items 6 and 7 (see Table 2). Since item 6 was also a relevant problem in the German interviews and rather problematic for younger children, the team decided that this issue appeared to be age-related. Also, item 7 was decided by the reviewers to be an age-related problem for younger children.

Table 2 Comprehensibility issues in the UK

The results of the interviews in the Netherlands are depicted in table 3. The title, item 3 ("Over the last week, on how many days has your skin been intensely itchy because of your eczema?") and item 5 were rated by the reviewers as minor problems. However, these problems could be neglected, because only few young people had minor problems with understanding those, item 7 and the response options were very difficult for the young people to comprehend. As already discussed for the UK, item 7 was decided to be an age-related problem and therefore not to be altered. The response options were only problematic for item 7 because the participants did not understand the word "*acceptabel*" (acceptable). Since these problems only occurred for this specific item it was decided to not alter the response options.

Table 3 Comprehensibility issues in the Netherlands

For Germany, the results of the interviews are depicted in table 4. Some minor problems occurred with item 1 ("Over the last week, how has your eczema been?"), item 3 and item 7. Since these problems

were only stated by a few young people, these issues are rather negligible. The young people had major issues understanding the title of the questionnaire, item 4 ("Over the last week, how much has your sleep been disturbed because of your eczema?"), item 5 and item 6. Regarding the title, the gender-specific term "*Patient/innen*" (male and female patients) was difficult to understand for the young people. For this reason, the questionnaire was renamed as "*Fragebogen für Kinder und Jugendliche mit Neurodermitis*" ("RECAP for children and adolescents with atopic eczema"). This alteration does not change the meaning, but it is more comprehensible for the young people. Since the participants did not understand the translation of the word "disturbed" (item 4) this word was altered into "*gestört*", which is a more easily understandable translation for "disturbed". Regarding item 5, the translation of "getting in the way of" was slightly simplified. The same goes for item 6, as the word "affected" was changed into a more comprehensible expression in German. We have placed great attention to making these adaptations conceptually equivalent to the original version. All these changes were discussed within the German research team with the help of a primary school teacher and paediatric linguist (DG). Therefore, these changes should now be comprehensible for the majority of young people from the age of 8 years and the applied adaptions should not affect the meaning of the items.

Table 4 Comprehensibility issues in Germany

In summary, only minor changes were made to the questionnaire. Some major problems (see table 5) were identified for young people between the age of 8 and 11 years and therefore we recommend that the RECAP proxy questionnaire is used for children under 12 years. The translational changes that were made in Germany were related to only language-specific issues and did not change the meaning of the questions in any way. All changes were only made in order to enhance the comprehensibility of the PROM. Due to these changes, the German child-version of RECAP may be used in young people from the age of 8 years.

Table 5 Summary of all major problems regarding the comprehensibility of RECAP

Discussion

Main findings

In this study, we assessed content validity (comprehensibility, relevance, and comprehensiveness) of the self-reported version of RECAP among young people with atopic eczema across the United Kingdom, Germany and the Netherlands. No comprehensibility issues were reported in adolescents above the age of 12 years. These children only had minor problems with the questionnaire and were able to fully complete it by themselves. Children younger than 12 years old reported problems with several items of RECAP and were thus unable to complete the questionnaires by themselves. In addition, all items and response options were considered relevant. Finally, children and adolescents did not report problems with comprehensiveness.

Linguistic comprehension and abstract thinking

In our study, children below the age of 12 reported difficulty understanding several terms which lead to an inability to complete RECAP without help. These terms included the terms "day to day activities" (item 5), "affected" (item 6) and "acceptable" (item 7). Interestingly, when explaining the terms "day to day activities" (item 5) or "affected" (item 6), children could understand these items and were able to provide an answer. This suggests a problem with the vocabulary of the children and not with the construct of these items. Adding an example would help children understanding these items. However, adding examples to the questionnaire leads to a restriction of the construct that each item is trying to capture and is therefore not preferable. Since these items are designed to leave room for individual interpretation, adding examples could restrict the patients in doing so. Furthermore, we did not want to introduce issues of cross-cultural validity by including inappropriate examples. A more pragmatic approach would be to encourage children and their caregivers to complete RECAP together. This provides children the opportunity to report their perspective of eczema control, without restricting the construct that is measured. Difficulties with the term "acceptable" (item 7) could be more complex. Although none of the children possessed understanding of the term "acceptable", explanation of the meaning of this item did not result in the ability to complete this item in all children younger than 12 years old. "Acceptability" could be a more complex concept that requires greater abstraction ability, which is not yet present in young children.[22] However, only limited struggles with this item were reported in the German version of RECAP which uses a specific term "*klarkommen*" (get along, cope). This would suggest a problem with linguistic comprehension instead of a problem in abstraction ability. Creating a new child version of RECAP could be an option. However, for uniformity purposes a single version of RECAP that captures exactly the same construct in all age groups should be pursued.

Importance of involving young people

With the increasing number of potential treatment options for young people with AE, it becomes more important to assess effectiveness in ways important to young people.[23] In addition to measuring patient-reported symptoms and quality of life, patients and professionals recently agreed that long-term control should be a core outcome for all AE trials.[9] The added value of capturing young people's own reported outcome is known in pediatrics and is underlined by the Food and Drug Administration (FDA).[17,24] In our study, we found that adolescents had no problems completing RECAP, while most younger children struggled with completing RECAP by themselves. Self-completion of RECAP by adolescents and capable children, provides clinicians and researcher with better information on perceived control over AE. For children with AE, this means that their care providers can better inform them how their peers perceived effectiveness of treatment options, which can help with the shared-decision process. In addition, self-completion promotes patient engagement and could therefore lead to greater treatment adherence.[16,25]

Strengths and limitations

A strength of this study was its multinational, multilingual approach to the content validity of RECAP among young people. Additionally, in accordance with COSMIN criteria for good content validity studies, we included at least seven participants per language and a topic guide was used during the cognitive interviews, making our findings more robust.[20] A limitation of our study was a lack of information on AE severity and the educational and cognitive level of the included participants which may influence both relevance as well as comprehensiveness. However, several approaches were used to recruit patients from both dermatology clinics as well as the community, which should have ensured inclusion of people with a range of eczema severities. However, since the study population was recruited differently for the UK than for the Netherlands and Germany, this might have also influenced the results (e.g. a better understanding through patient education at the dermatological departments). This study only assessed the content validity of the languages German, English and Dutch and it is possible that further studies are required in other languages.

Key recommendations

With the increasing number of trials in children and the movement of clinicians to capture patient-reported effectiveness of treatment in clinical[26,27], it is important to use validated and reliable outcome measure. RECAP, alongside another instrument called the ADCT, is recommended by the HOME initiative as a core outcome measurement instrument for long term control in AE.[9,28] Based on our findings, RECAP could be recommended as outcome measure for long term control in young people. In general, the self-reported version of RECAP is likely to be appropriate for children aged 12 years and older. Additionally, the German version is probably understood by lower ages (8 years and older) due to the linguistic changes. Nevertheless, in all three languages, there might be some situations where the proxy-version is needed for older children as well. Furthermore, since children below the age of 12 and children reported several comprehensibility issues with RECAP, the proxy version should be used in children younger than 12 years or when children are cognitively or physically incapable of reporting their experience of eczema control. If there are any doubts from the parents' side that their child is not capable to self-complete the questionnaire, the proxy version should rather be used. This should be decided individually with the involvement of the parents. While using the proxy version of RECAP, we would encourage caregivers to complete RECAP together with their child for optimal assessment of perceived eczema control.

Future research

Further research is necessary to investigate validity, responsiveness, reliability and interpretability of RECAP among different populations and age groups. Uptake of the HOME initiative core outcome set is needed to enable trials to be compared and combined in meta-analyses. For successful implementation of the HOME initiative core outcome set, it is important that future clinical trials include HOME

instruments such as RECAP. Trials involving children and young people now have guidance available on which version of RECAP to use.

Conclusion

In conclusion, RECAP is an outcome measure to capture 'eczema control' which can be used among all age groups; by proxy in children younger than 12 years and self-reported by adolescents and adults.

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Table 1 Demographic characteristics of Study Participants ($N = 23$)

		United Kingdom (n = 7)	**Netherlands (n = 7)**	**Germany (n = 9)**	**Total (n=23)**
Age	8-11 yrs	5	3	7	15
	12-16 yrs	2	4	2	8
	range	8-15	8-16	8-14	8-16
Sex		Female: 2 Male: 5	Female: 3 Male: 4	Female: 5 Male: 4	Female: 10 Male: 13
Ethnicity		White: 5, Asian: 2	White: 3, Mixed: 2, Black: 1, Arab: 1	Not reported (1 girl non-native)	Not available

Table 2 Comprehensibility issues in the UK

	Type of problem	Age (gender)	Examples
Instructions	Minor	8 years (female)	**Mother**: […] Did you understand this bit where it says the questions below provide a snapshot of your eczema. Do you understand that bit? **Participant**: No. (female, 8 years)
Item 6	Minor	11 years (male), 13 years (male)	**Interviewer**: So, what is your answer? **Participant**: I'm not sure. (male, 13 years)
Item 7	Major	8 years (female), 11 years (male)	**Interviewer**: Do you know what it means? **Participant**: No. (female, 8 years)

Table 3 Comprehensibility issues in the Netherlands

	Type of problem	Age (gender)	Examples
Title	Minor	8 years (male), 15 years (female)	**Participant**: What is "atopic"? (male, 8 years)
Item 3	Minor	12 years (female)	Participant had difficulty estimating symptom severity. (female, 12 years)
Item 5	Minor	9 years (male)	**Participant**: What are "*bezigheden*" (day to day activities)? (male, 9 years)
Item 7	Minor	8 years (male), 8 years (male)	Participant thinks, "*acceptabel*" (acceptable) is a difficult word. (male, 8 years)
	Major	9 years (male)	Participant doesn´t know the meaning of "*acceptabel*" (acceptable). (male, 9 years)
Response options	Major	8 years (male), 9 years (male)	Participant does not know meaning of "*acceptabel*" (acceptable). (male, 8 years)

Table 4 Comprehensibility issues in Germany

	Type of problem	Age (gender)	Examples
Title	Minor	9 years (female), 9 years (female), 10 years (male)	Participant stalled while reading "*Patient/innen*" (patients) and needed explanation from parent. (female, 9 years)
	Major	8 years (male), 10 years (male)	**Participant**: I don´t know what "*Patient/innen*" means. (male, 10 years)
Item 1	Minor	10 years (male), 10 years (male)	**Interviewer**: Do you know the word "*beurteilen*"? **Participant**: Not so well. (male, 10 years)
Item 3	Minor	9 years (female), 9 years (female), 9 years (female)	Interviewer had to explain to the participant the difference between item 2 and item 3. (female, 9 years)
Item 4	Minor	9 years (female)	Participant had problems understanding the word "*beeinträchtigt*" (disturbed). (female, 9 years)
	Major	8 years (female)	**Interviewer**: What do you not understand? **Participant**: "*Beeinträchtigt*" (disturbed). (female, 8 years)
Item 5	Minor	9 years (female), 12 years (male)	Participant struggled with the word "*alltägliche Aktivitäten*" (day to day activities) but actually understood it very well. (male, 12 years)
	Major	8 years (female), 8 years (male), 9 years (female), 10 years (male)	**Interviewer**: Do you know, what "*alltägliche Aktivitäten*" (day to day activities) means? **Participant**: No. (male, 8 years)
Item 6	Major	8 years (female), 9 years (female), 10 years (male)	**Participant**: I don´t understand the word "*beeinflusst*" (affected). (female, 8 years)
Item 7	Minor	14 years (female)	Participant struggled with the word "*klarkommen*" (how acceptable has your eczema been to you?). (female, 14 years)

Table 5 Summary of all major problems regarding the comprehensibility of RECAP

	Age range	Number of participants	Examples
Title	8 – 10 years	2	**Participant**: I don´t know what "*Patient/innen*" means. (male, 10 years)
Item 4	8 years	1	**Interviewer**: What do you not understand? **Participant**: "*Beeinträchtigt*" (disturbed). (female, 8 years)
Item 5	8 – 10 years	4	**Interviewer**: Do you know, what "*alltägliche Aktivitäten*" (day to day activities) means? **Participant**: No. (male, 8 years)
Item 6	8 – 10 years	3	**Participant**: I don´t understand the word "*beeinflusst*" (affected). (female, 8 years)
Item 7	8 – 11 years	3	Participant does not know the meaning of "*acceptabel*" (acceptable). (male, 9 years)
Response options	8 – 9 years	2	Participant does not know meaning of "*acceptabel*" (acceptable). (male, 8 years)

Appendix A Interview guide

	Questions	**Prompts**
Introduction	Thank you very much for your time. With this interview, you are supporting a project of … We would like to investigate whether the questions of the subsequent questionnaire are easily understood and feel relevant to you when describing how well controlled your eczema is. comprehensible, comprehensive and relevant. Atopic eczema often flares and then improves again. This questionnaire has been designed to measure how well you feel your eczema is controlled. However, this questionnaire is new in … (language) and with these interviews, we would like to ask you about your thoughts when trying to complete the questionnaire.	- You said that … - Did I understand correctly that … - Can you explain that to me? - Could you tell me more about that? - Can you give me an example?
	The interview will be recorded. Data will be assessed anonymized, thus conclusions on personal data won't be possible. ***(DECLARATION OF CONSENT & START RECORDING)***	
	Before we start, I would like to mention that there are no right or wrong answers. This interview is about your views and thoughts whilst completing the questionnaire, not about knowledge. I am guiding you through the interview. However, please feel free to add any additional thoughts that you might have along the way. I would ask you now to respond to the questions of the questionnaire. Please read the single questions out loud and say out loud what goes through your mind as you read it. ***(Participant completes the 7 items of the RECAP scale while thinking aloud.*** ***Probe either during that stage as much as possible or use the following questions afterwards)***	

General impression of the questionnaire	How was your impression of the questionnaire? What did you think when completing the questionnaire? What did you feel when completing the questionnaire?	Unsure/glad to tell something about this topic/overstrained/…
Comprehensibility	How easy to understand were the instructions for you? How easy to understand were the questions for you? How easy to understand were the response options for you? Were there any questions which should have been formulated differently? For each question, did you know what it was aimed at?	
Relevance	In your opinion, were there any questions which you think are redundant, double or very similar? In your opinion, are the response options appropriate? In your opinion, is the recall period of "last week" appropriate? Which aspect seems most relevant to you?	
Comprehensiveness	In your opinion, are there any key concepts missing in the questionnaire?	
Suggestions for improvement	Do you have any suggestions for improvement of the questionnaire?	
Conclusion	Is there anything you would like to add? Is there any important aspect which had not been mentioned until now?	You have already said …, are there also …?
	This is the end of the interview. Thank you very much for your time.	

Appendix B COSMIN Reporting guideline for studies on measurement properties of PROMs

General reporting recommendations relevant for all studies on measurement properties		
Item Number	**Item Name**	**Item Description**
Report section: Title		
T1	Patient Reported Outcome Measure (PROM)	The name of the PROM instrument(s) (and version if relevant) being studied.
T2	Measurement Property (MP)	What MPs are being studied or more generally, that MPs are being studied (if there are many properties being investigated, for example).
T3	Study sample	General description of relevant study sample characteristics (e.g., condition of interest, language) and also any intervention or exposure (e.g., treatments) if applicable.
Report section: Abstract		
A1	PROM	The name of the PROM instrument(s) (and version if relevant) being studied (i.e. the SF-36 or SF-12; language version) or if it concerns an item bank (e.g., PROMIS instruments). The type of instrument (e.g. a self reported questionnaire or interview).
A2	Measurement Property	What MPs are being studied or more generally, that MPs are being studied (if there are many properties being investigated, for example).
A3	Design	The type of study being used to test the properties (e.g., testretest design, longitudinal study, cohort, cross sectional, case series, randomized etc.). Other details of the study design if relevant (intervention/exposure, description of comparison instruments, outcomes other than PROMs).
A4	Sample	Inclusion / exclusion criteria. General description of relevant study sample characteristics (e.g., condition of interest, geographic location, language, other relevant demographic and baseline characteristics).
A5	Methods	A brief description of the methods for investigating each MP including statistical analyses.
A6	Results	The main results for all MPs investigated reporting statistics for each result with measures of precision where appropriate.
A7	Discussion/Conclusions	A brief description of the results in the context of existing evidence, main strengths and drawbacks and the need for future research on the PROM(s) investigated.
Report section: Introduction		
I1	Name and describe the PROM of interest	Specify the name, type, language, and version of the PROM being investigated and how it was developed. Describe the construct the PROM aims to measure and its subscales; describe the structure of the PROM (e.g., the number of factors, the number of items, scoring algorithm); describe relevant instructions (like time period), and number or type of response categories. State whether the PROM is based on a reflective or

		formative model. Note: This information may also appear in the methods section in greater detail.
I2	Target population	Describe the specific target population that the PROM was designed for. The authors need to provide the appropriate and necessary characteristics of this population.
I3	Citation for the original development of the PROM	The citation for the original development paper(s) should be provided and other highly relevant citations related to the quality of the specific PROM under investigation.
I4	State of Knowledge & Rationale	A description of the current scientific knowledge (what is known) regarding the MPs of? the PROM under investigation. The authors should provide a literature review or refer to a recent review of all existing evidence of the specific version (e.g., language, short 6 form) of the PROM and explain why the new study is necessary and important. The rational for the current proposed study should be given.
I5	Definitions	Specialized terms should be defined or explained.
I6	Objectives and Hypotheses	State the specific objective(s) of the research and hypotheses related to the specific PROM under investigation.
Report section: General Methods		
GM1	Study Design	State the key elements of the study design.
GM2	Participants	State how the participants were chosen; the inclusion and exclusion criteria. (e.g., if a PROM for a specific condition, then the eligibility and selection criteria should reflect this).
GM3	PROM administration	An explicit description of how and when the PROM(s) were administered (e.g., in what setting) including data collection devices/system used (e.g. paper based, electronic administration / ePRO) should be provided.
GM4	Data collection procedures	Provide information about other data collection, exposure methods (e.g., allocation to interventions) and time points / follow-up points.
GM5	Power/sample size calculation	Provide a power calculation for all MP analyses. Alternatively, if a rule of thumb is used, state it and the source/citation.
GM6	Statistical analyses	Statistical analyses and tests corresponding to all hypotheses or objectives for all MPs should be reported. Where appropriate, a cut-off for statistical significance should be reported (e.g., p-value less than 0.05). A description of all statistics to be used to estimate the magnitude and direction of effect should also be reported, together with measures of variability or precision. Report statistical package used.
GM7	Missing data	State approaches or plan for dealing with missing data.
GM8	Post hoc analysis	The report should specify analyses that used data after the data collection period concluded (i.e., if the analyses were post hoc; secondary data analyses) and describe the rationale for any post hoc analyses.

Report section: General results		
GR1	Missing data	The amount and reasons for missing data should be explained for all analyses for all PROMs (or other outcome measurement instruments) and relevant groups.
GR2	Participant/patient Characteristics	The study patients' characteristics should be described, including baseline PROM scores.
GR3	Sample size	If one study contained analyses using different sample sizes, the authors should report the sample size for each analysis.
Report section: Discussion		
D1	MP evidence	Per measurement property the authors should compare the result to the criteria for good measurement properties (e.g., COSMIN criteria)[27], and determine if the specific MP is sufficient or not. Note: This information may also appear in the results section in greater detail in a table for example.
D2	Practical relevance	The authors need to discuss the practical relevance of the findings.
D3	Strengths and limitations	Strengths and limitations of the study should be discussed. For example, discuss if there were any significant potential biases in the study that could have impacted the results.
D4	Generalizability	Generalizability issues related to the PROM results should be discussed. For example, discuss if the results could be generalized to other populations given the sample studied.
D5	Instrument changes	Discuss the need for modifications to the existing PROM or new 7 PROM development. If you conclude that one of the measurement properties is insufficient, you could suggest some modification, or if it is really poor, you could suggest stopping use of the PROM (in the specific population or in general).
D6	Future Research	Report specifically the type of research needed to answer new questions arising out of these findings for the particular MP and PROM investigated.
Report section: Conclusions		
C1	Conclusions	State the overall conclusions for each MP and of the use PROM investigated.
Report section: Other information		
O1	Conflict of interest	State any relevant conflict of interest related to the PROM under investigation (e.g., an author being the PROM developer, funding body etc).

Specific Reporting recommendations for studies on Content Validity		
Item Number	**Item Name**	**Item Description**
CV1	Relevance	Report if and how patients and/or professionals were asked whether each item is relevant for their experience with the condition.
CV2	Comprehensiveness	Report if and how patients and/or professionals were asked whether all key concepts are included.
CV3	Comprehensibility	Report if and how the comprehensibility of the PROM instructions, items, response options, and recall period was assessed.
CV4	Relevance results	Report if all items were considered relevant for the construct, population, and context of use of interest by patients and/or professionals.
CV5	Response options and recall period	Report whether the response options and recall period were considered appropriate by patients and/or professionals.
CV6	Comprehensiveness results	Report whether patients and/or professionals considered all key concepts to be included in the PROM.
CV7	Comprehensibility results	Report whether patients understood the PROM instructions, items, and response options as intended.

Appendix C Problem-focused coding manual

Code	Label	Elaboration
1	**Comprehension**	Item has ambiguous meaning, lack of clarity in wording, uses obscure or difficult language
2	**Intended construct**	Raised a concern about if participant is responding in a way that is capturing the intended construct
2.1	**Beliefs about their eczema and/or treatments affecting response**	i.e. related to eczema but not the concept we are trying to capture
2.2	**None eczema related issues affecting response**	i.e. not related to the eczema, other diseases, other reasons
3	**Knowledge**	Participant lacked the information needed to answer the question
4	**Applicability**	Item was not relevant or applicable to the participant, question had made assumptions
5	**Sensitivity / Desirability**	Item raised concerns or wording was too sensitive, desirability bias likely to occur
6	**Memory retrieval**	Participant had difficulty recalling information required, high level of detail required, recall period too long, felt they had a shortage of cues
7	**Calculating response**	Participant had to make a complex estimation to decide upon a judgement or evaluation, had to use heuristics to provide answer
8	**Assigning response options**	Response options were undefined or vague, used inappropriate units, unclear what they referred to, overlapping categories, missing categories
8.1	**Distinguishing between response option types**	i.e. not clearly distinguishing frequency response options from intensity response options
9	**Other concerns raised**	Problems identified that do not fit within the above codes
9.1	**Aim of the questions**	Uncertainty about the aims of the questions
9.2	**Uncertainties when making comparisons**	Uncertainties about what experience to compare current experience to