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BRIEF REPORT

Responsiveness and Minimal Clinically Important Difference of the Infants and Toddlers Dermatology Quality of Life Questionnaire

Pavel V. Chernyshov · Servando E. Marron · Dimitra Koumaki · Nives Pustišek · Liana Manolache · Carmen Salavastru · Alina Suru · Adelina Sendrea · Tetiana Svyatenko · Olha Statkevych · Michael J. Boffa · Sara Borg Grech · Sergii Zemskov · Volodymyr V. Kuts · Pavlo Lishchynskyi · Andrii V. Chernyshov · Lucia Tomas-Aragones

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ABSTRACT

Background: The Infants and Toddlers Dermatology Quality of Life (InToDermQoL) is the dermatology-specific proxy health-related quality of life (HRQoL) instrument for children from birth to 4 years. The aim of the present study was to confirm the responsiveness and establish minimal clinically important difference (MCID) for the InToDermQoL.

Methods: Parents of children with skin diseases were asked to fill in the InToDermQoL at the initial visit (T1) and subsequent consultation (T2). We hypothesized that correlations between change scores of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents should be above 0.3. The receiver operating characteristic (ROC) curves method was also used for confirmation of responsive-

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P. V. Chernyshov (✉)
Department of Dermatology and Venereology, National Medical University, Bulvar Shevchenko, 13, Kiev 01601, Ukraine
e-mail: chernyshovpavel@ukr.net

S. E. Marron
Department of Dermatology, Aragon Psychodermatology Research Group (GAI+PD), University Hospital Miguel Servet, Zaragoza, Spain

D. Koumaki
Department of Dermatology and Venereology, University Hospital of Heraklion, Heraklion, Crete, Greece

N. Pustišek
Children's Hospital Zagreb, Zagreb, Croatia

L. Manolache
Dermatology, Dali Medical, Bucharest, Romania

C. Salavastru · A. Suru · A. Sendrea
Department of Paediatric Dermatology, Colentina Clinical Hospital, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

T. Svyatenko · O. Statkevych
Department of Skin and Venereal Diseases, Dnipro State Medical University, Dnipro, Ukraine

M. J. Boffa · S. B. Grech
Department of Dermatology, Mater Dei Hospital, Msida, Malta

S. Zemskov
Department of General Surgery, Bogomolets National Medical University, Kiev, Ukraine

V. V. Kuts
Department of Information and Computer Technologies, State Organization "National Institute of Phthisiology and Pulmonology Named After F.G. Yanovsky, National Academy of Medical Sciences of Ukraine", Kiev, Ukraine

ness and determination of MCIDs of the InToDermQoL. The area under the ROC curve (AUC) was used as an indicator of responsiveness.
Results: Results of 442 patients were included. Correlations between change scores of age-specific versions of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents were above 0.3 (0.46-0.74). AUCs for age-specific versions of the InToDermQoL were acceptable (above 0.7) or excellent (above 0.8). Estimated MCIDs for the InToDermQoL were as follows: 3 points of total score change for 0–-11 months, 5 for 1–2 years and 3 or 4 for 3–-4 years version. Estimated MCIDs for the InToDermQoL version for 1–2-year-old children was higher than MCIDs for the 3–4-year-old version despite the higher number of items in the latter. Therefore a MCID of 5 was recommended for both these versions.
Conclusions: Responsiveness for all age-specific versions of the InToDermQoL questionnaire was confirmed. MCIDs for the InToDermQoL are proposed as follows: 3-point change of the total score for age version 0–11 months and 5-point for the age versions 1–2 years and 3–4 years.

Keywords: Children; Dermatology; Infants and Toddlers Dermatology Quality of Life; Minimal clinically important difference; Quality of life; Responsiveness

P. Lishchynskyi
Ukrainian Scientific and Practical Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of the Ministry of Health of Ukraine, Kiev, Ukraine

A. V. Chernyshov
Department of Cellular Radiobiology, State Institution "National Research Center for Radiation Medicine of National Academy of Medical Sciences of Ukraine", Kiev, Ukraine

L. Tomas-Aragones
Department of Psychology, University of Zaragoza, Zaragoza, Spain

Key Summary Points

Why carry out this study?

Responsiveness is an important validation characteristic of the health-related quality of life (HRQoL) instruments.

Knowledge of what constitutes a minimal clinically important difference (MCID) allows clinicians and researchers to interpret the clinical meaning of a change in score of the HRQoL instrument.

What did the study ask?

The aim of the present study was to confirm the responsiveness and establish MCID for the Infants and Toddlers Dermatology Quality of Life (InToDermQoL) questionnaire.

What was learned from the study?

Responsiveness for all age-specific versions of the InToDermQoL questionnaire was confirmed.

MCIDs for age-specific versions of the InToDermQoL were proposed.

INTRODUCTION

The Infants and Toddlers Dermatology Quality of Life (InToDermQoL) questionnaire is the dermatology-specific proxy health-related quality of life (HRQoL) instrument for children from birth to 4 years [1]. Prior to the development of the InToDermQoL questionnaire, there were no dermatology-specific HRQoL instruments for this age group of patients. This resulted in attempts to use disease-specific questionnaires as dermatology-specific, to use dermatology-specific tools for children younger than the questionnaire minimal age limit, or to skip assessment of HRQoL in this age group [2, 3]. To avoid the problem of cross-cultural inequivalence, development and validation of the

InToDermQoL were performed simultaneously in different national centers of the project [1, 4]. Results of the international field tests confirmed internal consistency, test–retest reliability, convergent and discriminant validity, and sensitivity to treatment of the InToDermQoL questionnaire [4, 5]. The first variant of score bands for the InToDermQoL questionnaire has been proposed [5]. The InToDermQoL was used to study QoL in children with seborrheic, allergic contact, and atopic dermatitis before and during the coronavirus disease 2019 (COVID-19) pandemic [6]. Furthermore, an epidermolysis-bullosa-specific module of the InToDermQoL was developed and underwent initial validation [7–9].

Responsiveness is one of the measurement properties that reflects the quality of outcome measurement. Responsiveness means that the instrument should detect change in the purported construct, but also that it should detect the right amount of change, that is, it should not under- or overestimate the real change in the construct that has occurred [10]. The European Academy of Dermatology and Venereology (EADV) Task Force on QoL and Patient-Oriented Outcomes consider responsiveness an important validation characteristic of the HRQoL instruments [11]. A clinically important difference represents a change that would be considered meaningful and worthwhile by the patient. The minimally clinically important difference (MCID) is a threshold value for such a change. The definition of a MCID would be particularly helpful in the evaluation of patient-reported outcomes [12]. The knowledge of what constitutes a MCID allows clinicians and researchers to interpret the clinical meaning of a change in score [13]. Some national and international guidelines contain detailed recommendations on treatment goals and changes of treatment approaches based on MCID [14].

The aim of the present study was to confirm the responsiveness and establish MCID for the InToDermQoL questionnaire.

METHODS

National centers of the InToDermQoL project were invited to participate in the study. Parents or other adult relatives of children with skin diseases from birth to 4 years old were asked to fill in the InToDermQoL questionnaire at the initial visit (T1) and subsequent consultation after 4–6 weeks (T2). Diagnoses of skin diseases were confirmed by dermatologists in all cases.

The data for the study were collected from September 2022 until May 2023.

The InToDermQoL (Table 1) questionnaire consists of three versions: 10 items for children under 1 year of age, 12 items for children 1–-2 years of age, and 15 items for children 3–-4 years of age. Responses of the InToDermQoL questionnaire are on a 4-point scale, from 0 to 3. The total score is calculated by summing the score of each question. Maximum total score for children under 1 year of age is 30. Maximum total score for children 1–2 years of age is 36, and maximum total score for children 3–4 years of age is 45 [1].

The anchor-based approach was used to study the responsiveness of the InToDermQoL questionnaire. There is no gold standard available, and therefore, the anchors used were the levels of improvement based on the global assessment of clinical severity by dermatologists and by patients' parents. Hypotheses about the expected direction and magnitude of correlations between change scores on the instrument of interest and change scores of instruments that measure similar constructs (strong relationships, above 0.5) or instruments that measure unrelated constructs (weaker relationships, below 0.3) were used [10]. We consider disease severity and HRQoL as related but not similar constructs. Therefore, we hypothesized that correlations between change scores of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents should be above 0.3. We also hypothesized that correlations between change scores of global assessment of clinical severity by dermatologists and change scores of global assessment of clinical severity by patients' parents should be higher than

Table 1 The Infants and Toddlers Dermatology Quality of Life Questionnaire

Infants and Toddlers Dermatology Quality of Life (InToDermQoL)		
The aim of this questionnaire is to measure how much your child's skin problem has affected them over the last week		
Child's name: **Diagnosis:**	**Child's age:** **Disease severity:**	**Child's gender:** **Date:** **Filled in by: mother/father/another person**
1. Your child's itching or scratching because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
2. Your child's bleeding (from injured skin and/or mucosa) because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
3. Your child's pain because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
4. Your child's sleep problems because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
5. Your child's mood changes because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
6. Your child's bathing problems because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
7. Your child's problems with dressing/undressing (irritation of lesions, pain) because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐

Table 1 continued

Infants and Toddlers Dermatology Quality of Life (InToDermQoL)		
The aim of this questionnaire is to measure how much your child's skin problem has affected them over the last week		
Child's name: **Diagnosis:**	**Child's age:** **Disease severity:**	**Child's gender:** **Date:** **Filled in by: mother/father/another person**
8. Your child's feeding problems because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
9. Your child's problems during physical activity (infant's movements or walking, running, crawling, etc.)	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
10. Your child's problems with treatment (e.g., home treatment, bandaging, skin care, etc.)	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
If your child is over 1 year of age		
11. Your child's tiredness because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
12. Restrictions and limitations (social, nutritional, physical activity, and sports, pets, etc.) your child had because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
If your child is over 3 years of age		
13. Do other peoples' questions about your child's skin disease affect your child?	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐

Table 1 continued

Infants and Toddlers Dermatology Quality of Life (InToDermQoL)		
The aim of this questionnaire is to measure how much your child's skin problem has affected them over the last week		
Child's name: **Diagnosis:**	**Child's age:** **Disease severity:**	**Child's gender:** **Date:** **Filled in by: mother/father/another person**
14. Your child's feeling of being different from peers because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐
15. Rejection by other children because of their skin disease	Very much	☐
	Quite a lot	☐
	Only a little	☐
	Not at all	☐

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correlations between change scores of the InToDermQoL, and that change scores of global assessment of clinical severity by dermatologists and by patients' parents should be above 0.5 because they measure similar constructs. Pearson's correlation coefficient was used to measure correlation between scores.

The receiver operating characteristic (ROC) curves method was also used for confirmation of responsiveness and determination of MCIDs of the age-specific versions of the InToDermQoL questionnaire. The area under the ROC curve (AUC) was used as an indicator of responsiveness. The AUC of an ROC curve represents the probability that scores will correctly discriminate between improved and non-improved patients. An area of 0.7–0.8 is considered acceptable and an area of 0.8–0.9 excellent [12]. MCIDs of the age-specific versions of the InToDermQoL questionnaire were estimated using the ROC method by comparing children with and without improvement assessed by dermatologists and by patients' parents. The optimal cut-offs on the ROC curves were determined by using the optimal Youden's index [15]. The nearest integers above the cut-off values were determined as MCIDs. The software StatPlus, AnalystSoft Inc., Version v7 was used in the analysis.

The EADV Task Force on Quality of Life and Patient Oriented Outcomes recommends using the word ''quimp'' (quality of life impairment) in routine clinical work and research [16, 17], and this word was used in this study.

This study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments. Ethical approval was obtained from the Commission on Bioethical Expertise and Ethics in Scientific Studies and other local ethical research committees where required. Informed consent from patients' parents or guardians to participate and for publication was obtained in all cases.

RESULTS

Parents or grandmothers of 442 children with skin diseases from Spain, Greece, Croatia,

Table 2 Diagnoses of children with skin diseases whose parents filled in the Infants and Toddlers Dermatology Quality of Life questionnaire

Diagnosis	0–11 months (n = 169)	1–2 years (n = 145)	3–4 years (n = 128)
Atopic dermatitis	79	67	36
Seborrheic dermatitis	6	–	–
Pityriasis alba	4	5	–
Milia	1	–	–
Intertrigo	–	1	–
Pyoderma	1	2	6
Nevi	7	3	4
Giant nevus	2	–	–
Diaper dermatitis	6	2	–
Perioral dermatitis	1	6	3
Contact dermatitis	3	3	2
Impetigo	2	2	2
Urticaria	2	2	3
Papular urticaria	8	2	3
Urticaria pigmentosa	3	2	1
Hemangiomas	8	3	2
Xeroderma	3	–	–
Pediculosis	–	1	2
Ichtyosis	–	–	1
Prurigo	2	3	2
Eczema	4	6	11
Fungal infection	–	5	10
Hand eczema	5	3	2
Warts	2	2	5
Folliculitis	2	–	–
Molluscum contagiosum	3	4	5
Psoriasis	1	1	1
Keratosis pilaris	–	–	1
Scabies	3	5	3

Table 2 continued

Diagnosis	0–11 months (n = 169)	1–2 years (n = 145)	3–4 years (n = 128)
Vitiligo	1	1	–
Pyogenic granuloma	1	–	–
Incontinentia pigmenti	1	–	–
Infantile cephalic pustulosis	1	–	–
Eczema herpeticum	1	–	–
Viral exanthem	1	1	1
Hypertrichosis	1	–	–
Epidermolysis bullosa	1	1	2
Capillary malformation	1	–	–
Aplasia cutis	1	–	–
Café au lait macule	1	1	–
Herpes	–	2	2
Nail dystrophy	–	1	–
Pityriasis rubra pilaris	–	1	–
Pilomatricoma	–	1	–
Alopecia areata	–	1	9
Gianotti–Crosti syndrome	–	2	–
Staphylococcal scaled skin syndrome	–	1	–
Cutaneous mosaicism	–	1	–
Bullous pemphigoid	–	1	–
Granuloma anulare	–	–	3
Pityriasis rosea	–	–	3
Dermatitis herpetiformis	–	–	1
Pigmented purpuric dermatitis	–	–	1
Xantogranuloma	–	–	1

Romania, Malta, and Ukraine filled in national language versions of the InToDermQoL questionnaire at T1 and T2. Data from 20 parents were incomplete and 422 results were used for further analysis. Information on diagnoses of children with skin diseases is presented in Table 2. The questionnaires were filled in by mothers (87.79%), fathers (10.91%), and grandmothers (1.30%) of children with skin diseases.

Correlations between change scores of age-specific versions of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients'

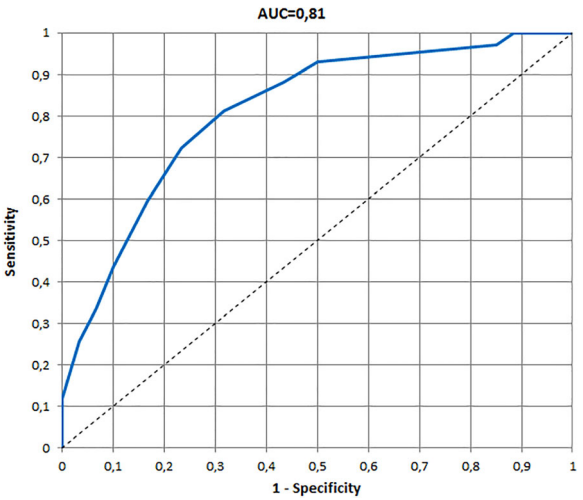

Fig. 1 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 0–11 months version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by dermatologists

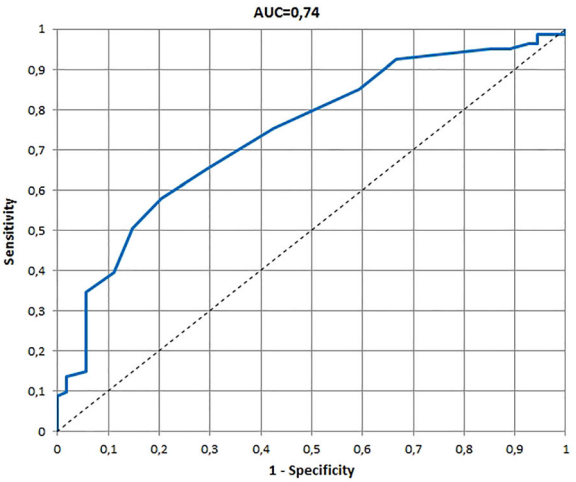

Fig. 3 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 1–2 years version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by dermatologists

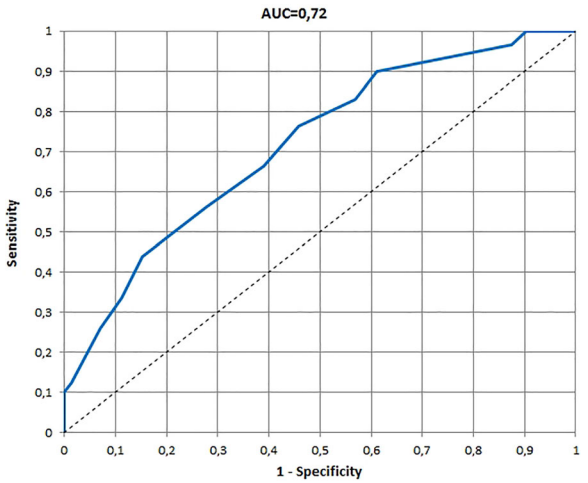

Fig. 2 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 0–11 months version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by patients' parents

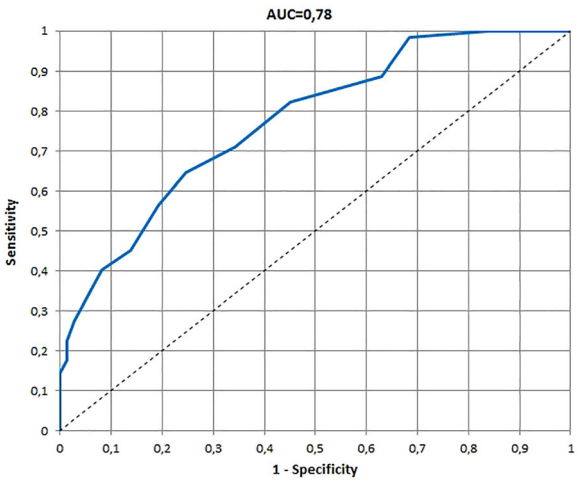

Fig. 4 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 1–2 years version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by patients' parents

parents, as well as between change scores of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents, are presented in Table 3. Our hypotheses that correlations between change scores of the InToDermQoL and change scores of global assessment of

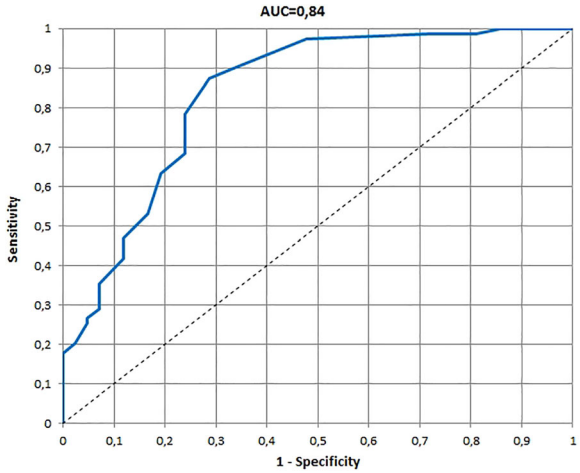

Fig. 5 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 3–4 years version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by dermatologists

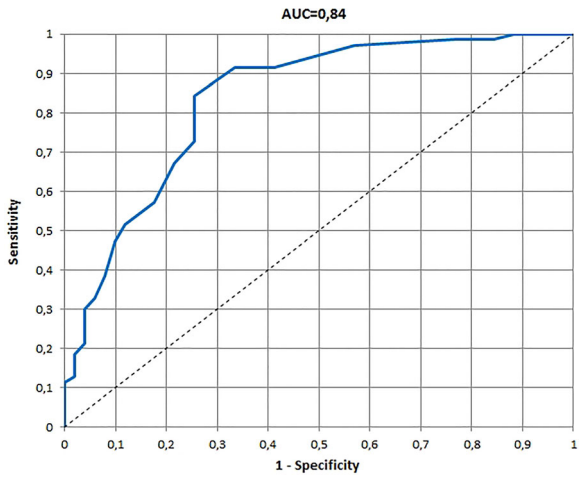

Fig. 6 The receiver operating characteristic (ROC) and area under the ROC curve (AUC) for 3–4 years version of the Infants and Toddlers Dermatology Quality of Life questionnaire developed on the basis of the global assessment of clinical severity by patients' parents

clinical severity by dermatologists and by patients' parents should be above 0.3 and that correlations between change scores of global assessment of clinical severity by dermatologists and change scores of global assessment of clinical severity by patients' parents should be higher than correlations between change scores of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents and should be above 0.5 were confirmed.

The ROCs and AUCs for age-specific versions of the InToDermQoL developed on the basis of the global assessment of clinical severity by dermatologists and by patients' parents are presented in Figs. 1, 2, 3, 4, 5, 6. AUCs for all age-specific versions of the InToDermQoL were acceptable (above 0.7) or excellent (above 0.8).

The 95% confidence intervals for AUCs, cut-off values, sensitivity, specificity, and MCIDs for age-specific versions of the InToDermQoL questionnaire are presented in Table 4. Estimated MCIDs for the InToDermQoL version for 3–4-year-old children appeared to be lower than the MCIDs for the InToDermQoL version for 1–2-year-old children despite a higher number of items in the version for 3–4-year-old children. Therefore, the highest MCID (five) was recommended for both these age-specific versions of the InToDermQoL questionnaire.

DISCUSSION

The anchor-based approach used in our study confirmed the responsiveness of the InToDermQoL questionnaire. Our initial hypotheses were confirmed for all age-specific versions of the InToDermQoL questionnaire. AUCs based on either global assessment of clinical severity by dermatologists or on global assessment of clinical severity by patients' parents were acceptable or excellent for all age-specific versions of the InToDermQoL. MCIDs based on cut-off values were proposed.

It was previously reported that the variety of possible anchors and uncertainty in the anchor cut point that defines a minimal difference makes a single estimate of MCID problematic. It is recommended that the estimation of MCID for an instrument should be based primarily on relevant patient-based and clinical anchors. Multiple approaches to estimating the MCID will produce a range of different values, and decision guidance may often be needed to select a single value or narrow range of MCID values

Table 3 Correlations between change scores of age-specific versions of the Infants and Toddlers Dermatology Quality of Life (InToDermQoL) questionnaire and change scores of global assessment of clinical severity by dermatologists and by patients' parents, and between change scores of the InToDermQoL and change scores of global assessment of clinical severity by dermatologists and by patients' parents

Age-specific versions of the InToDermQoL questionnaire	Correlation between change scores of the InToDermQoL and global disease severity assessed by dermatologists	Correlation between change scores of the InToDermQoL and global disease severity assessed by patients' parents	Correlation between change scores of the global disease severity assessed by dermatologists and global disease severity assessed by patients' parents
InToDermQoL version for 0–11 months (n = 164)	r = 0.57	r = 0.53	r = 0.76
InToDermQoL version for 1–2 years (n = 137)	r = 0.46	r = 0.59	r = 0.63
InToDermQoL version for 3–4 years (n = 121)	r = 0.68	r = 0.74	r = 0.85

Table 4 The 95% confidence intervals for areas under the receiver operating characteristic curves (AUCs), cut-off values, sensitivity, specificity, and minimal clinically important differences (MCIDs) for age-specific versions of the Infants and Toddlers Dermatology Quality of Life questionnaire

	AUC (95% CI)	Cut-off	Sensitivity (95% CI)	Specificity (95% CI)	MCID
0–11 months (n = 161)					
Dermatologists' assessment	0.81 (0.74; 0.88)	2	0.81 (0.74; 0.89)	0.68 (0.57; 0.80)	3
Parental assessment	0.72 (0.64; 0.79)	2	0.77 (0.68; 0.85)	0.54 (0.43; 0.66)	3
1–2 years (n = 135)					
Dermatologists' assessment	0.74 (0.66; 0.82)	4	0.58 (0.47; 0.69)	0.80 (0.69; 0.90)	5
Parental assessment	0.76 (0.70; 0.85)	4	0.65 (0.53; 0.76)	0.75 (0.66; 0.85)	5
3–4 years (n = 121)					
Dermatologists' assessment	0.84 (0.76; 0.92)	2	0.87 (0.80; 0.95)	0.71 (0.58; 0.85)	3
Parental assessment	0.84 (0.76; 0.91)	3	0.84 (0.76; 0.928)	0.75 (0.63; 0.87)	4

[18]. The only problem we encountered was that MCIDs for the version for 1–2 year olds appeared to be higher than MCIDs for the version for 3–4 year olds. On the basis of the higher number of items in the version for 3–4 year olds, the same MCID as for the version for 1–-2 years old children was selected and approved.

There are a number of problems in defining a MCID, specifically those developed from patient-reported data. Problems may be associated with patients' ability to understand the context of improvement. Retrospective judgments are subject to recall bias as the patients may fail to truly remember the intrinsic nature of their prior condition. Baseline severity of symptoms can also influence the outcome of the MCID. The MCID can vary depending on the variability of the health of the population ahead of time. Other forms of patient variation that can influence report of change include descriptive factors such as age, socioeconomic status, or education [19].

The choice of a subjective assessment as an external criterion is not ideal but is due to the lack of satisfying objective assessment, a situation that spurred the use of PRO in the first place. Global assessment scales have been shown to be very sensitive to change, both positive and negative. Anchor-based methods will produce different MCIDs depending on the criterion scale and the arbitrary selection or grouping of scale levels. Conceptually, a minimal difference is a difference between two adjacent levels on a scale, such as ''unchanged'' and ''slightly better.'' MCID would then depend on the number of levels on a scale: the larger the number of levels, the smaller the difference between two adjacent levels and the smaller the MCID [12].

We decided not to analyze answers of fathers and mothers separately because in almost 90% of cases, the person who fills in the InToDermQoL questionnaire was the mother and no significant difference between mothers' and fathers' assessment of disease-specific proxy questionnaire was previously reported [20, 21]. We used real-life data from dermatologic clinics and included patients with a wide spectrum of diagnoses. For some skin diseases, symptoms have the highest effects on quimp [7, 22]. Meanwhile, psychosocial problems have the main impact on quimp in other skin diseases [11, 23]. This may lead to a minimal or absence of quimp in children with a number of skin diseases because feelings of stigmatization are unlikely before the age of 3 years, and during the age period of 3–10 years of age, the majority of children are very optimistic and the memory of experiences of bullying might not persist [24]. However, such facts may be better reflected in proxy reports by parents. Here we should mention that skin disease in children often cause quimp in parents and other family members. Therefore, the EADV Task Force on QoL and Patient-Oriented Outcomes recommends that the measurement of the impact of a skin disease on family and caregivers should also be included in a thorough evaluation of the burden of disease [25].

It seems in any case irrelevant for clinical practice to provide different MCIDs for sexes, and difference of HRQoL instrument scores among the sexes should be studied in children matched by other factors [26, 27]. Parental assessment of HRQoL of their children with skin diseases may not be identical among different countries because of cultural, social, and climatic factors [28, 29]. External factors, as in the case of the COVID-19 pandemic, may have multidirectional effects on patient's HRQoL [6, 30].

HRQoL instruments may vary by validation characteristics, scoring systems, included topics, and recall periods [31]. Use of validated international instruments with established score meaning bands and MCID makes comparison and interpretation of HRQoL assessment easy (as in case of the dermatology-specific HRQoL instrument for adults, the Dermatology Life Quality Index [32], and dermatology-specific HRQoL instrument for older children, the Children's Dermatology Life Quality Index [33]). Such instruments may be included in guidelines, core outcome sets, and used in clinical trials and practice [14, 34]. There are many reasons to assess HRQoL in dermatologic clinical practice [35], and we hope that the InToDermQoL will be used internationally in pediatric dermatology for research and practical needs.

CONCLUSIONS

Acceptable or excellent responsiveness was confirmed for all age-specific versions of the InToDermQoL questionnaire. MCIDs for all three age-specific versions of the InToDermQoL were proposed as follows: 3 points of the InToDermQoL total score for age version 0–-11 months and 5 points of the InToDermQoL total score for age versions 1–2 years and 3–4 years.

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Declarations

Conflict of Interest. The authors have nothing to disclose.

Ethical Approval. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Ethical approval was obtained from the Commission on Bioethical Expertise and Ethics in Scientific Studies and other local ethical research committees where required. Informed consent from patients' parents or guardians to participate and for publication was obtained in all cases.

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