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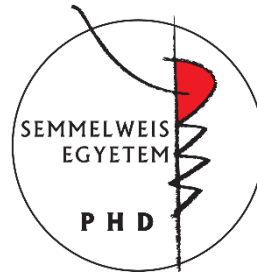
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Disease burden of atopic dermatitis

PhD Thesis

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List of Abbreviations

AD: Atopic dermatitis

DALY: Disability-Adjusted Life Year

DLQI: Dermatology Life Quality Index

DLQI-R: Dermatology Life Quality Index Relevant

EASI: Eczema Area and Severity Index

ES: Effect size

HOME: Harmonising Outcome Measures for Eczema

HRQoL: Health-related quality of life

HS: Hidradenitis suppurativa

IGA: Investigator Global Assessment scale

IL: Interleukin

INF γ : Interferon gamma

IQR: Interquartile range

JAK: Janus kinase

NRR: Not relevant response

oSCORAD: Objective Scoring Atopic Dermatitis

QALY: Quality-Adjusted Life Year

RE: Relative efficiency

SD: Standard deviation

Th1: Type 1 helper T-lymphocyte

Th2: Type 2 helper T-lymphocyte

VAS: Visual Analogue Scale

1. Introduction

The term atopy refers to the predisposition of an individual for developing allergy-related inflammatory diseases such as rhinoconjunctivitis, bronchial asthma, atopic dermatitis (AD), or food allergies. The manifestation of atopic diseases is determined by genetic and environmental factors simultaneously. With growing socio-economic wealth, urbanization, and the spread of Western lifestyle over the past decades, the environment of billions of people has changed substantially. These major changes of life circumstances including the diet, better sanitary conditions, and less exposure to microorganisms may have significantly impacted our immune system, allowing atopic diseases to become widespread [1,2]. Beside efficient removal of pathogens, increasing hygiene has a direct impact on the skin barrier; frequent bathing, and regular use of detergents may disrupt it in susceptible individuals, subsequently decreasing the protection against allergens and pathogens [3]. Probably due to these reasons, AD has become one of the most common inflammatory skin disorders in industrialized countries today, affecting up to 20-25% of children and 10% of adults [2,4-8]. The prevalence in Hungary is around 17% in children and 5% in adults [9]. Even though it seems to plateau in developed countries, a lower but increasing prevalence is seen in many developing countries [2,10].

1.1. Atopic dermatitis

1.1.1. Clinical presentation

It is a chronic inflammatory skin disease with relapsing-remitting disease course, characterized by acute flares and remissions. Patients with AD are at increased risk for developing allergic, type 2 inflammatory diseases such as allergic rhinoconjunctivitis, nasal polyps, bronchial asthma, contact dermatitis, and food allergies. The onset of AD is typically in infancy or early childhood. It may spontaneously resolve before adulthood; however, it persists in many cases throughout life [4]. Because of a defective skin barrier, atopic skin is dry, easily irritated, and prone to infections and sensitization against allergens. The diagnosis of AD is based on the clinical presentation as summarized by the Hanifin-Rajka criteria [11].

The clinical presentation is heterogenous, ranging from localized, mild eczematous skin lesions to extensive, severe forms (Figure 1). Acute lesions appear as red, exudative plaques sometimes with vesicles and crusts. As a lesion turns chronic over

time, redness fades, the skin becomes thickened, lichenified, scaly, and painful fissures may develop. Furthermore, atopic skin is dry and itchy, resulting in frequent scratching and the development of excoriations. In infancy and childhood, skin lesions are often exudative, and are typically localized in the face and on the extensor sides of the extremities. In older children and adults, flexural localization is seen, and skin lesions usually appear rather chronic with lichenification. Other typical sites include the hands, feet, neck, face, and mamillae in adults. The signs and symptoms of AD vary continuously, as acute and chronic phases alternate. Acute exacerbations are sometimes triggered by viral and bacterial superinfections; in other cases, stress, and environmental factors (i.e., cold, dry weather, contact with allergens) are responsible for the worsening of the disease.



Figure 1. Clinical signs of atopic dermatitis on one of our patients' skin. Dry skin, erythematous papules and plaques with scaling, excoriations, and lichenification all over the body of a 24-year-old woman.

Genetic background does not just affect the skin barrier, but it also makes patients susceptible for selective immunodeficiency against specific microbes leading to frequent infections by these germs. Eczema herpeticum (i.e., superinfection with herpes simplex virus) presents with vesicles, pustules, and crusted erosions over large skin surfaces. The most common bacterial superinfection is impetiginization, mostly caused by *Staphylococcus aureus*. It manifests with itchy, red, eroded plaques with honey-colored crusts, and it is highly contagious. In severe cases of acute flares, erythroderma can develop, which is an indication for hospitalization. Patients with AD are also at increased risk for developing verruca vulgaris, molluscum contagiosum, and yeast infections.

Further clinical characteristics of AD are summarized by the Hanifin-Rajka criteria, which are used as a basis for diagnosing AD [11]. They consist of four major and several minor criteria; if at least 3 of both are present, the diagnosis of AD can be established. Major criteria are pruritus, chronic relapsing dermatitis persisting for at least 2 years, positive personal or family medical history for atopic disease, and the typical morphology and distribution of skin lesions as presented above. Minor features are the followings: early onset, xerosis, type I hypersensitivity (skin test reactivity), elevated serum IgE, facial pallor/erythema, orbital darkening, Dennie-Morgan infraorbital fold, recurrent allergic conjunctivitis, keratoconus, anterior subcapsular cataract, cheilitis, anterior neck folds, nipple eczema, hand or foot dermatitis, ichthyosis/palmar hyperlinearity/keratosis pilaris, pityriasis alba, perifollicular accentuation, white dermographism, recurrent skin infections, itch when sweating, intolerance to wool and detergents, skin lesions influenced by environmental/emotional factors, and food intolerance.

1.1.2. Pathomechanism

The pathomechanism is summarized in Figure 2. AD is multifactorial in etiology: genetic, immunologic, and environmental factors lead to a disrupted skin barrier, a key feature of AD. The skin barrier is a complex protective system, it is the first line of defense against injuries, pathogens, allergens, and has an essential role in maintaining homeostasis; in AD, this barrier is damaged as a result of various pathological events.

As one of the main factors of genetic predisposition, loss-of-function mutations in the FLG gene have been identified [12]. The gene product, filaggrin, is a barrier protein

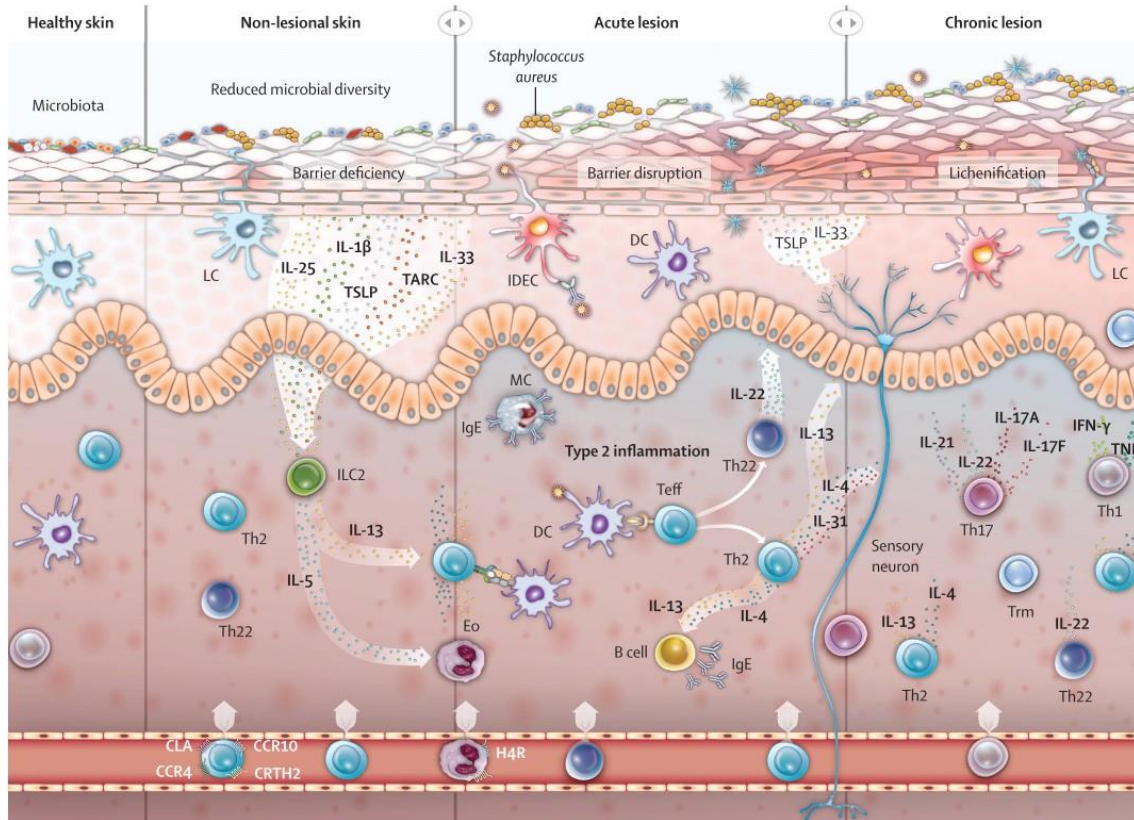


Figure 2. Pathomechanism of AD. Reprinted from *The Lancet*, 396:345-360, Langan SM, et al., *Atopic dermatitis*, Copyright (2020) [4], with permission from Elsevier [license number: 5443620654072].

responsible for the aggregation of keratin intermediate filaments in corneocytes, and its degradation products regulate skin hydration and pH. When filaggrin expression is reduced or absent, or if its mutation(s) lead to insufficient function, the structure and protective function of the stratum corneum is disrupted: transepidermal water loss and pH are increased, and microbes and allergens penetrate more easily. There is a bilateral interaction between the barrier and the immune system. Through the damaged barrier, the increased stimulation of the immune system leads to an excessive production of type 2 inflammatory cytokines (i.e., IL-4 and IL-13), which further enhances the barrier damage (e.g., by suppressing filaggrin expression) [13]. Also, IL-4 and IL-13 promote the production of IL-24, which inhibits the expression of filaggrin through the activation of the Janus kinase (JAK)/STAT pathway [14,15].

The immune pathomechanism of AD can be described as a biphasic process: in acute lesions, type 2 helper T-lymphocytes (Th2 cells) and their cytokines are dominant but over time, in the chronic phase, a shift towards type 1 helper T-lymphocytes (Th1

cells) and their cytokines is observed [16]. First, antigens and allergens penetrate the skin through the disturbed barrier, Langerhans cells recognize them and promote the activation of Th2 cells, which initiate type 2 inflammation by producing the cytokines IL-4, IL-5, IL-13, and IL-31 [17]. This Th2 milieu and the barrier disruption potentiate keratinocytes to produce thymic stromal lymphopoietin (TSLP), IL-25, and IL-33, which further enhance Th2 activation, maintaining inflammation [14]. Furthermore, this environment promotes eosinophilia and IgE production in B-lymphocytes [14,17]. Langerhans cells release chemoattractants as well, thus monocytes are recruited to the skin, where they differentiate into inflammatory dendritic epidermal cells over time and produce IL-12 and IL-18. These cytokines potentiate Th1 polarization, increasing the role of Th1 cells and their IL-12 and INF γ production in chronic AD [16]. Apart from maintaining immune dysregulation, some of these mediators (i.e., IL-4, IL-13, IL-31, TSLP) induce itching as well [14]. Eventually, a vicious circle is formed: chronic inflammation and mechanical injury by scratching further weaken the skin barrier.

There are some additional structural and functional characteristics of atopic skin contributing to the decreased barrier function. First, both IL-4 and IL-13 have been reported to negatively affect the production of antimicrobial peptides (AMP) in keratinocytes, such as cathelicidins and β -defensins [18]. As a result, atopic skin has a microbiome with decreased diversity and is susceptible to colonization and superinfection with *Staphylococcus aureus* (a common trigger of exacerbations) [19]. Second, ceramides are essential components of the lipid layer surrounding corneocytes, however, the overall ceramide content of atopic skin is decreased with a lower proportion of long-chain ceramides and relatively increased proportion of short-chain ceramides [20]. The disorganized lipid structure supports transepidermal water loss and penetration of foreign antigens [14]. Third, located beneath the stratum corneum, tight junctions are intercellular structures of stratum granulosum; they control the selective paracellular permeability. However, a decreased expression of tight junction proteins claudin-1 and claudin-23 has been described in AD [21]. All these factors contribute to the complex network of interactions maintaining AD.

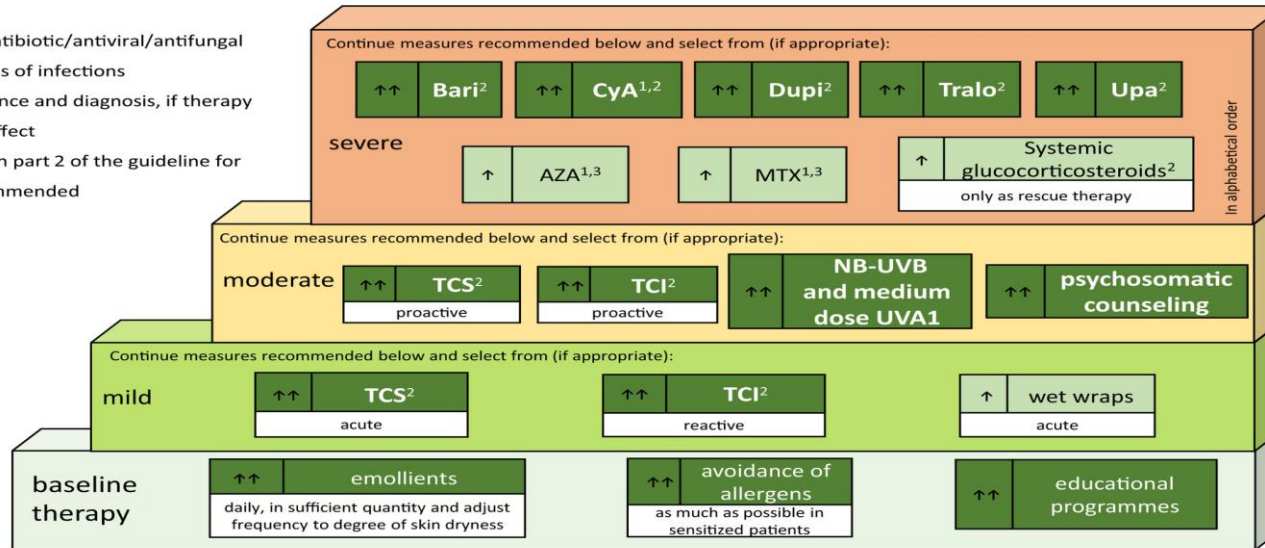
1.1.3. Diagnosis and treatment

Characteristic clinical features and medical history are key to establish the diagnosis of AD. Based on the Hanifin-Rajka criteria, the American Academy of Dermatology suggested revised diagnostic criteria for use in clinical practice [22,23]. This includes essential features that must be present (pruritus, eczema with typical morphology, and chronic or relapsing history), important features that support the diagnosis (early age of onset, xerosis, positive history for atopy, and IgE reactivity), and associated features that are less specific for AD but suggest the diagnosis (such as white dermographism). This guideline also highlights exclusionary conditions that should be ruled out before diagnosing AD (i.e., scabies, seborrheic dermatitis, contact dermatitis, ichthyoses, etc.).

In the following, treatment principles are summarized according to the recently released EuroGuiDerm guideline [24,25] (Figure 3). The management of AD patients is based on a continuous baseline therapy, which can be supplemented with additional treatment steps if needed, according to current disease severity. Three bedrocks of baseline therapy are patient education, daily use of emollients, and avoidance of allergens and other provoking factors. The first step is added to baseline therapy as necessary; in mild AD, topical corticosteroids and/or topical calcineurin inhibitors are usually sufficient for flare management. However, patients with moderate AD or frequent flares usually require the second step which includes proactive treatment with topical corticosteroids or calcineurin inhibitors, phototherapy, and/or psychosomatic counseling.

Stepped-care plan for adults with atopic eczema

- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to Table 2 in part 2 of the guideline for TCS classes recommended



¹ refer to guideline text for restrictions, ² licensed indication, ³ off-label treatment
 ↑↑ (dark green) strong recommendation for the use of an intervention / ↑ (light green) weak recommendation for the use of an intervention
 For definitions of disease severity, acute, reactive, proactive see section 'VII' and section 'Introduction to systemic treatment' of the EuroGuiDerm Atopic Eczema Guideline
 Abro= abrocitinib; AZA=azathioprine; Bari=baricitinib; CyA=ciclosporin; Dupi=dupilumab; MTX=methotrexate; TCl=topical calcineurin inhibitors; TCS= topical corticosteroids; Tralo=tralokinumab; Upa=upadacitinib; UVA1=ultraviolet A1; NB-UVB=narrow-band ultraviolet B

100% Agreement

Symbols	Implications (adapted from GRADE ¹)
↑↑	We believe that all or almost all informed people would make that choice.
↑	We believe that most informed people would make that choice, but a substantial number would not.
0	We cannot make a recommendation.
↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
↓↓	We believe that all or almost all informed people would make a choice against that choice.
	No recommendation.

Figure 3. European guideline on AD treatment. Reprinted from *J Eur Acad Dermatol Venereol*, 36:1409-1431, Wollenberg A, et al., European guideline (EuroGuiDerm) on atopic eczema: part I - systemic therapy. John Wiley & Sons Ltd. Copyright (2022) [25].

The proactive regimen is initiated after lesions have healed; topical anti-inflammatory therapy is applied to previously affected sites long-term, usually twice a week. The third step includes systemic therapy for severe AD, which has changed substantially over the past few years. Cyclosporine has been the first-line option for systemic immunosuppressive treatment for a long time, and it still has a strong recommendation. However, dupilumab (a monoclonal IL-4/IL-13 inhibitor) and JAK inhibitors (i.e., baricitinib and upadacitinib) have become available in several countries and may be recommended as first-line systemic therapies. These drugs are much more efficient and safer than other immunosuppressants such as azathioprine, methotrexate, and systemic corticosteroids which consequently have a weak recommendation; the latter may only be used as rescue therapy. Each step in this guideline is an add-on to previous steps and may be complemented with antiseptic/antibiotic/antiviral/antifungal treatment in case of infections.

As reflected in this guideline, the emerging novel drugs have substantially expanded the therapeutic options in AD over the past few years and the intensive development does not seem to have stopped [26]. There are several alternatives under development, or already available in some countries, i.e., tralokinumab and lebrikizumab (IL-13 inhibitors), nemolizumab (IL-31 inhibitor), tepezelumab (TSLP inhibitor), etc. [27]. However, biologics and small molecule JAK inhibitors are highly effective, but at the same time these are costly therapies. High quality data on disease burden and the cost-effectiveness of such treatments is therefore essential to appropriately inform decision makers and support optimal allocation of health resources.

1.2. Disease burden

1.2.1. The concept of disease burden and its practical implications

The Encyclopedia of Public Health defines burden of disease as “the total, cumulative consequences of a defined disease or a range of harmful diseases with respect to disabilities in a community”, which include “health, social aspects, and costs to society” [28]. For health systems to work effectively, comprehensive and systematic information on population health and the cost-effectiveness of health interventions is fundamental. The Global Burden of Disease study was launched by the World Health Organization and the World Bank in 1991 with the aim of exploring mortality and the number of years lived

with disability by cause on a global level. Led by the Institute for Health Metrics and Evaluation (IHME), a report is released every few years with up-to-date data on global disease burden [29-31]. In this study, burden of disease was defined as loss of health and a new indicator named disability-adjusted life year (DALY) was introduced for its assessment [32]. DALY combines the number of life years lost due to premature death (years of life lost, YLL) in the population and the number of healthy years lost due to disability (years lost due to disability, YLD) in one unit [33]. It can be described as a health gap, i.e., the difference between a hypothetical ideal health state and the actual health status. In other words, one DALY is one year lost, which could have been lived in full health [34].

In addition to loss of function and mortality, disease burden includes several other factors such as loss of health-related quality of life (HRQoL), and the costs of the disease. An important practical implication of measuring the burden of certain diseases roots in the fact that the available resources in health systems are limited while decision makers face a multitude of various health problems, each demanding action. Evaluating health interventions in an objective way is essential to allocate resources appropriately [35,36]. The term quality-adjusted life years (QALY) was first used in 1976 as an indicator of health outcome, which combines duration with HRQoL [37]. Today it is a universal measure of health gain (or loss), which allows to assess the cost-effectiveness of medical interventions [36,38,39]. In Hungary, the National Health Insurance Fund determines the funding of treatments and medical interventions based on the achieved QALY gain [40]. The QALY captures the benefit of an intervention in terms of morbidity (HRQoL gain) and mortality (increase in survival) in one single indicator; it can be calculated by weighting the number of life-years gained by the individual's HRQoL over those years [38].

One of the most widely used methods for gaining HRQoL weights is the estimation of health utilities (a value from 0 to 1), which express societal preferences for a given health state (i.e., how desirable that certain state is) [39,41]. A utility of 1 means full health, 0 is the state, which is as bad as being dead, while negative values represent health states worse than being dead. Generic preference-based HRQoL measures (e.g. EQ-5D, Health Utilities Index 3, Short Form 6 dimensions, etc.) can be used in different patient populations to generate utilities [42]. For instance, answering the five questions

in EQ-5D-5L (5L) yields a unique health state described by five digits. Then, by applying a country-specific value set, a utility can be assigned to that specific health state [43]. A detailed description of the EQ-5D utility calculation is provided in the methods chapter.

1.2.2. The societal burden of skin diseases, particularly AD

Even though skin diseases may seem less severe compared to other chronic diseases such as diabetes or kidney disease, they are responsible for a considerable burden affecting people of all ages and cultures. In 2013, 1.79% of global disease burden was attributed to skin diseases, among which dermatitis (including atopic, seborrheic, and contact dermatitis) was responsible for the largest number of DALYs [44]. In the 2019 evaluation of the Global Burden of Disease Study, skin diseases in general caused the 7th largest nonfatal disease burden worldwide (as for reference, the 1st were musculoskeletal disorders followed by mental disorders, while cardiovascular diseases and chronic respiratory diseases ranked 10th and 11th, respectively) [45]. Dermatitis was still the leading cause of disease burden caused by skin diseases, attributing to a similar amount of nonfatal burden as e.g., drug use, alcohol use, asthma, diarrheal diseases, and chronic kidney disease [45,46]. Among specific skin conditions, AD caused the largest number of DALYs in 2019, followed by acne vulgaris, scabies, viral skin diseases, urticaria, and psoriasis. The amount of disability (excluding mortality) caused by AD was also similar to that of Alzheimer's disease, idiopathic epilepsy, bipolar disorder, and periodontal diseases [45]. The burden of dermatitis, particularly AD, was found to be larger in regions with high socioeconomic development compared to low-income countries [46].

Several other studies have been conducted to assess patient reported burden of AD. A US population-based study found that patients with moderate and severe AD had lower generic HRQoL than patients with other chronic conditions such as heart disease, diabetes, and high blood pressure [47]. A European study of adult patients showed that AD is associated with HRQoL impairment, decreased work productivity, increased healthcare utilization, and psychological comorbidities [48]. Results of a Japanese survey also support that adult patients with AD have higher rates of depression, anxiety, sleep disorders, HRQoL impairment, and decreased work productivity [49]. All these findings underline the importance of measuring disease burden and the need to identify cost-effective health interventions for reducing it.

1.2.3. The individual burden of AD

Given its chronic nature and debilitating symptoms, the impact of AD on patients' and their loved ones' HRQoL is extensive. Negative effects may arise in several areas of life including physical activity, mental health, social functioning, relationships, sexual life, sleep quality, work productivity, leisure time, and financial aspects [50]. Direct medical costs and indirect costs such as decreased work productivity and work absenteeism not only have substantial economic implications, but also place financial burden on patients [4,51]. Everyday skin care and topical treatment of lesions, especially during acute flares, is time-consuming and costly. Pruritus, a hallmark of AD, leads to sleep disturbance, often resulting in the impairment of daily activity [52]. Moreover, itching is worsened by stress and sweating, which restricts physical activity as well. Lesions on visible skin surfaces may cause stigmatization, low self-esteem, and psychological stress; studies have shown that AD is associated with anxiety, depression, and increased risk of suicidal ideation [53,54]. Furthermore, patients are at increased risk of developing other atopic diseases, and bacterial, viral, and fungal skin infections [55,56]. All these factors contribute to a substantial disease burden and indicate the need for HRQoL assessment in clinical practice. Identifying the most important individual problems caused by AD can help to find the optimal treatment strategy, monitor the therapeutic effect, and change the treatment whenever it is necessary.

1.3. Health-related quality of life (HRQoL) measurement in AD

The concept of HRQoL refers to the individuals' perceived physical and mental health; it measures the impact of diseases and different health conditions on everyday life [57]. Instruments for HRQoL assessment in dermatological patients can be divided into three categories [58]. Generic HRQoL instruments are applicable in any healthy or patient population, allowing comparisons with non-dermatologic conditions and the general population; some of them are also suitable for gaining health utilities, and calculating QALYs for cost-effectiveness analyses [42]. Skin-specific instruments are suitable for use in any dermatological disease and measure the HRQoL in relation to the skin's condition. Disease-specific instruments are designed to assess specific problems related to a certain dermatological disorder. Skin- and disease-specific instruments are more sensitive to HRQoL changes compared to generic ones in dermatological diseases. Applying validated disease severity and HRQoL instruments is indispensable not only for

effective and personalized patient care, but also for the optimal allocation of healthcare resources.

Some of the most frequently used generic HRQoL instruments in adult AD are the EQ-5D descriptive system, the Short-Form-36, Short-Form-12, and Health Utilities Index Mark 3 [58]. Common skin-specific measures are the Skindex instrument family (e.g., Skindex-29, Skindex-17, Skindex-16) and Dermatology Life Quality Index (DLQI), while Quality of Life Index for AD (QoLIAD) and Atopic Dermatitis Burden Scale for Adults (ABS-A) are widely used AD-specific instruments. As validated Hungarian versions of AD-specific measures are not available, we only applied generic (two versions of EQ-5D: EQ-5D-3L [3L] and EQ-5D-5L [5L]) and skin-specific (DLQI, DLQI-Relevant [DLQI-R], and Skindex-16) instruments in our study.

1.3.1. The generic EQ-5D instrument family

The EQ-5D descriptive system is the preferred method by pharmacoeconomic guidelines for obtaining health utilities in around 30 countries, including Hungary [59,60]. As health utilities can be translated into QALYs, EQ-5D outputs are useful for cost-effectiveness analyses [42]. The original version, 3L was developed in 1990 and has been broadly used in clinical trials and economic evaluations [61]. It is a generic instrument with a descriptive system that allows the measurement of HRQoL in five dimensions, with three response levels in each. However, some issues have been identified with the 3L, particularly in terms of sensitivity and ceiling effect [62]. To improve measurement properties, the EuroQol group has developed a more recent version, the 5L, which offers five response levels in each dimension instead of only three [62].

The two versions have been compared in psoriasis and hidradenitis suppurativa (HS), but not in AD [63,64]. Furthermore, while more evidence is available with 3L, only few studies reported 5L utilities in AD, with limited information on its measurement properties [65-70]. Both 3L and 5L are generic HRQoL measures but may yield different health utility outcomes. Therefore, in order to choose the right instrument in different settings, understanding their psychometric properties is essential. This was the rationale for a detailed comparison of the two versions in our study.

1.3.2. The skin-specific DLQI, DLQI-R, and Skindex-16

The DLQI is among the most frequently used skin-specific HRQoL instruments in several dermatological diseases including AD and it is the recommended measure for assessing HRQoL outcomes in AD trials [58,71,72]. Nevertheless, some doubts have been raised about the measurement properties of the questionnaire [73-78]. It has been reported that almost 40% of psoriasis patients mark at least one “not relevant” response (NRR), suggesting content validity problems with DLQI [79]. As all items where the NRR response is marked are scored as if they had no impact on the patients’ HRQoL, NRRs falsely improve the total DLQI score, potentially leading to the underestimation of burden. With the aim of avoiding potential bias arising from the NRR option, these findings led to the proposal of an alternative scoring formula, the DLQI-R, which allows to adjust the total score to the number of NRRs [80]. This new formula has been tested in psoriasis, pemphigus, morphea, HS, and vitiligo, and it has been shown to provide similar or improved validity, responsiveness, and discriminatory power as the original DLQI scoring in these patient populations [80-83]. However, there is less data available on the validity of DLQI-R in AD. Only one study has been conducted; it involved patients with mild AD and found that over half of them marked at least one NRR [79]. Nevertheless, this paper reported no significant difference between the performance of DLQI and DLQI-R and concluded that further studies are needed involving patients with moderate and severe AD as well.

Along with DLQI, the Skindex instrument family is also frequently used in dermatologic conditions [58]. The newer Skindex-16 version was developed based on the original Skindex-29 with the aim of constructing a shorter HRQoL outcome measure which assesses the amount of burden rather than the frequency of patient experiences [84]. It involves the items which had the best performance in the longer version along with additional items that were originally not included, but many patients found relevant [85]. However, very few AD studies have reported Skindex-16 data so far and there is a lack of knowledge about its validity in this patient population [86-89].

1.3.3. The Harmonising Outcome Measures for Eczema (HOME) initiative

Founded in 2008, the HOME initiative was set up with the goal of establishing a minimum core outcome set for AD clinical trials and clinical practice [90]. The concept behind

standardizing outcome measures is to improve scientific communication, evidence-based decision making, and patient care. Patients, healthcare professionals, regulatory bodies, journal editors, and the pharmaceutical industry are all represented in the group. Following several international meetings, after the assessment of measurement properties and feasibility of available instruments, consensus-based recommendations have been released [91]. The four outcome domains that should be measured in all AD clinical trials are clinical signs (by Eczema Area and Severity Index [EASI]), patient-reported symptoms (by Patient Oriented Eczema Measure and Numerical Rating Scale 11 for itch intensity), HRQoL (by the DLQI series for adults, children, and infants), and long-term control (by Recap of atopic eczema, or Atopic Dermatitis Control Tool). The outcome set for clinical practice is still subject to discussion. In the present study we measured clinical signs and HRQoL with various instruments, including those recommended by the HOME group (EASI and DLQI, respectively).

2. Objectives

The main objectives of our study were:

- To assess the degree of HRQoL impairment in adult AD patients in Hungary and to identify the most problematic areas.
 - As the COVID-19 outbreak started during our study, we also sought to compare HRQoL in AD patients before and during the pandemic.
 - Using previous data from our research group, we aimed to compare HRQoL loss in AD and other chronic skin diseases including HS, psoriasis, and pemphigus.
- To assess and compare measurement properties of DLQI, DLQI-R, Skindex-16, and 5L in terms of ceiling and floor effects, convergent validity, and known-group validity.
 - As DLQI-R has been studied only in mild AD [79], we aimed to further investigate the relevance of NRRs in a sample with heterogeneous disease severity.
- To compare psychometric properties of 3L and the newer 5L version in AD regarding both the descriptive system and utilities.
 - To obtain health utilities using 3L and 5L.

3. Methods

The study was carried out in collaboration with the Department of Health Economics, Corvinus University of Budapest. Ethics approval was granted by the Scientific and Ethics Committee of the Medical Research Council in Hungary (reference No.: 29655/2018/EKU).

3.1. Study design

We conducted a multicentric, cross-sectional, survey-based clinical study between March 2018 and January 2021, in Hungary [92,93]. Adult AD patients were recruited at three institutions:

- Department of Dermatology, Venereology and Dermatooncology, Semmelweis University, Budapest, Hungary;
- Department of Dermatological Allergology, University of Debrecen, Debrecen, Hungary;
- Saint Martin Outpatient Center, Pannonhalma, Hungary.

Both inpatients and outpatients were approached to participate regardless of disease severity. Inclusion criteria were being aged 18 years or above and having AD diagnosed by a dermatologist according to the Hanifin-Rajka criteria [11]. After signing an informed consent form, patients completed the questionnaire and were examined by one of the investigators.

The questionnaire was written in Hungarian and consisted of two parts (Appendix 1). The first section was completed by the patient and, along with sociodemographic questions, it included the 3L [61], 5L [62], DLQI [71], and Skindex-16 [84], as well as 0-10 visual analogue scales (VAS) for itching and sleep disturbance in the preceding month and a 0-10 patient global assessment (PtGA) VAS for self-reported severity assessment. Data on AD-related expenditure, the impact of AD on work and sick leave, as well as health care use related to AD were also obtained in this part. The second section was completed by the investigator who collected clinical information about treatment, comorbidities, and AD severity using the Investigator Global Assessment (IGA) as described by Eichenfield et al. [94], the objective SCORing Atopic Dermatitis (oSCORAD) [95,96], and the EASI scales [97]. Physicians participating in the study were

trained for the proper completion of these severity measures to minimize bias due to multiple investigators. Only the validated, Hungarian versions of the HRQoL and severity instruments were used.

To determine how the COVID-19 pandemic has influenced the HRQoL of AD patients, participants were divided into two groups: “before COVID-19” (patients recruited from March 5, 2018 to March 11, 2020 [i.e. the date on which the state of emergency was announced in Hungary]) and “since COVID-19” (patients recruited from June 5, 2020 to January 27, 2021). Due to the lock-down, no patients were included between March 11 and June 5, 2020.

3.2. Health-related quality of life (HRQoL) instruments

3.2.1. EQ-5D-3L, EQ-5D-5L, and EQ VAS

To measure generic HRQoL, we applied the 3L and 5L in our study [61,62]. These questionnaires measure HRQoL in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Respondents are asked to choose the option in each dimension which best describes their health on the day of completion. In the 3L version, each dimension has a three-level response scale (1 = no problems, 2 = some/moderate problems, or 3 = extreme problems/unable to/confined to bed), allowing to identify $3^5 = 243$ different health states. In 5L, respondents can choose from five options in each dimension (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, and 5 = unable to/extreme problems), resulting in $5^5 = 3125$ distinct health states. The answers given in the five dimensions yield a five-digit EQ-5D profile: the worst possible health state is “33333” on the 3L, and “55555” on the 5L, while the best possible health state is “11111” on both. To this EQ-5D profile, a health utility (0-1) can be assigned, which represents people’s preferences in average about how good or bad that health state is. These utilities may be used in economic evaluations: value 1 means full health, 0 means a state which is regarded as bad as being dead, while negative values represent health states worse than being dead. The utilities are defined using a value set, which is a list of values for every possible EQ-5D profile, and is specific for a certain community (i.e., the general public of a country) [98]. We computed EQ-5D utilities using the Hungarian value sets, which allow utilities to range from -0.865 to 1 on the 3L and from -0.848 to 1 on the 5L [43].

Additionally, the EQ visual analogue scale (EQ VAS) is also part of the EQ-5D instruments. It is a 20-cm vertical scale anchored at 0 (“the worst health you can imagine”) and 100 (“the best health you can imagine”); respondents are asked to rate their overall health on the day of completion.

3.2.2. *DLQI and DLQI-Relevant (DLQI-R)*

The DLQI consists of ten items, which refer to the preceding seven days of completion [71]. Respondents are asked about the extent of symptom- and treatment-related problems, and how their skin condition affects their daily activities, work/studying, leisure time, and personal relationships. There are four response options to each question (0: “not at all” or “not relevant”, 1: “a little”, 2: “a lot”, 3: “very much”), resulting in a final score of 0 to 30, where higher scores mean larger impact on HRQoL (worse HRQoL). In addition to DLQI, we calculated DLQI-R scores as well, using the following formula:

$$DLQI-R = DLQI \times \frac{10}{10-NRR}.$$

This way, the final score is adjusted for the number of NRRs, which helps to avoid possible bias caused by considering not relevant items as having no impact on HRQoL [80].

3.2.3 *Skindex-16*

Along with DLQI, we applied Skindex-16 for measuring skin-specific HRQoL [84]. The questionnaire includes sixteen questions, which refer to the preceding seven days of completion and are grouped into three subscales: symptoms, emotions, and functioning. Respondents are asked about certain effects of their skin condition (e.g., “Have you been bothered by your skin condition itching”?) and responses are given on a rating scale anchored at 0 “never bothered” and 6 “always bothered”. To calculate subscale scores, answers to the corresponding questions are summed up and transformed to a 0-100 scale. The Skindex-16 total score is estimated by averaging the three subscale scores yielding a final score of 0-100 (0: the skin condition has no impact on HRQoL, 100: maximal impact on HRQoL).

3.2.4. Itching and sleeping visual analogue scales (VAS)

The survey included VASs for the evaluation of self-reported itching and sleep disturbance related to AD in the preceding one month of completion. These are horizontal numerical scales anchored at 0 and 10. On the itching VAS, 0 represents no itching, and 10 represents the worst possible itching. On the sleeping VAS, 0 means that AD had no negative effect on sleeping, while 10 means the worst possible sleep disturbance.

3.3. Assessment of disease severity

3.3.1. Patient global assessment (PtGA)

The PtGA is another 0-10 VAS where patients are asked to evaluate the severity of their disease at the time of completion; 0 means no negative effect caused by AD, while 10 means the worst possible effect.

3.3.2. Investigator global assessment (IGA)

The IGA scale is designed for an overall evaluation of AD severity by a physician. There are several variations available however, we applied the IGA described by Eichenfield et al.: the scale ranges from 0-6 and higher scores indicate more severe disease (0: clear, 1: almost clear, 2: mild disease, 3: moderate disease, 4: severe disease, 5: very severe disease) [94].

3.3.3. Eczema Area and Severity Index (EASI)

The EASI is the recommended instrument for measuring severity in AD patients by the HOME group [97,99]. The percentage of affected skin surface is scored by a physician from 0 to 6 (0: no eruption; 1: 1-9%; 2: 10-29%; 3: 30-49%; 4: 50-69%; 5: 70-89%; 6: 90-100%) in four body regions. The intensity of lesions (erythema, edema/papulation, excoriation, lichenification) is then scored from 0 to 3 (0: none, 1: mild, 2: moderate, 3: severe) in each body region separately. Eventually, a multiplier is applied for each region (head/neck: 0.1, upper limbs: 0.2, trunk: 0.3, lower limbs: 0.4). The final score ranges from 0 to 72 where higher scores indicate more severe disease. We determined EASI severity groups according to the cut-off values described by Chopra et al. (0: clear, 0.1-5.9: mild, 6.0-22.9: moderate, 23.0-72.0: severe) [100].

3.3.4. Objective SCORing Atopic Dermatitis (oSCORAD)

The SCORAD index was developed by the European Task Force on Atopic Dermatitis with the aim of obtaining a consensus on severity assessment in AD [95]. The instrument combines objective and subjective criteria; the extent and intensity of skin lesions are evaluated by a physician, while pruritus and sleep loss are reported by the patient using two 0-10 VASs. The involved body surface is assessed according to the Wallace rule of nines. The intensity of lesions (erythema, edema/papulation, oozing/crust, excoriation, lichenification, dryness) is scored from 0 to 3. In this study, we applied the oSCORAD, which includes only the objective domains of the original instrument and yields a final score between 0-83, where higher scores indicate more severe disease [96]. To determine oSCORAD severity groups, we also applied severity strata as described by Chopra et al. (0-7.9: clear, 8.0-23.9: mild, 24.0-37.9: moderate, 38.0-83.0: severe) [100].

3.4. Statistical analyses

First, a descriptive statistical analysis of demographic and clinical characteristics of the patient population was performed. Frequency and relative frequency were calculated for categorical variables, while mean and standard deviation (SD), as well as median and interquartile range (IQR) were determined for continuous variables. The proportion of patients with NRRs on the DLQI, the number of NRRs in certain items of the DLQI, and the proportion of participants enrolled before vs. during the COVID-19 pandemic were determined. Groups of patients (with vs. without NRRs and before vs. since COVID-19) were compared in terms of age and disease duration (independent samples *t*-test), HRQoL and disease severity outcomes (Mann-Whitney *U*-test), and categorical variables i.e., sex, employment, comorbidities, etc. (Fisher's exact test).

Statistical analyses were carried out in SPSS 25.0 (IBM, Armonk, NY, USA), Stata 14 (StataCorp LP., College Station, TX, USA), and R Statistical Software (v4.1.2 Vienna, Austria) [101]. A *p*-value of <0.05 was considered statistically significant.

3.4.1. Impact of the COVID-19 pandemic on HRQoL

To compare total scores on the HRQoL instruments among the “before COVID-19” and “since COVID-19” groups we performed multivariate linear regressions; for the comparison of HRQoL item responses ordinal logistic regressions were performed. We controlled the regression models for age, sex, level of education, disease severity

(oSCORAD score) and type of treatment. Robust standard errors were used in cases when heteroscedasticity was present.

3.4.2. Measurement properties of DLQI, DLQI-R, Skindex-16, and EQ-5D-5L

Measurement properties of DLQI, DLQI-R, Skindex-16, and EQ-5D-5L were tested in the total sample in terms of floor and ceiling effect, convergent validity, and known-group validity.

First, we determined the proportion of respondents reporting the worst or best possible health states on each scale; floor or ceiling effects were present if at least 15% of patients achieved the lowest or highest score on a given instrument [102]. We used floor and ceiling effects to compare the overall HRQoL of the before and since COVID-19 subgroups. If a HRQoL measure showed relevant floor or ceiling effect, it was considered as a limitation of the given instrument, as it may not be able to make sensitive distinctions among patients with very mild or very severe disease.

Convergent validity assessment of HRQoL and severity instruments was carried out by calculating Spearman's correlations coefficients ($r_s < 0.20$: very weak, $0.20-0.39$: weak, $0.40-0.60$: moderate, > 0.60 : strong) [103]. Based on previous reports, we expected skin-specific instruments to correlate more strongly with disease severity than generic ones [66]. Also, strong correlations were expected among skin-specific measures, while moderate correlations between skin-specific and generic ones [65].

To assess the known-group validity of HRQoL instruments, patients were divided into EASI and oSCORAD severity groups according to the cut-off values described above. We applied the Kruskal-Wallis test to compare HRQoL scores among severity groups and the H -statistic obtained in the Kruskal-Wallis test was used to compute effect size (ES, η^2 ; ≥ 0.01 : small, ≥ 0.06 : moderate, ≥ 0.14 : large) [104,105]. To compare the efficiency of HRQoL instruments at discriminating between known severity groups, we computed relative efficiency (RE: the ratio of the ESs of two HRQoL instruments, with DLQI as reference; a value of > 1 means that the given measure is more efficient than DLQI).

3.4.3. Comparing EQ-5D-3L and EQ-5D-5L

The two instruments have been compared in previous psychometric studies in various healthy and patient populations; our statistical analysis was based on the methods of these studies [63,64,106-108]. In the questionnaire, the 5L was placed before the 3L version, to prevent the underuse of the additional two levels in the 5L.

We assessed feasibility by comparing the number of missing responses in 3L and 5L (missing values were not imputed).

The distributions of 3L and 5L utilities were visualized using histograms, and the proportion of patients reporting no problems across all five EQ-5D dimensions was calculated to estimate the ceiling effect. Due to the two additional response levels, a reduced ceiling effect was expected in the 5L compared to the 3L. First, we computed the difference in the proportion of patients reporting no problems (absolute ceiling effect reduction). Then, the relative reduction was calculated as $(\text{ceiling}_{3L} - \text{ceiling}_{5L}) / \text{ceiling}_{3L}$. The difference in ceiling effect between the 3L and 5L was compared using McNemar's test.

The difference between 3L and 5L utilities was tested by Wilcoxon signed-rank test. We displayed the agreement between the 3L and 5L using a Bland-Altman plot [109], with the mean of the 3L and 5L utilities on the x-axis and their difference on the y-axis. The 95% confidence interval for the difference was calculated as the mean difference $\pm 1.96 \times$ standard deviation (SD). The points outside the upper and lower limits were considered outliers. The intraclass correlation coefficient (ICC) was used to test parallel forms reliability, which reflects both the agreement and degree of correlation between the two descriptive systems [110]. We used a two-way random model with absolute agreement to estimate ICCs [111]. The ICC values were classified as follows: poor: 0-0.39, fair: 0.40-0.59, good: 0.60-0.74, and excellent: 0.75-1.0 [112]. Based on previously reported data, good or excellent agreement was expected between 3L and 5L [107].

The proportion of consistent and inconsistent 3L-5L response pairs was calculated using cross-tabulations. A 3L response at least two levels away from its 5L pair was considered inconsistent (e.g. the respondent chooses some problems [level 2] on the 3L and severe problems [level 4] on the 5L) [106]. To calculate the average size of

inconsistency, 3L responses were recoded on a 5L scale (level 13L = level 15L, level 23L = level 35L and level 33L = level 55L) and the following formula was used: $|3L-5L| - 1$ [106].

Informativity reflects the ability of an instrument to differentiate between different levels of health [113]. We determined the informativity of the five dimensions in 3L and 5L using Shannon's (H') and Shannon's evenness (J') indices [113,114]. The H' expresses the absolute information content (the number of possible responses) combined with how evenly the information is distributed across all responses, while J' represents the evenness of distribution exclusively. Our hypothesis was that with its two additional levels, the 5L improves the informativity of 3L [115]. We calculated the H' and J' indices according to the following formulas (L : number of levels in one dimension of the EQ-5D; p_i : percentage of patients choosing the i th level):

$$H' = - \sum_{i=1}^L p_i \log_2 p_i$$

$$J' = \frac{H'}{H'_{max}}, \text{ where } H'_{max} = \log_2 L$$

Higher H' indicates better informativity (range: 0 to $\log_2 L$, where $\log_2 L$ is 1.85 for the 3L and 2.32 for the 5L). The value of J' ranges from 0 to 1, where 0 corresponds to the worst discriminatory power, when all responses are in the same response level and 1 indicates the best discriminatory power with even distribution of responses across all levels [107].

Convergent validity was assessed by calculating Spearman's rank order correlation coefficients (r_s) between the 3L and 5L dimensions and utilities, and previously validated other instruments. Based on earlier reports, we expected the EQ-5D dimensions and utilities to correlate at least moderately with EQ VAS, DLQI, and Skindex-16 [65], and weakly with severity measures including IGA, oSCORAD, EASI, and PtGA VAS [66]. In general, we expected most EQ-5D dimensions and utilities to correlate weakly or very weakly with sleeping and itching VAS, as these problems are not included in the EQ-5D descriptive system [116]. The only exception was the

pain/discomfort dimension for which we hypothesized a moderate correlation with itching based on a previous study [117]. Also, we expected the 5L to correlate more strongly with disease severity and skin-specific HRQoL instruments than the 3L.

Due to the skewed distribution of EQ-5D utilities, we used non-parametric Mann-Whitney and Kruskal-Wallis tests to assess and compare the ability of 3L and 5L to distinguish between known groups of patients defined by severity scores on IGA, oSCORAD, and EASI or skin-specific HRQoL on DLQI. Our hypothesis was that patients with higher disease severity or worse skin-specific HRQoL have significantly lower utilities and the 5L can better differentiate across known groups. Effect sizes (ES) were calculated as follows:

$$ES(Z) = \frac{\text{Mann-Whitney } Z}{n - 1}$$

$$ES(H) = \frac{\text{Kruskal-Wallis } H - k + 1}{n - k}$$

where k is the number of groups, and n is the sample size; ESs were interpreted as described above. The RE was computed as the ratio of the ESs of 5L and 3L utilities. A RE larger than 1 indicated that the 5L was more efficient in differentiating between known groups.

4. Results

4.1. Study population

Demographic and clinical characteristics of patients are summarized in Table 1. Altogether, 224 adult AD patients were approached to participate and a total of 218 completed the questionnaire (2 submitted it incomplete, 4 did not wish to participate). Mean age was 31.3 years (range: 18 to 73), 57.8% were female. More than a quarter of patients (27.5%) were students and 61.0% were full- or part-time employed. The disease duration at the time of completion ranged from 0 to 68 years (mean: 19). Data collection was conducted in two waves: 125 patients were recruited before the COVID-19 pandemic (“before COVID-19” group: from March 5, 2018 to March 11, 2020 [i.e., the date on which the state of emergency was announced in Hungary]) and 93 patients during the COVID-19 pandemic (“since COVID-19” group, from June 2020 to January 2021). When comparing sociodemographic characteristics in the two groups, more patients marked the “other” employment option in the since COVID-19 group, but no other relevant difference occurred. Anxiety was significantly more common in the since COVID-19 group (32.3% vs. 14.4%) and the occurrence of some other comorbidities and applied treatments also varied. Few patients (9.6%) were untreated at the time of completion, 23.4% received solely topical therapy, 3% had UVB phototherapy, 2.3% was treated with dupilumab and 63.3% received some other systemic treatment (Table 1). Systemic therapies included antihistamines, antibacterial and antiviral agents, as well as traditional immunosuppressants (i.e., cyclosporin, azathioprine, corticosteroids, and methotrexate). Some patients were treated with more than one systemic agent at the same time and some of them used topical treatment along with systemic medication(s). No patient received JAK inhibitors as they were not yet available in Hungary at the time of our survey.

Disease severity scores are summarized in Table 2. When applying the severity bands developed by Chopra et al., the average severity of AD was moderate in the whole sample as measured by EASI and oSCORAD [100]. According to EASI, 23.5% had clear or mild AD, 54.4% had moderate, and 22.1% had severe disease. No significant difference occurred in the total HRQoL, itching VAS, sleeping VAS, and disease severity scores between the “before COVID-19” and “since COVID-19” groups, except for a

slight decrease of oSCORAD score in the latter group. On 0-10 VASs, the average severity scores of itching and sleep disturbance were 7.01 and 5.51, respectively.

Table 1. Demographic and clinical characteristics of patients with atopic dermatitis. Modified from [93].

	Mean (SD) or N (%)			p-value ^b
	Total sample (N=218)	Before COVID-19 (N=125)	Since COVID-19 ^a (N=93)	
Age (years)	31.34 (11.68)	31.88 (12.64)	30.61 (10.27)	0.429
Disease duration (years) (missing=3)	19.02 (12.91)	18.44 (12.84)	19.80 (13.02)	0.444
Family history of AD	74 (33.9%)	36 (28.8%)	38 (40.9%)	0.082
Sex				
Female	126 (57.8%)	72 (57.6%)	54 (58.1%)	1.000
Male	92 (42.2%)	53 (42.4%)	39 (41.9%)	
Education (missing=2)				
Primary	12 (5.6%)	8 (6.4%)	4 (4.3%)	0.315
Secondary	112 (51.9%)	68 (54.4%)	44 (47.3%)	
Tertiary	92 (42.6%)	47 (37.6%)	45 (48.4%)	
Employment^c				
Employed full-time	109 (50.0%)	67 (53.6%)	42 (45.2%)	0.273
Employed part time	24 (11.0%)	15 (12.0%)	9 (9.7%)	0.665
Retired or disability pensioner	13 (6.0%)	8 (6.4%)	5 (5.4%)	1.000
Unemployed	12 (5.5%)	8 (6.4%)	4 (4.3%)	0.563
Student	60 (27.5%)	34 (27.2%)	26 (28.0%)	1.000
Other	23 (10.6%)	5 (4.0%)	18 (19.4%)	0.010
Non-dermatologic comorbidities				
Allergic rhinitis	129 (59.2%)	75 (60.0%)	54 (58.1%)	0.782
Bronchial asthma	74 (33.9%)	51 (40.8%)	23 (24.7%)	0.014
Allergic conjunctivitis	50 (22.9%)	35 (28.0%)	15 (16.1%)	0.050
Anxiety	48 (22.0%)	18 (14.4%)	30 (32.3%)	0.003
Other non-dermatologic conditions	11 (5.0%)	4 (3.2%)	7 (7.5%)	0.105
Sinusitis	8 (3.7%)	6 (4.8%)	2 (2.2%)	0.471
Depression	8 (3.7%)	6 (4.8%)	2 (2.2%)	0.471
Other	58 (26.6%)	28 (22.4%)	30 (32.3%)	0.042
Allergies				
Pollen allergy	106 (48.6%)	55 (44.0%)	51 (54.8%)	0.132
Dust allergy	80 (36.7%)	45 (36.0%)	35 (37.6%)	0.887
Food allergy	49 (22.5%)	24 (19.2%)	25 (26.9%)	0.193
Metal allergy	14 (6.4%)	12 (9.6%)	2 (2.2%)	0.028
Other allergies	70 (32.1%)	25 (20.0%)	45 (48.4%)	<0.001
Current treatment				
None	21 (9.6%)	9 (7.2%)	12 (12.9%)	0.007
Solely topical therapy	51 (23.4%)	35 (28.0%)	16 (17.2%)	
Phototherapy (UVB) ^d	3 (1.4%)	3 (2.4%)	0 (0.0%)	
Biological therapy (dupilumab)	5 (2.3%)	0 (0.0%)	5 (5.4%)	
Systemic non-biological treatment ^e	138 (63.3%)	78 (62.4%)	60 (64.5%)	
Antihistamines ^d	115 (52.8%)	65 (52.0%)	50 (53.8%)	
Antibiotics ^d	45 (20.6%)	22 (17.6%)	23 (24.7%)	
Antiviral therapy (acyclovir) ^f	4 (1.8%)	3 (2.4%)	1 (1.1%)	

	Mean (SD) or N (%)			<i>p</i> -value ^b
	Total sample (N=218)	Before COVID- 19 (N=125)	Since COVID- 19 ^a (N=93)	
Immunosuppressant therapy ^f	68 (31.2%)	37 (29.6%)	31 (3.4%)	
<i>Cyclosporin</i>	21 (9.6%)	12 (9.6%)	9 (9.7%)	
<i>Azathioprine</i>	1 (0.5%)	1 (0.8%)	0 (0.0%)	
<i>Corticosteroids</i>	34 (15.6%)	17 (13.6%)	17 (18.3%)	
<i>Methotrexate</i>	11 (5.0%)	9 (7.2%)	2 (2.2%)	
<i>Acitretin</i>	1 (0.5%)	0 (0.0%)	1 (1.1%)	
Topical therapy ^d	162 (74.3%)	97 (77.6%)	65 (69.9%)	
Topical corticosteroids	159 (72.9%)	94 (75.2%)	65 (69.9%)	
Topical tacrolimus	20 (9.1%)	15 (12.0%)	5 (5.4%)	

^aAfter March 11, 2020. ^bIndependent samples t-test or Fisher's exact test. ^cMultiple responses could be marked. ^dIn the preceding one month. ^eIn monotherapy or more than one systemic treatment combined; some patients used topical agents along with systemic therapy. ^fIn the preceding one year.

Table 2. Disease severity and HRQoL scores of AD patients [93].

Outcome measures ^a		Total sample (n=218)						Before COVID-19 (N=125)		Since COVID-19 (N=93) ^b		p-value ^c
		Mean (SD)	Median (IQR)	Minimum	Maximum	Floor effect, N (%)	Ceiling effect, N (%)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
DLQI (0-30)		13.44 (8.46)	14.00 (6.00-20.00)	0	30	9 (4.1%)	3 (1.4%)	13.57 (8.56)	15.00 (6.00-20.00)	13.28 (8.36)	13.00 (6.00-19.50)	0.801
DLQI-R (0-30)		13.76 (8.60)	14.44 (6.00-21.00)	0	30	9 (4.1%)	3 (1.4%)	13.85 (8.68)	15.00 (6.00-21.00)	13.64 (8.53)	14.00 (6.00-21.00)	0.867
Skindex-16 (0-100)	Symptoms subscale	62.44 (29.64)	68.75 (37.50-87.50)	0	100	4 (1.8%)	33 (15.1%)	60.87 (30.90)	66.67 (33.33-89.59)	64.56 (27.89)	70.83 (45.83-87.50)	0.465
	Emotions subscale	61.21 (29.18)	69.05 (40.48-85.71)	0	100	6 (2.8%)	13 (6.0%)	60.88 (30.28)	69.05 (40.48-88.10)	61.65 (27.80)	69.05 (42.86-85.71)	0.945
	Functioning subscale	46.87 (31.48)	46.67 (20.00-74.17)	0	100	22 (10.1%)	10 (4.6%)	47.49 (32.30)	50.00 (16.67-78.34)	46.02 (30.49)	43.33 (20.00-73.33)	0.786
	Total score	56.84 (27.46)	61.49 (35.64-80.04)	0	100	3 (1.4%)	3 (1.4%)	56.41 (28.90)	63.33 (31.99-81.65)	57.41 (25.54)	60.79 (40.32-78.52)	0.975
EQ-5D-5L utility (-0.848 to 1)		0.82 (0.22)	0.89 (0.78-0.97)	-0.357	1.000	0 (0%)	49 (22.5%)	0.83 (0.21)	0.89 (0.76-1.00)	0.82 (0.23)	0.88 (0.79-0.96)	0.455
EQ VAS (0-100) (missing=1)		69.15 (20.50)	75.00 (57.00-85.00)	0	100	1 (0.5%)	6 (2.8%)	69.11 (21.28)	75.00 (55.50-85.00)	69.19 (19.54)	75.00 (58.50-85.00)	0.797
Itching VAS (1-month average) (0-10) (missing=1)		7.01 (2.92)	8.00 (5.00-9.00)	0	10	6 (2.8%)	51 (23.4%)	6.75 (3.13)	8.00 (4.00-9.00)	7.36 (2.58)	8.00 (6.00-10.00)	0.285
Sleeping VAS (1-month average) (0-10) (missing=3)		5.51 (3.53)	6.00 (2.00-9.00)	0	10	25 (11.5%)	36 (16.5%)	5.30 (3.52)	6.00 (2.00-8.00)	5.79 (3.55)	6.50 (2.00-9.00)	0.280
PtGA VAS (0-10) (missing=1)		6.04 (2.74)	7.00 (4.00-8.00)	0	10	7 (3.2%)	21 (9.7%)	5.97 (2.94)	7.00 (4.00-8.00)	6.14 (2.45)	6.50 (4.00-8.00)	0.967
oSCORAD (0-83)		35.91 (14.61)	36.90 (26.60-46.73)	0	71.10	2 (0.9%)	0 (0%)	34.36 (24.48)	31.00 (16.00-48.75)	27.89 (20.79)	23.00 (12.25-41.50)	0.029
EASI (0-72)		15.76 (11.99)	14.40 (6.10-21.98)	0	59.40	4 (1.8%)	0 (0%)	17.16 (12.64)	16.55 (6.20-23.75)	13.88 (10.84)	12.00 (6.10-20.25)	0.063
IGA scale (0-5)		2.77 (1.04)	3.00 (2.00-3.00)	0	5	5 (2.3%)	5 (2.3%)	2.80 (1.10)	3.00 (2.00-4.00)	2.73 (0.96)	3.00 (2.00-3.00)	0.362

^aHigher scores represent better health status for the EQ VAS and EQ-5D-5L utility and worse health status for all other measures. ^bAfter March 11, 2020. ^cMann-Whitney *U* test.

4.2. HRQoL results

4.2.1. HRQoL impairment in AD

Results of the HRQoL instruments are presented in Table 2. Mean DLQI, DLQI-R, Skindex-16 scores, and 5L utilities indicate quite severe HRQoL impairment among AD patients. The most troublesome items on DLQI were item 1 (itchy, sore, painful skin), item 2 (embarrassment), and item 4 (clothes), where 91.7%, 83.5%, and 75.7% of patients reported problems, respectively (Figure 4). On Skindex-16, most problems occurred in item 1 (itching), item 5 (persistence/recurrence), and item 6 (worry), where 97.2%, 94.9%, and 94.9% reported feeling bothered, respectively (Figure 5). On the generic 5L, the most problems were reported in the pain/discomfort dimension, followed by usual activities and anxiety/depression, with 65.6%, 56.0%, and 52.3% of patients having at least slight problems, respectively (Figure 6).

Using previous data from our research group, we could compare 5L utilities of AD patients by age groups with those of patients with different skin diseases, and the general population (Figure 7). The mean 5L utilities in the general population and in AD, HS, psoriasis, and pemphigus were 0.93 ± 0.14 , 0.82 ± 0.22 , 0.76 ± 0.21 , 0.84 ± 0.19 , and 0.82 ± 0.21 , respectively [43,63,82,118].

4.2.2. Impact of the COVID-19 pandemic on HRQoL

The HRQoL outcomes in the before and since COVID-19 groups are summarized in Table 2; there was no significant difference in the total DLQI, DLQI-R, Skindex-16 scores, and 5L utilities between the two groups. Nevertheless, after evaluation of sociodemographic and clinical variables individually, we found that patients reported significantly more problems during COVID-19 in some specific areas such as skin symptoms, pain/discomfort, worrying, social interactions, shopping/home/garden, and fear of persistence/reoccurrence of symptoms (Table 3).

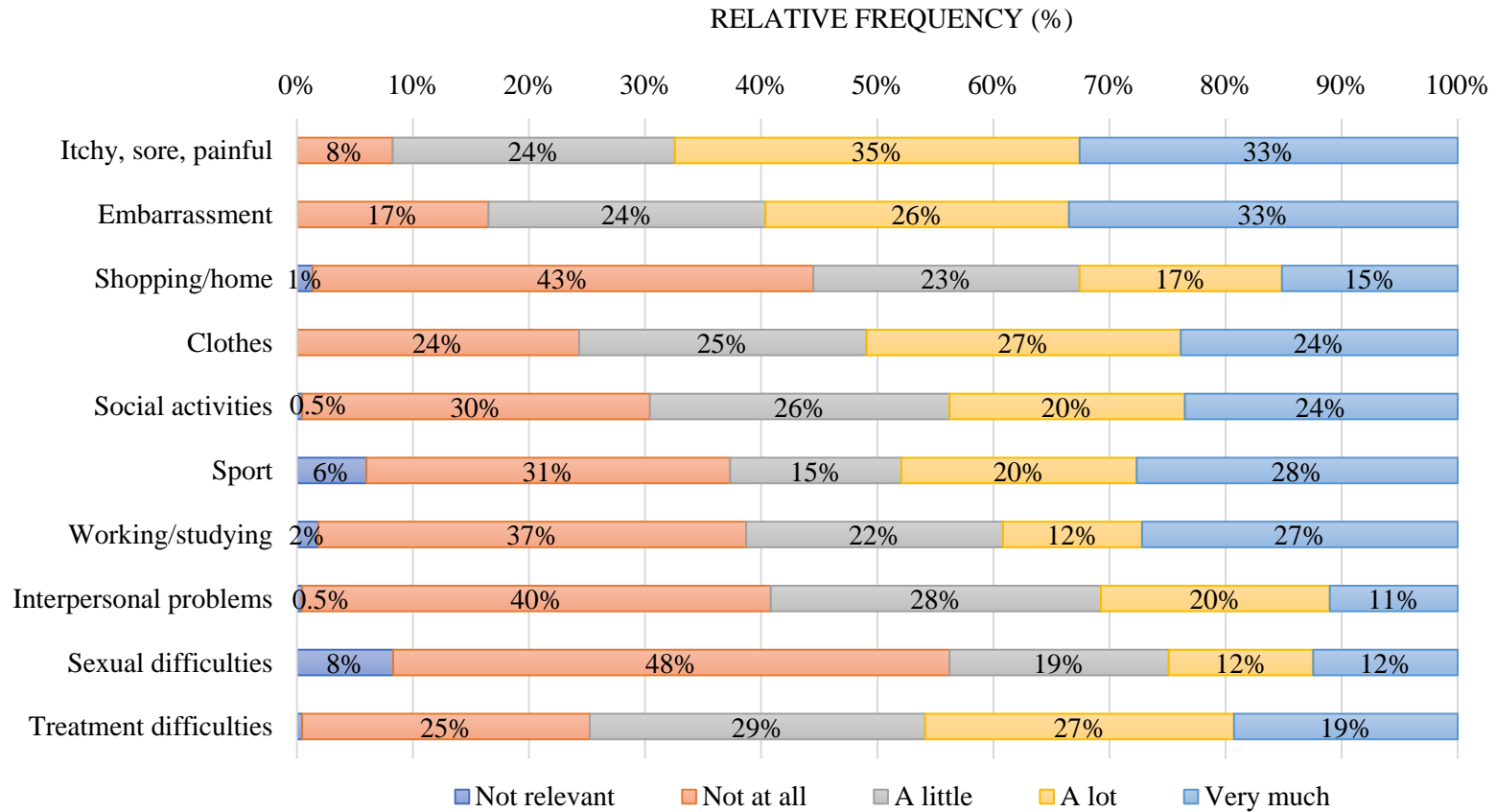


Figure 4. Frequency of problems reported on DLQI.

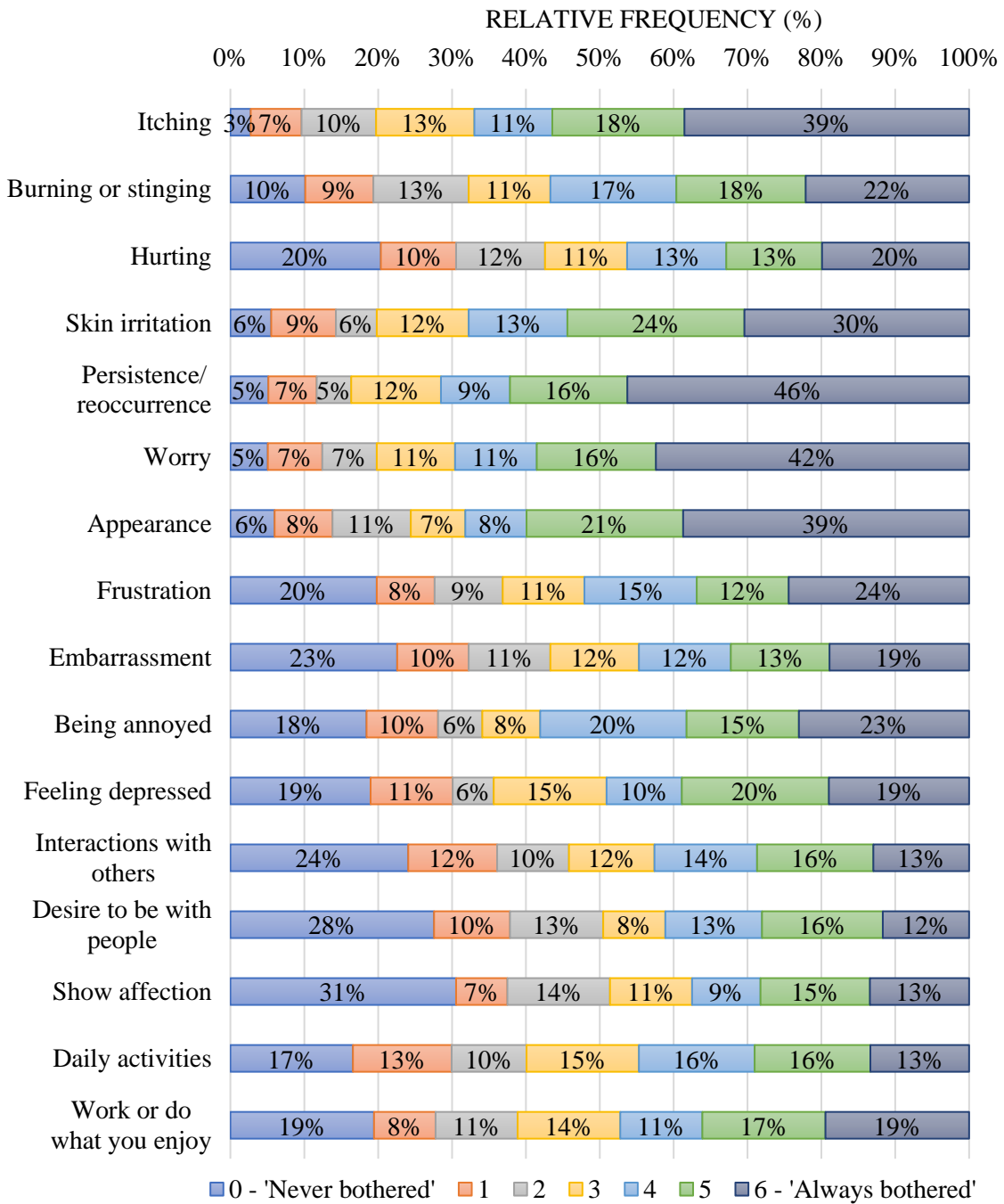


Figure 5. Frequency of problems reported on Skindex-16.

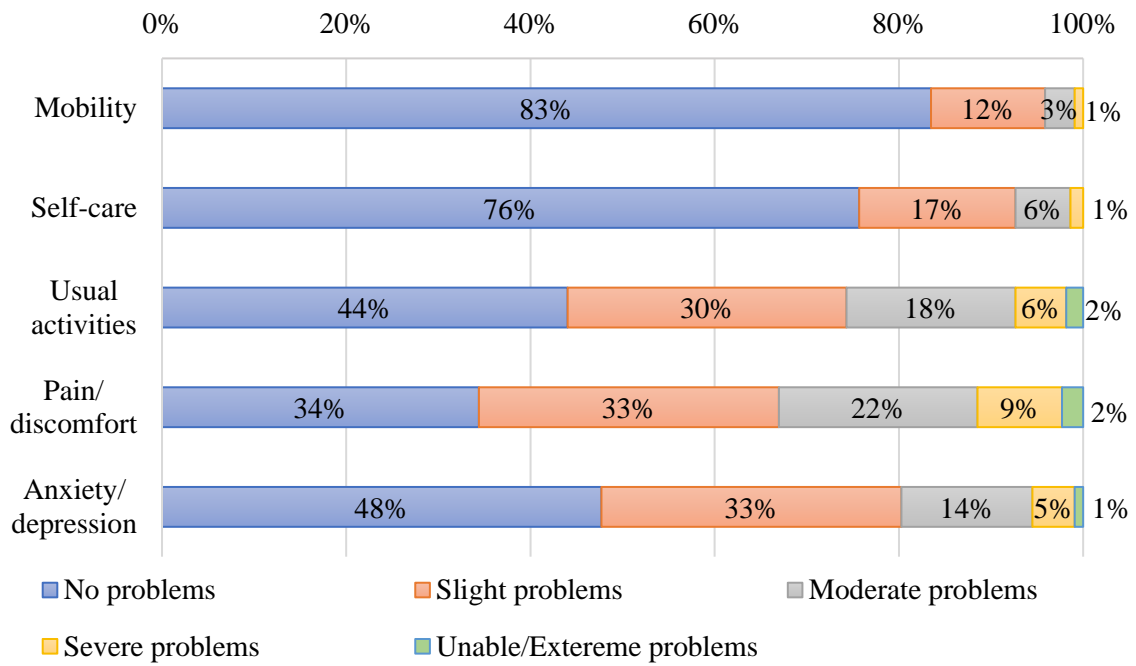


Figure 6. Frequency of problems reported on EQ-5D-5L.

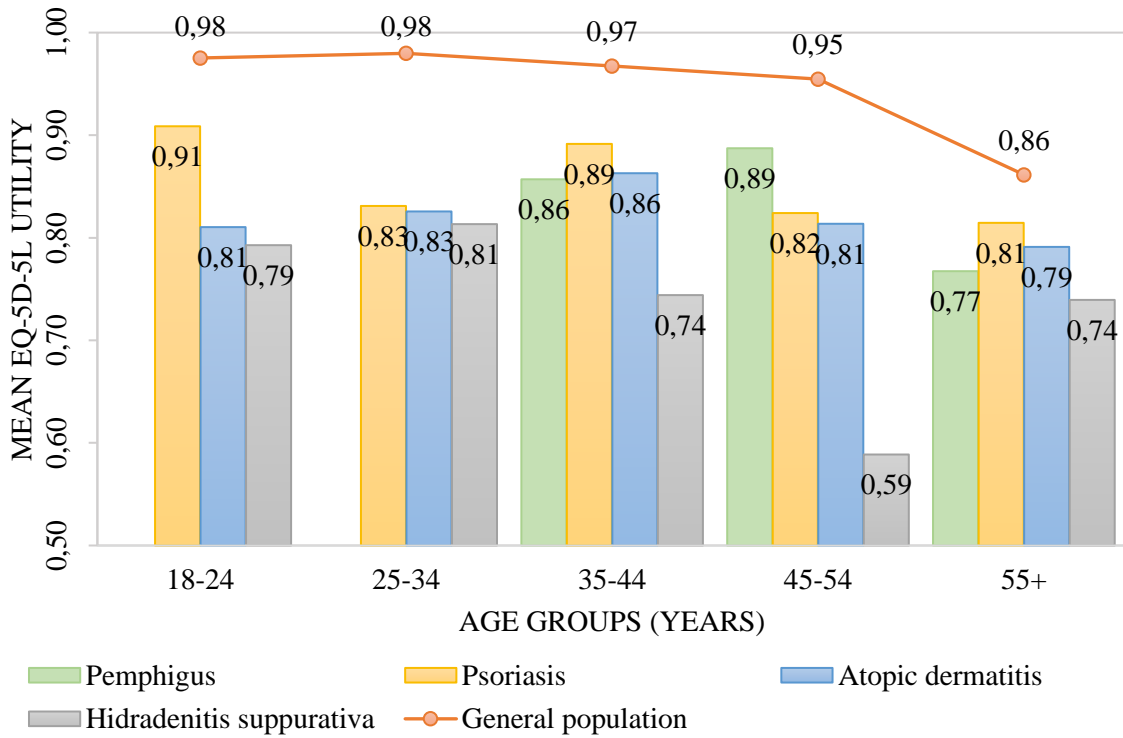


Figure 7. Comparing EQ-5D-5L utilities in skin diseases and the general population in Hungary.

Table 3. Comparison of HRQoL outcomes before and since COVID-19 controlled for age, sex, level of education, disease severity (oSCORAD) and type of treatment (N=218) [93].

Item	OR (95%CI) or marginal effect (95%CI)	p-value
EQ-5D-5L		
dimension 1 (mobility)	1.26 (0.58-2.74)	0.564
dimension 2 (self-care)	1.24 (0.64-2.38)	0.525
dimension 3 (usual activities)	1.14 (0.67-1.93)	0.628
dimension 4 (pain/discomfort)	1.78 (1.06-2.99)	0.028
dimension 5 (anxiety/depression)	1.33 (0.78-2.27)	0.300
EQ-5D-5L utility	-0.03 (-0.09-0.03)	0.313
EQ VAS	-2.18 (-7.20-2.84)	0.393
DLQI		
item 1 (itchy, sore, painful, stinging)	1.28 (0.76-2.17)	0.358
item 2 (embarrassed, self-conscious)	1.45 (0.85-2.45)	0.170
item 3 (shopping, home, garden)	1.86 (1.08-3.20)	0.026
item 4 (clothing)	0.83 (0.50-1.37)	0.460
item 5 (social, leisure)	0.90 (0.54-1.51)	0.692
item 6 (sport)	1.23 (0.72-2.09)	0.445
item 7 (working, studying)	0.84 (0.50-1.42)	0.523
item 8 (interpersonal problems)	1.33 (0.79-2.25)	0.289
item 9 (sexual difficulties)	1.55 (0.87-2.77)	0.141
item 10 (treatment difficulties)	1.57 (0.94-2.62)	0.084
DLQI total score	0.94 (-0.91-2.80)	0.317
DLQI-R total score	1.06 (-0.82-2.94)	0.266
Skindex-16		
item 1 (itching)	1.68 (1.00-2.82)	0.051
item 2 (burning or stinging)	1.48 (0.91-2.43)	0.118
item 3 (hurting)	1.87 (1.13-3.08)	0.015
item 4 (skin irritation)	1.48 (0.89-2.45)	0.134
item 5 (persistence / reoccurrence)	1.88 (1.09-3.23)	0.022
item 6 (worry)	1.89 (1.11-3.22)	0.019
item 7 (appearance)	1.00 (0.60-1.67)	0.994
item 8 (frustration)	1.51 (0.91-2.49)	0.108
item 9 (embarrassment)	1.17 (0.71-1.93)	0.540
item 10 (being annoyed)	1.20 (0.74-1.97)	0.460
item 11 (feeling depressed)	1.44 (0.87-2.37)	0.156
item 12 (interactions with others)	1.69 (1.03-2.78)	0.039
item 13 (desire to be with people)	1.16 (0.70-1.92)	0.568
item 14 (show affection)	1.59 (0.96-2.63)	0.072
item 15 (daily activities)	1.21 (0.74-1.98)	0.447
item 16 (work or do what you enjoy)	1.25 (0.76-2.04)	0.383
Skindex-16 symptoms subscale	7.41 (0.68-14.14)	0.031
Skindex-16 emotions subscale	4.66 (-1.88-11.19)	0.162
Skindex-16 functioning subscale	3.48 (-3.79-10.75)	0.345
Skindex-16 total score	5.18 (-0.78-11.15)	0.088

4.3. Measurement properties of DLQI, DLQI-R, Skindex-16, and EQ-5D-5L

No floor or ceiling effects were found for DLQI, DLQI-R, and Skindex-16 (Table 2). Also no floor effect, but a mild ceiling effect was present for 5L (22.5% achieved full health in the whole sample) which showed a reduction when comparing the before and since COVID-19 groups (27.2% vs. 16.1%, Table 4).

The 5L utility had strong correlations with the generic EQ VAS (r_s : 0.67) and skin-specific DLQI, DLQI-R, and Skindex-16 total scores (range of r_s : |0.68| to |0.73|, Table 5). There were very strong correlations among skin-specific HRQoL instruments (r_s : 0.83 to 0.99). The severity scales oSCORAD, EASI, and IGA correlated weakly with generic HRQoL instruments (r_s : |0.31| to |0.36|) and moderately with skin-specific instruments (r_s : 0.44 to 0.54). Itching and sleep disturbance in the preceding one month had moderate correlations with 5L and EQ VAS (r_s : |0.45| to |0.48|), and moderate to strong correlations with skin-specific HRQoL instruments (r_s : 0.58 to 0.63). All correlations were statistically significant ($p < 0.05$).

The HRQoL instruments demonstrated good known-group validity; patients with more severe disease had worse HRQoL scores on each instrument ($p < 0.001$, Table 6). Skin-specific HRQoL measures could differentiate across known severity groups with large effect sizes (0.20 to 0.23), while generic instruments demonstrated moderate effect sizes (0.08 to 0.13) ($p < 0.001$ for all). The DLQI outperformed most HRQoL instruments in terms of known-group validity; however, DLQI-R could better distinguish across severity groups defined by EASI (relative efficiency, RE: 1.037) and IGA (RE: 1.033), and Skindex-16 across severity groups defined by EASI (RE: 1.064).

The mean DLQI-R scores were slightly higher compared to DLQI (13.76 vs. 13.44). Overall, 30 patients (13.8%) had at least one NRR on the DLQI; 21 (9.6%) marked one NRR, 7 (3.2%) marked two NRRs and 2 (0.9%) marked three NRRs. The highest number of NRRs were reported regarding sexual difficulties, sports, and work/school (Figure 4). We found no significant difference between patients with and without NRRs in terms of age, sex, level of education, and disease severity; however, those who were not employed at the time of completion, were more likely to have at least one NRR ($p = 0.043$).

Table 4. Ceiling and floor effects of outcome measures before and since COVID-19 [93].

Outcome measures ^a		Before COVID-19 (N=125)				Since COVID-19 (N=93) ^b			
		Minimum	Maximum	Floor effect, N (%)	Ceiling effect, N (%)	Minimum	Maximum	Floor effect, N (%)	Ceiling effect, N (%)
DLQI (0-30)		0	30	7 (5.6%)	3 (2.4%)	0	29	2 (2.2%)	0 (0.0%)
DLQI-R (0-30)		0	30	7 (5.6%)	3 (2.4%)	0	29	2 (2.2%)	0 (0.0%)
Skindex-16 (0-100)	Total score	0	100	2 (1.6%)	3 (2.4%)	0	29	1 (1.1%)	0 (0.0%)
	Symptoms subscale	0	100	2 (1.6%)	20 (16.0%)	0	98.89	2 (2.2%)	13 (14.0%)
	Emotions subscale	0	100	5 (4.0%)	9 (7.2%)	0	100	1 (1.1%)	4 (4.3%)
	Functioning subscale	0	100	16 (12.8%)	7 (5.6%)	0	100	6 (6.5%)	3 (3.2%)
EQ-5D-5L utility (-0.848 to 1)		0.154	1.000	0 (0.00%)	34 (27.2%)	-0.357	1.000	0 (0.00%)	15 (16.1%)
EQ VAS (0-100) (missing=1)		0	100	1 (0.8%)	4 (3.2%)	8	100	0 (0.0%)	2 (2.2%)
Itching VAS (1-month average) (0-10) (missing=1)		0	10	5 (4.0%)	27 (21.6%)	0	100	1 (1.1%)	24 (25.8%)
Sleeping VAS (1-month average) (0-10) (missing=3)		0	10	16 (12.8%)	18 (14.4%)	0	10	9 (9.7%)	18 (19.4%)
PtGA VAS (0-10) (missing=1)		0	10	7 (5.6%)	13 (10.4%)	1	10	0 (0.0%)	7 (7.5%)
oSCORAD (0-83)		0	69.20	1 (0.8%)	0 (0.0%)	0	71.10	1 (1.1%)	0 (0.0%)
EASI (0-72)		0	59.40	3 (2.4%)	0 (0.0%)	0	58.80	1 (1.1%)	0 (0.0%)
IGA scale (0-5)		0	5	3 (2.4%)	3 (2.4%)	0	5	2 (2.2%)	2 (2.2%)

^aHigher scores represent better health status for the EQ VAS and EQ-5D-5L utility and worse health status for all other measures. ^bAfter March 11, 2020.

Table 5. Spearman's correlations between outcome measures (N=218) [93].

Measures ^a	DLQI	DLQI-R	Skindex-16				EQ VAS	EQ-5D-5L	Itching VAS ^b	Sleeping VAS ^b	PtGA VAS	oSCORAD	EASI
			Symptoms subscale	Emotions subscale	Functioning subscale	Total							
DLQI (0-30)	-	-	-	-	-	-	-	-	-	-	-	-	-
DLQI-R (0-30)	0.993	-	-	-	-	-	-	-	-	-	-	-	-
Skindex-16 (0-100)	Symptoms subscale	0.730	0.725	-	-	-	-	-	-	-	-	-	-
	Emotions subscale	0.697	0.693	0.722	-	-	-	-	-	-	-	-	-
	Functioning subscale	0.827	0.822	0.687	0.771	-	-	-	-	-	-	-	-
	Total	0.839	0.834	0.877	0.904	0.918	-	-	-	-	-	-	-
EQ VAS (0-100)	-0.598	-0.592	-0.529	-0.542	-0.591	-0.610	-	-	-	-	-	-	-
EQ-5D-5L (-0.848-1)	-0.731	-0.733	-0.572	-0.574	-0.691	-0.684	0.665	-	-	-	-	-	-
Itching VAS (0-10)^b	0.579	0.575	0.662	0.583	0.492	0.625	-0.460	-0.452	-	-	-	-	-
Sleeping VAS (0-10)^b	0.633	0.632	0.647	0.545	0.535	0.630	-0.459	-0.479	0.726	-	-	-	-
PtGA VAS (0-10)	0.672	0.670	0.682	0.633	0.592	0.695	-0.578	-0.583	0.696	0.620	-	-	-
oSCORAD (0-83)	0.485	0.538	0.461	0.428	0.492	0.516	-0.354	-0.359	0.382	0.385	0.465	-	-
EASI (0-72)	0.485	0.487	0.430	0.384	0.445	0.464	-0.334	-0.308	0.369	0.381	0.409	0.886	-
IGA (0-5)	0.472	0.480	0.377	0.363	0.448	0.443	-0.353	-0.349	0.271	0.320	0.436	0.821	0.809

^aHigher scores represent better health status for the EQ VAS and EQ-5D-5L utility and worse health status for all other measures. ^bFor the past one month.

All correlation coefficients were significant ($p < 0.05$)

Table 6. Known-group validity across the EASI, oSCORAD and IGA severity bands (mean scores, effect size, relative efficiency) (N=218) [93].

EASI degree of severity (missing = 1)		Clear or mild (0.0-5.9)		Moderate (6-22.9)	Severe (23-72)	Effect size	Relative efficiency
N (%)		51 (23.50%)	-	118 (54.38%)	48 (22.12%)	-	-
DLQI (0-30)		8.04 (6.80)	-	13.24 (7.86)	19.46 (7.45)	0.197	-
DLQI-R (0-30)		8.15 (6.91)	-	13.59 (8.02)	19.92 (7.39)	0.204	1.037
Skindex-16 (0-100)	Total score	37.14 (26.16)	-	57.84 (25.15)	74.89 (20.37)	0.209	1.064
	Symptoms subscale	42.57 (30.69)	-	63.95 (26.52)	80.04 (23.51)	0.174	0.883
	Emotions subscale	42.58 (29.96)	-	62.41 (27.82)	77.33 (19.49)	0.148	0.754
	Functioning subscale	26.28 (27.54)	-	47.18 (29.20)	67.29 (27.14)	0.188	0.957
EQ VAS (0-100)		79.22 (14.95)	-	68.03 (20.87)	61.92 (20.61)	0.086	0.437
EQ-5D-5L (-0.848-1)		0.91 (0.14)	-	0.82 (0.21)	0.75 (0.27)	0.080	0.407
oSCORAD degree of severity (missing = 1)		Clear or mild (0.0-23.9)		Moderate (24-37.9)	Severe (38-83)	Effect size	Relative efficiency
N (%)		45 (20.74%)	-	73 (33.64%)	99 (45.62%)	-	-
DLQI (0-30)		7.07 (6.31)	-	11.95 (7.14)	17.59 (7.97)	0.228	-
DLQI-R (0-30)		7.19 (6.46)	-	12.34 (7.35)	17.94 (8.03)	0.227	0.997
Skindex-16 (0-100)	Total score	36.40 (25.70)	-	52.83 (23.25)	69.66 (23.94)	0.227	0.997
	Symptoms subscale	40.28 (29.33)	-	59.93 (24.70)	75.00 (26.12)	0.198	0.868
	Emotions subscale	44.02 (30.83)	-	56.78 (26.65)	72.90 (24.72)	0.148	0.651
	Functioning subscale	24.89 (28.36)	-	41.78 (27.27)	61.08 (28.62)	0.200	0.879
EQ VAS (0-100)		79.98 (13.15)	-	70.73 (18.43)	62.73 (22.37)	0.091	0.398
EQ-5D-5L (-0.848-1)		0.92 (0.11)	-	0.86 (0.18)	0.76 (0.26)	0.089	0.391
IGA		Clear or almost clear	Mild	Moderate	Severe	Effect size	Relative efficiency
N (%)		32 (14.68%)	32 (14.68%)	108 (49.54%)	46 (21.10%)	-	-
DLQI (0-30)		5.44 (5.42)	10.31 (6.70)	14.57 (7.67)	18.54 (8.47)	0.224	-
DLQI-R (0-30)		5.53 (5.56)	10.52 (6.89)	14.93 (7.85)	19.00 (8.34)	0.231	1.033
Skindex-16 (0-100)	Total score	26.88 (22.59)	51.53 (21.77)	62.00 (24.85)	69.25 (24.70)	0.215	0.963
	Symptoms subscale	32.81 (30.08)	56.12 (21.92)	68.91 (26.89)	72.28 (26.68)	0.166	0.744
	Emotions subscale	30.43 (26.30)	60.86 (25.51)	65.96 (26.49)	71.69 (25.94)	0.167	0.744
	Functioning subscale	17.40 (21.03)	37.61 (28.05)	51.14 (29.88)	63.77 (28.19)	0.204	0.912
EQ VAS (0-100)		83.53 (12.81)	76.50 (15.98)	65.74 (19.87)	61.93 (23.01)	0.130	0.580
EQ-5D-5L (-0.848-1)		0.92 (0.11)	0.91 (0.08)	0.82 (0.20)	0.71 (0.31)	0.110	0.492

$p < 0.001$ for all groups (Kruskal-Wallis H). Bolded relative efficiency values indicate that the measure is more efficient than DLQI at discriminating between known severity groups.

4.4. Comparing the performance of EQ-5D-3L and EQ-5D-5L in AD

The two versions of EQ-5D were compared in the whole sample. Each participant completed both the 3L and 5L instruments with no missing responses in either dimension; however, one patient left the EQ VAS blank.

No floor effect occurred on 3L, 5L, or EQ VAS. On the EQ VAS, 6 (2.8%) patients reached the maximum score (“the best health you can imagine”). Ceiling effects of the 3L and 5L utilities and dimensions are shown in Table 7. A statistically significant reduction of ceiling effect was observed in the mobility, self-care, and usual activities dimensions of the 5L compared to the 3L, while in the anxiety/depression dimension the ceiling effect slightly (but not significantly) increased. The overall ceiling effect was also reduced when moving from 3L to 5L (27.5% vs. 22.5%; $p=0.029$).

Figure 8 shows the distribution of 3L and 5L utilities in the whole sample. Overall, 33 unique health states were reported on the 3L and 84 on the 5L. One patient had a negative utility (meaning a health state worse than being dead) on 5L and no one on 3L. The mean utility was slightly lower on 5L compared to 3L (0.82 vs. 0.85, $p=0.928$). There was a good agreement between 3L and 5L with an ICC of 0.815 (95% CI: 0.758–0.859, $p<0.001$). The agreement between the two measures is displayed on a Bland-Altman plot (Figure 9).

Overall, 64 (5.9%) inconsistent response pairs (i.e., where the 3L response is inconsistent with the 5L response) were marked by 50 (22.9%) patients. The proportion of inconsistent response pairs in each dimension is shown in Table 8. The fewest inconsistencies occurred in the mobility dimension. The largest average size of inconsistency and highest percentage of inconsistent response pairs were present in the anxiety/depression domain (Table 7).

Absolute informativity (H' , i.e., the number of possible responses on an instrument, combined with how evenly the information is distributed across these responses) was increased in each dimension of 5L compared to 3L (Table 7). Relative informativity (J' , i.e., how evenly the responses are distributed) increased in the first four dimensions, but not in the anxiety/depression dimension.

Table 7. Ceiling effect, inconsistencies and informativity of the EQ-5D-3L and EQ-5D-5L in AD [92].

Dimensions	Ceiling effects							Inconsistencies		Informativity			
	EQ-5D-3L		EQ-5D-5L		Ceiling effect reduction		McNemar's test <i>p</i> -value			EQ-5D-3L		EQ-5D-5L	
	n	Ceiling (n, %)	n	Ceiling (n, %)	Absolute (%)	Relative (%)		Inconsistent response pairs (n, %) ^a	Average size of inconsistencies	H'	J'	H'	J'
Mobility	218	192 (88.1%)	218	182 (83.5%)	4.59%	5.21%	0.016	3 (1.4%)	1.00	0.53	0.33	0.81	0.35
Self-care	218	190 (87.2%)	218	165 (75.7%)	11.47%	13.16%	<0.001	9 (4.1%)	1.11	0.55	0.35	1.07	0.46
Usual activities	218	116 (53.2%)	218	96 (44.0%)	9.17%	17.24%	0.002	15 (6.9%)	1.07	1.15	0.73	1.83	0.79
Pain/discomfort	218	86 (39.4%)	218	75 (34.4%)	5.05%	12.79%	0.054	17 (7.8%)	1.12	1.17	0.74	1.98	0.85
Anxiety/depression	218	99 (45.4%)	218	104 (47.7%)	-2.29%	-5.05%	0.404	20 (9.2%)	1.15	1.27	0.80	1.70	0.73
Overall (11111) or average	-	60 (27.5%)	-	49 (22.5%)	5.05%	18.33%	0.029	64 (5.9%)	1.09	0.93	0.59	1.48	0.64

H' = Shannon's index; J' = Shannon's evenness index

^aThe total number of pairs is 218 for all dimensions.

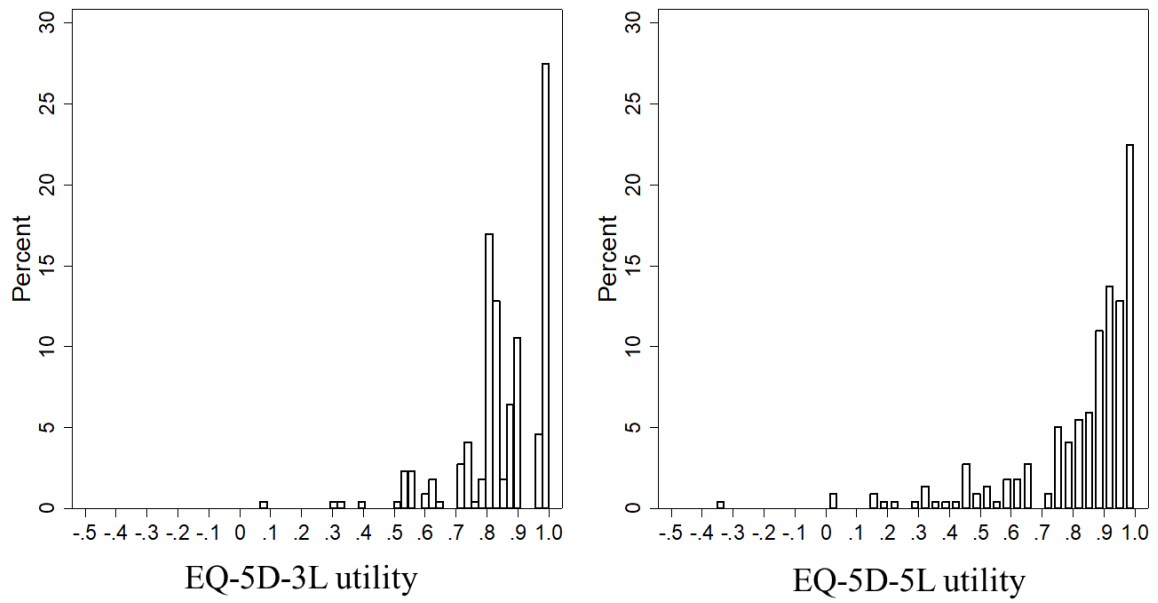


Figure 8. Distribution of EQ-5D-3L and EQ-5D-5L utilities in AD patients [92].

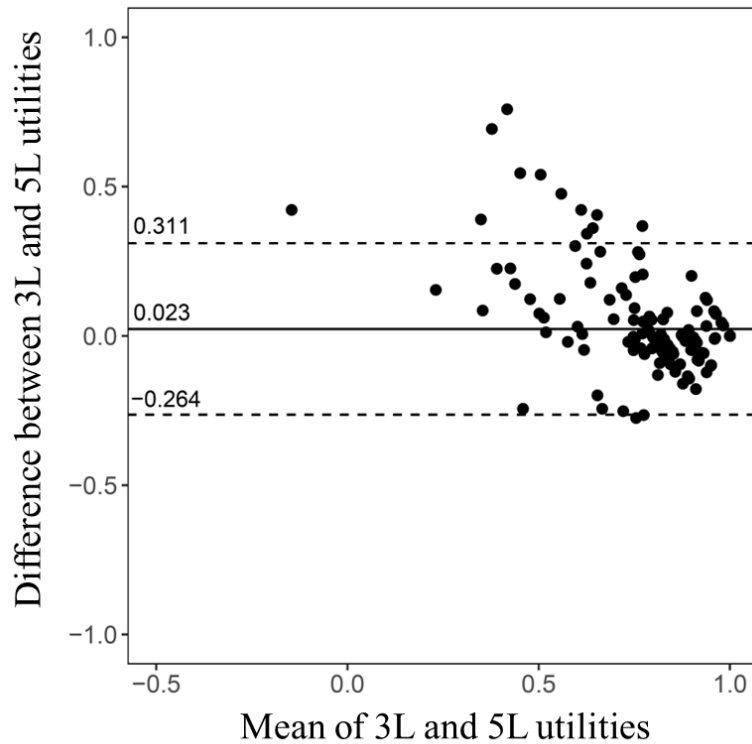


Figure 9. Bland-Altman plot of EQ-5D-3L and EQ-5D-5L utilities [92].

Table 8. Redistribution properties: cross-tabulation of EQ-5D-3L and EQ-5D-5L responses [92].

3L	5L				
Dimensions	Level 1	Level 2	Level 3	Level 4	Level 5
Mobility, n (%)					
Level 1	180 (93.8%)	11 (5.7%)	1 (0.5%)	0 (0.0%)	0 (0.0%)
Level 2	2 (7.7%)	16 (61.5%)	6 (23.1%)	2 (7.7%)	0 (0.0%)
Level 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Self-care, n (%)					
Level 1	163 (85.8%)	20 (10.5%)	6 (3.2%)	1 (0.5%)	0 (0.0%)
Level 2	2 (7.1%)	17 (60.7%)	7 (25.0%)	2 (7.1%)	0 (0.0%)
Level 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Usual activities, n (%)					
Level 1	88 (75.9%)	22 (19.0%)	5 (4.3%)	1 (0.9%)	0 (0.0%)
Level 2	8 (8.3%)	44 (45.8%)	34 (35.4%)	10 (10.4%)	0 (0.0%)
Level 3	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (16.7%)	4 (66.7%)
Pain/discomfort, n (%)					
Level 1	67 (77.9%)	15 (17.4%)	2 (2.3%)	2 (2.3%)	0 (0.0%)
Level 2	8 (6.5%)	56 (45.2%)	43 (34.7%)	14 (11.3%)	3 (2.4%)
Level 3	0 (0.0%)	0 (0.0%)	2 (25.0%)	4 (50.0%)	2 (25.0%)
Anxiety/depression, n (%)					
Level 1	90 (90.9%)	6 (6.1%)	3 (3.0%)	0 (0.0%)	0 (0.0%)
Level 2	13 (12.3%)	64 (60.4%)	26 (24.5%)	3 (2.8%)	0 (0.0%)
Level 3	1 (7.7%)	1 (7.7%)	2 (15.4%)	7 (53.8%)	2 (15.4%)

The size of inconsistency is represented in grayscale with more inconsistency in darker fields. White fields contain consistent response pairs.

Percentages may not total 100 by row due to rounding.

Correlations of 3L and 5L dimensions and utilities with other instruments are shown in Table 9. Both 3L and 5L utilities correlated strongly with EQ VAS, DLQI, and Skindex-16 total score, and weakly with EASI, oSCORAD, and IGA severity scores. When analyzing each dimension, we found that the mobility and self-care dimensions had weak or no correlations with other HRQoL instruments, while the usual activities, pain/discomfort, and anxiety/depression dimensions correlated moderately or strongly with DLQI and Skindex-16. Itching and sleep disturbance in the preceding one month exhibited weak correlations with 3L and moderate correlations with 5L utilities. In terms of convergent validity, the 5L outperformed 3L in almost all instances with only two exceptions: the anxiety/depression dimension of 3L correlated slightly stronger with IGA and oSCORAD scores.

Results of the known-group validity comparison of 3L and 5L are shown in Table 10. Both instruments could differentiate across groups of patients based on severity and DLQI score bands with moderate to large effect sizes. In other words, patients with more severe disease and worse skin-specific HRQoL had lower 5L and 3L utilities ($p < 0.001$). The 5L could better distinguish across EASI (RE: 1.033) and DLQI (RE: 1.275) groups, while 3L performed slightly better with IGA (RE: 0.978) and oSCORAD (RE: 0.966) groups.

Table 9. Convergent validity of 3L and 5L dimensions and utilities: Spearman's correlation coefficients [92].

Outcome measures	EQ-5D						
	Version	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression	Utility
EQ VAS (0-100)	3L	-0.255	-0.246	-0.483	-0.547	-0.507	0.626
	5L	-0.333	-0.316	-0.495	-0.676	-0.531	0.665
Itching VAS (0-10) (1-month average)	3L	0.096*	0.106*	0.299	0.351	0.305	-0.383
	5L	0.186	0.159	0.379	0.476	0.361	-0.452
Sleeping VAS (0-10) (1-month average)	3L	0.147	0.091*	0.312	0.381	0.276	-0.397
	5L	0.167	0.195	0.364	0.484	0.368	-0.479
IGA scale (0-5)	3L	0.171	0.130*	0.241	0.326	0.236	-0.328
	5L	0.207	0.202	0.289	0.389	0.223	-0.349
EASI (0-72)	3L	0.098*	0.113*	0.171	0.254	0.244	-0.274
	5L	0.196	0.128*	0.215	0.328	0.262	-0.308
oSCORAD score (0-83)	3L	0.174	0.139	0.236	0.312	0.271	-0.342
	5L	0.273	0.226	0.280	0.375	0.254	-0.359
Skindex-16 total (0-100)	3L	0.181	0.237	0.526	0.515	0.521	-0.622
	5L	0.302	0.329	0.566	0.657	0.556	-0.684
Skindex-16 symptoms (0-100)	3L	0.136	0.136	0.429	0.488	0.380	-0.513
	5L	0.217	0.212	0.459	0.612	0.392	-0.572
Skindex-16 emotions (0-100)	3L	0.105*	0.195	0.429	0.444	0.511	-0.549
	5L	0.248	0.260	0.460	0.551	0.531	-0.574
Skindex-16 functioning (0-100)	3L	0.239	0.298	0.535	0.492	0.510	-0.619
	5L	0.339	0.375	0.594	0.617	0.556	-0.691
DLQI (0-30)	3L	0.267	0.338	0.570	0.557	0.509	-0.669
	5L	0.354	0.376	0.651	0.670	0.545	-0.731

* $p > 0.05$. Bold and italic values indicate a lower correlation coefficient for the 5L compared to 3L.

Table 10. Known-group validity of EQ-5D-3L and EQ-5D-5L compared [92].

		EQ-5D-5L utility					EQ-5D-3L utility					RE ^b
		n	Mean (SD)	Median (Q1-Q3)	<i>p</i> -value ^a	ES	n	Mean (SD)	Median (Q1-Q3)	<i>p</i> -value ^a	ES	
Total sample		218	0.82 (0.22)	0.89 (0.78-0.97)	-	-	218	0.85 (0.15)	0.85 (0.80-1.00)	-	-	-
IGA	Clear	5	0.95 (0.09)	1.00 (0.96-1.00)	<0.001	0.105	5	0.97 (0.07)	1.00 (1.00-1.00)	<0.001	0.108	0.978
	Minimal	27	0.93 (0.11)	0.97 (0.91-1.00)			27	0.93 (0.11)	1.00 (0.88-1.00)			
	Mild	32	0.91 (0.08)	0.92 (0.87-0.96)			32	0.87 (0.09)	0.88 (0.80-0.96)			
	Moderate	108	0.82 (0.20)	0.88 (0.76-0.96)			108	0.85 (0.13)	0.82 (0.80-0.96)			
	Marked	41	0.70 (0.32)	0.83 (0.49-0.92)			41	0.78 (0.20)	0.80 (0.72-0.90)			
	Severe	5	0.77 (0.07)	0.79 (0.75-0.80)			5	0.70 (0.15)	0.72 (0.55-0.82)			
EASI	Clear (0.0-0.1)	5	0.80 (0.33)	0.96 (0.80-1.00)	<0.001	0.083	5	0.93 (0.11)	1.00 (0.85-1.00)	<0.001	0.080	1.033
	Mild (0.2-5.9)	46	0.92 (0.10)	0.96 (0.88-1.00)			46	0.91 (0.10)	0.96 (0.82-1.00)			
	Moderate (6-22.9)	118	0.82 (0.21)	0.90 (0.77-0.96)			118	0.85 (0.14)	0.88 (0.80-0.96)			
	Severe (23-72)	49	0.74 (0.28)	0.85 (0.67-0.92)			49	0.78 (0.18)	0.80 (0.78-0.85)			
oSCORAD	Clear (0-7.9)	8	0.97 (0.07)	1.00 (0.99-1.00)	<0.001	0.099	8	0.98 (0.05)	1.00 (1.00-1.00)	<0.001	0.103	0.966
	Mild (8-23.9)	38	0.91 (0.11)	0.94 (0.87-1.00)			38	0.90 (0.10)	0.93 (0.82-1.00)			
	Moderate (24-37.9)	73	0.86 (0.17)	0.92 (0.81-0.97)			73	0.86 (0.12)	0.88 (0.80-0.96)			
	Severe (38-83)	99	0.76 (0.26)	0.85 (0.65-0.92)			99	0.80 (0.17)	0.82 (0.78-0.90)			
DLQI	No effect (0-1)	15	0.99 (0.01)	1.00 (1.00-1.00)	<0.001	0.489	15	0.99 (0.03)	1.00 (1.00-1.00)	<0.001	0.384	1.275
	Small effect (2-5)	37	0.96 (0.05)	1.00 (0.93-1.00)			37	0.94 (0.09)	1.00 (0.90-1.00)			
	Moderate effect (6-10)	40	0.93 (0.08)	0.94 (0.92-0.96)			40	0.91 (0.07)	0.90 (0.88-1.00)			
	Very large effect (11-20)	76	0.80 (0.17)	0.84 (0.76-0.92)			76	0.82 (0.11)	0.82 (0.80-0.88)			
	Extremely large effect (21-30)	50	0.62 (0.29)	0.66 (0.45-0.85)			50	0.73 (0.19)	0.80 (0.62-0.82)			

^aMann-Whitney test or Kruskal Wallis test, where $p < 0.05$ was considered statistically significant. ^bRelative efficiency compared to the EQ-5D-3L.

5. Discussion

We conducted an extensive, multicenter survey on the HRQoL of adult AD patients in Hungary. According to the available global literature, our study was the first to provide comprehensive data on multiple measurement properties of DLQI, DLQI-R, Skindex-16, and 5L, and to compare the 3L and 5L versions of EQ-5D in AD patients. The results have important implications for clinicians, researchers, and healthcare decision makers. This study is also among the first attempts to evaluate the effect of the COVID-19 pandemic on the HRQoL of AD patients.

5.1. Health-related quality of life (HRQoL) in AD

5.1.1. HRQoL impairment in AD

Our patients reported substantially reduced HRQoL in several aspects of life; most problems occurred regarding skin symptoms (i.e., itching, pain) and mental health (i.e., worrying, anxiety, depression). The impairment of mental HRQoL among AD patients has been extensively studied and previous research also found increased rates of anxiety, depression, and even suicidal ideation [53,54,119]. It is also known that skin symptoms directly impact several areas of life such as sleep quality, daily activities, social interactions, and sexual life [52,120,121]. As predictors of HRQoL impairment, we identified disease severity, sleep disturbance, and pruritus which findings are in line with previous reports [122].

Nevertheless, we observed some exceptions when patients with clear or mild AD had severe HRQoL impairment and vice versa, suggesting that the main factors contributing to HRQoL loss may vary across individuals. For instance, some people are more bothered by their physical appearance, while others feel less embarrassed because of visible skin lesions. Given the different individual needs and the wide variety of available AD therapies, the treatment strategy should be determined in a personalized way and measuring HRQoL can be helpful during this process [123]. This highlights the importance of applying HRQoL measures not only in clinical trials but also in daily practice, which is often overlooked by dermatologists [124]. Self-administered instruments can be quickly completed during visits (even in the waiting room prior to the consultation) and may enable to explore the personal components of HRQoL impairment

and thereby to identify the optimal treatment strategy and to monitor the therapeutic effect [125]. On the long run, regular use of HRQoL instruments in clinical practice may also contribute to an increased quality of patient care [125]. According to the recommendations of the European Academy of Dermatology and Venereology (EADV), clinicians should use a skin- and/or AD-specific instrument, while researchers should apply a combination of generic and skin-specific instruments [58]. There is a currently ongoing work by the HOME group to identify the most suitable HRQoL instrument for AD patients in clinical practice.

5.1.2. Comparison of HRQoL in AD and other chronic diseases

The 5L is widely used for generic HRQoL assessment in many diseases and the general population. It has been described several times that AD patients have significantly lower HRQoL than healthy controls [122]. Using previous data from our research group, we found a similar HRQoL reduction in AD (mean 5L utility: 0.82), HS (0.75), psoriasis (0.84), and pemphigus (0.81) compared to the general population (0.93) in Hungary [43,63,82,118]. As for non-dermatologic conditions, a systematic review summarized available 5L studies and reported that mean 5L utilities ranged from 0.31-0.99 in diabetes, 0.62-0.90 in neoplasms, 0.56-0.85 in cardiovascular diseases, 0.65-0.90 in HIV infection, and 0.68-0.79 in COPD [126]. Furthermore, we found that AD patients had similar mean 5L utilities to values reported in partly controlled asthma (0.80) [127]. Nevertheless, we have to emphasize that the comparability of utilities across different studies is limited due to variances of disease severity in patient populations and different value sets applied for utility calculation.

Regarding 5L dimensions, the most burdensome area was pain/discomfort in AD, where 65.6% of our patients reported problems. In the Hungarian general population and in HS, psoriasis, and pemphigus, 28.9%, 77.4%, 53.0%, and 49.5% had problems in this dimension, respectively. As reference, in liver disease, diabetes, cardiovascular disease, COPD/asthma, and arthritis, 42.2%, 58.5%, 74.5%, 77.8%, and 93.0% of patients reported problems, respectively [108]. When comparing DLQI outcomes with different skin conditions, we found that AD patients had worse mean DLQI scores (13.44) than patients with HS (11.75), psoriasis (7.13), vitiligo (9.30), pemphigus (5.40), and morphea (3.99) [81-83,118,128].

5.1.3. Impact of the COVID-19 pandemic on HRQoL

Mean DLQI, DLQI-R, Skindex-16, and 5L scores have indicated quite severe HRQoL impairment both prior to and since the COVID-19 pandemic; however, some specific problems have become more common after the outbreak. For instance, more worrying and pain/discomfort has been reported in the new epidemiological situation. This corresponds to previous studies which reported increased anxiety during the pandemic [129,130]. An important implication of these findings is that psychosocial stress is known to negatively impact the course of chronic inflammatory skin diseases, including AD [131-133]. Higher stress levels and frequent hand-washing with detergents may be related to more reported problems regarding skin symptoms during COVID-19 [129]. Greater fear of persistence/reoccurrence of lesions may be explained by limited access to outpatient care during the lockdown. Increased difficulties with social interactions and shopping/home/garden are probably related to the lockdown restrictions. Furthermore, the ratio of patients reporting full health almost halved after the outbreak as attested by the reduction of ceiling effect in 5L. All these findings highlight that the COVID-19 pandemic placed substantial additional burden on AD patients.

5.2. Measurement properties of DLQI, DLQI-R, Skindex-16, and EQ-5D-5L

Each instrument demonstrated good overall validity. Ceiling and floor effects refer to the proportion of patients achieving the maximum or minimum score possible on the scale. No floor effect occurred and only 5L demonstrated a slight ceiling effect which may be explained by its generic nature and that some questions are therefore not relevant in AD. Compared to an earlier study, 5L had somewhat larger ceiling effect in psoriasis than in our sample, meaning that higher proportion of psoriasis patients reported full health on the instrument [63]. This finding is important because if a HRQoL measure shows substantial ceiling or floor effect, that is considered a limitation of the instrument as it may not be able to register slight differences in very mild or very severe HRQoL impairment.

The HRQoL instruments showed good convergent and known-group validity with each other and severity scales. As expected based on previous findings, skin-specific measures correlated stronger with disease severity than generic ones [66]. Interestingly, we observed strong correlations between generic and skin-specific HRQoL instruments,

which is in contrast with earlier studies reporting at most moderate correlations [65,134]. When assessing known-group validity, skin-specific DLQI, DLQI-R, and Skindex-16 had larger effect sizes than 5L, meaning that they were more effective at differentiating across known severity groups of patients. Measurement properties of Skindex-16 presented in this study are especially relevant, as most earlier studies that used Skindex-16 did not conduct comprehensive validation of the instrument. The only exception we found was a Japanese study [89]; however, evidence on measurement properties is usually needed from different settings and contexts (e.g., country, language, clinical setting) to confirm the validity and usefulness of an instrument.

On the DLQI form, much smaller proportion of patients had at least one NRR (13.8%) compared to what was observed in HS (20.7%), pemphigus (53.7%), morphea (36.6%), psoriasis (24.0-38.8%), or mild AD (55.2%) [74,79,81-83,135,136]. However, in this latter AD study, data were collected on an online platform, and it included patients with mild disease contrary to our sample. Interestingly, in our sample NRRs were slightly more frequent in the since COVID-19 group; lifestyle changes and restrictions may have contributed to the increase in NRRs during the pandemic, as it was also observed in psoriasis patients in Ireland [137]. Altogether, the overall performance of DLQI-R did not significantly differ from DLQI in our sample. Although some previous reports found that DLQI-R performs better than DLQI in skin diseases, others did not [81,136]. It seems that while DLQI-R scoring may help compensate the bias caused by NRRs, it does not solve the underlying issue of content validity with DLQI [79]. Given that AD patients are from different sociodemographic groups, it looks inevitable that some items of the questionnaire such as “shopping”, “work/study”, “sports”, and “sexual relationships” concern them differently. Further, the one-week recall period may also affect NRRs as some patients may not engage in these activities on a weekly basis. Still, DLQI is the recommended HRQoL outcome measure for adults in AD clinical trials. Clinicians, patients, industry representatives and methodologists took part in the discussion at the HOME VII consensus meeting which focused on the validity of available adult HRQoL instruments and DLQI was chosen as the most suitable one [72]. Our findings support the usefulness of DLQI in AD; however, the usefulness of DLQI-R needs further investigation in this patient population.

Overall, in our sample the three skin-specific instruments performed similarly well and slightly outperformed the generic 5L, as expected. This may be attributable to the fact that 5L dimensions are not specific to skin-related symptoms and the instrument is therefore less sensitive at detecting slight variances in HRQoL. Future research is needed to validate the 5L against AD-specific HRQoL measures, such as the QoLIAD [138].

5.3. Comparing the performance of EQ-5D-3L and EQ-5D-5L in AD

Both 3L and 5L demonstrated good psychometric properties with 5L being somewhat superior in most aspects. Earlier studies have also reported improved measurement properties for 5L in various patient groups (e.g., liver disease, diabetes, cardiovascular disease, COPD/asthma, and arthritis) and the general population [107,139]. Among skin diseases, the two versions have been compared in psoriasis and HS, but not yet in AD [63,64]. The performance of the two descriptive systems can vary a lot, even among dermatological conditions. However, it is important to determine how measurement properties of the instruments translate into the discriminatory power of utilities, as this may have an impact on QALYs, cost-effectiveness ratios and ultimately financial decisions in healthcare.

The improved overall discriminatory power of 5L in AD is attested by the increased relative informativity ($J'=0.59$ in 3L, vs. 0.65 in 5L). The absolute informativity also increased ($H'=0.93$ in 3L, vs. 0.48 in 5L) supporting the usefulness of the additional two response levels in 5L. Furthermore, when comparing the two descriptive systems, more than twice as many unique health states were observed in psoriasis (86 vs. 30), HS (101 vs. 43), and AD (84 vs. 33) with the 5L than with the 3L suggesting that 5L enables a more precise measurement of health status. Other concordant findings in psoriasis, HS, and AD are the ceiling effect reduction of 5L, the low proportion of inconsistent response pairs, and the increased average informativity of 5L. Similar improvements were reported in a European study of non-dermatological patient groups with different chronic diseases [108].

Mean utilities were lower in the 5L, compared to the 3L in HS (0.76 vs 0.78) and AD (0.82 vs. 0.85), but it was not the case in psoriasis (0.84 vs. 0.77). Of note, in the HS and AD studies the Hungarian value sets were used to calculate utilities, while in the

psoriasis study, the UK value sets. In AD patients, the difference between 3L and 5L values tended to increase at lower mean utilities (i.e., at worse health states), with lower utilities on 5L, suggesting that with its extra two levels, 5L can more precisely capture worse health states.

We observed some unexpected tendencies in the measurement properties of the anxiety/depression dimension. Interestingly, in all three dermatological conditions, ceiling effects decreased in each dimension when moving from 3L to 5L, except in this one, where a slight increase was observed. Furthermore, in our sample this was the only dimension where the relative informativity of 5L did not increase and the number of inconsistent response pairs was also the highest here. Similar observations were reported for the anxiety/depression dimension in other studies from Hungary [63,64,140]. These results may be explained by the altered wording of the two systems: in the Hungarian versions, the word “depression” was translated to “lehangoltság” (meaning feeling down) in 3L, while the word “depresszió” (meaning depression) was used in 5L. We may presume that people are more likely to say that they are feeling down than that they have depression.

Overall, the improved measurement properties of the 5L descriptive system seem to appear on the level of utilities as well; 5L utilities correlated stronger with disease severity and skin-specific HRQoL than 3L utilities. The particularly strong correlation of 5L utilities with DLQI and Skindex-16 support the excellent validity of 5L in the AD population. Nevertheless, regarding known-group validity, the 3L and 5L were equally effective at differentiating between known patient groups based on severity, as attested by the similar effect sizes. Future research may concentrate on the test–retest reliability and responsiveness of the instruments.

5.4. Limitations

The study has some limitations. First, most participants were enrolled at university hospitals, where patients with moderate and severe AD may be overrepresented compared to mild AD. Second, as AD-specific HRQoL questionnaires, such as QoLIAD, or ABS-A, are not available in Hungarian language, these were not applied although they would have contributed to the validation of skin-specific and generic instruments [138,141]. Third, there were some differences between the before COVID-19 and since COVID-19

groups in terms of comorbidities, current treatment, and the proportion of participants with “other” employment. A possible explanation for the difference in treatments may be the less frequent outpatient visits during the lockdown and the improved access to dupilumab in Hungary after 2020 (5 patients received dupilumab in the since COVID-19 group whereas none in the before one). However, in other demographic and clinical characteristics there was no significant difference between the two groups. Fourth, given the cross-sectional design, we could not collect longitudinal data from individual patients, which would have allowed a more precise analysis of the impact of COVID-19 on HRQoL. Also, because of the cross-sectional design, test-retest reliability, and responsiveness of the HRQoL instruments could not be assessed. Lastly, the comparability of HRQoL among skin diseases is limited due to differences in the study populations regarding disease severity and age distribution.

On the other hand, strengths of the study include its multicenter nature, the wide variety of HRQoL and disease severity instruments used, and the diverse patient population in terms of clinical and demographical characteristics.

6. Conclusions

Measuring HRQoL is an important tool for the assessment of individual and societal burden caused by chronic diseases. Adult patients with AD have substantially impaired HRQoL affecting several areas of life. Some specific problems regarding symptoms and mental wellbeing have become significantly more common since the COVID-19 pandemic. The results of our study contributed to the validation of three skin-specific (DLQI, DLQI-R, Skindex-16) and two generic (3L, 5L) HRQoL instruments in AD. Each instrument demonstrated good overall validity and could be applied for HRQoL assessment in AD. This study also provides 3L and 5L utilities stratified by disease severity that are suitable to estimate QALYs in cost-effectiveness analyses of AD treatments. When comparing the two adult versions of EQ-5D, the 5L was superior compared to 3L regarding both the descriptive system (except the anxiety/depression dimension in some instances) and the utilities. Our findings supported the importance of HRQoL assessment both in clinical and research settings. Skin-specific instruments are more sensitive to slight changes in HRQoL and are therefore more useful in clinical practice while the generic 5L can be recommended for QALY calculations. This is particularly important as the increasing number of novel but costly AD therapies create a growing need for high-quality inputs in cost-effectiveness analyses.

7. Summary

Atopic dermatitis (AD) is a chronic inflammatory skin disease with extensive individual and socioeconomic burden. There are several instruments for measuring skin-specific and generic health-related quality of life (HRQoL) of patients; the latter can also be used for creating inputs for cost-effectiveness analyses in economic evaluations of therapies.

The goal of this study was to assess the HRQoL of adult AD patients in Hungary, to identify the most problematic areas, and to explore how they were affected by the COVID-19 pandemic. We also aimed to compare measurement properties of DLQI, DLQI-R, Skindex-16, and EQ-5D-5L (5L) in terms of ceiling and floor effects as well as convergent and know-group validity. Further, the performance of two generic measures, the EQ-5D-3L (3L) and 5L were compared in AD.

We conducted a multicenter cross-sectional survey involving 218 adult AD patients in Hungary. Participants were asked to complete a survey including the five HRQoL instruments along with sociodemographic and medical questions. Disease severity was measured by EASI, oSCORAD, and IGA, and patients also completed 0-10 VASs for itching and sleep disturbance.

The HRQoL outcomes showed quite severe overall HRQoL impairment; mean DLQI, DLQI-R, and Skindex-16 scores were 13.44, 13.76, and 56.84, while mean 3L and 5L utilities were 0.85 and 0.82, respectively. Problems regarding skin symptoms, pain/discomfort, worrying, fear of persistence/reoccurrence of disease, and social relationships have become more common during the pandemic ($p < 0.05$ for all). Skin-specific instruments outperformed 5L in terms of ceiling effect, convergent and known-group validity. The 5L was superior to 3L regarding ceiling effect, informativity, and convergent validity.

To conclude, patients with AD reported considerable HRQoL impairment in several areas of life, and some problems regarding symptoms and mental health have become even more frequent since the start of the COVID-19 pandemic. Each instrument performed well against validity tests. The skin-specific DLQI, DLQI-R, and Skindex-16 can be recommended for use in clinical practice, and 5L should be preferred over 3L in economic evaluations of AD treatments.

8. Összefoglalás

Az atopiás dermatitis (AD) egy krónikus gyulladásoos bőrbetegség, mely jelentős terhet ró a betegekre és a társadalomra egyaránt. A bőr-specifikus és általános egészséggel kapcsolatos életminőség felmérésére számos mérce létezik, melyek közül az utóbbiak segítségével költséghatékonysági elemzések során is alkalmazható adatok (hasznosságértékek) nyerhetők.

Tanulmányunk célja volt, hogy felmérjük a felnőtt AD-s betegek életminőségét Magyarországon, hogy meghatározzuk a betegség által érintett leginkább problémás területeket és hogy megvizsgáljuk, mindez hogyan változott a COVID-19 pandémia során. További célunk volt, hogy összehasonlítsuk a DLQI, DLQI-R, Skindex-16 és EQ-5D-5L (5L) mérési tulajdonságait padló- és plafonhatás, konvergencia validitás és ismert csoportok szerinti validitás tekintetében. Összehasonlítottuk továbbá két általános életminőség mérce, az EQ-5D-3L (3L) és az 5L mérési tulajdonságait AD-ben.

Egy multicentrikus keresztmetszeti felmérést végeztünk 218 felnőtt AD-s beteg bevonásával. A résztvevők egy kérdőívet töltöttek ki, mely az életminőség mércék mellett szociodemográfiai és klinikai adatokra vonatkozó kérdéseket is tartalmazott. A betegség súlyosságát az EASI, oSCORAD és IGA skálák segítségével mértük fel, valamint a betegek 0-10-ig terjedő viszketés és alvászavar vizuális analóg skálákat is kitöltöttek.

Az átlagos DLQI, DLQI-R és Skindex-16 pontszámok (rendre 13,44, 13,76 és 56,84), valamint 3L és 5L hasznosság értékek (0,85 és 0,82) jelentős életminőség csökkenést jeleztek. A bőrtünetekkel, fájdalommal, aggodalommal, társas kapcsolatokkal és a betegség kiújulásával, fennmaradásával kapcsolatos problémák gyakoribbá váltak a pandémia idején ($p < 0,05$). A bőrspecifikus mércék jobban teljesítettek plafonhatás, konvergencia és ismert csoportok szerinti validitás tekintetében mint az általános 5L. Az 5L verzió pontosabbnak bizonyult a 3L verzióhoz képest a plafonhatás, informativitás és konvergencia validitás vonatkozásában.

Összességében az AD-s betegek jelentős életminőség-csökkenésről számoltak be az élet számos területén és néhány bőrtünetekkel és mentális egészséggel kapcsolatos probléma még gyakoribbá vált a pandémia alatt. A vizsgált mércék közül a betegellátás során a bőrspecifikus DLQI, DLQI-R és Skindex-16 használata, gazdasági elemzésekhez pedig elsősorban az 5L hasznosság értékek használata javasolt.

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10. Bibliography of own publications

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10.1.1. International peer reviewed journals (total IF: 11.478)

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10.1.2. Conference presentations and posters

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10.2. Other publications

10.2.1. Book chapters

1. Koszorú K, Sárdy M. Linear IgA Disease. In: Schmidt E (ed.), Diseases of the oral mucosa. Springer, Cham, 2021: 241-245.
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10.2.2. International peer reviewed journals (total IF: 6.356)

1. Koszorú K, Kovács A, Lőrincz K, Medvecz M, Sárdy M. (2023) Low dose oral glucocorticoid therapy in lichen planus: A retrospective cohort study. *Indian J Dermatol Venereol Leprol*, 89: 568-571. (IF: 2.217)
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1. Koszorú K, Kovács A, Lőrincz K, Medvecz M, Sárdy M. (2022) Low dose systemic corticosteroid treatment in lichen planus. *Bőrgyógy Venerol Sz*, 98: 174. Hungarian Dermatological Society Annual Meeting, Debrecen.

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Appendix 1. The questionnaire (Hungarian)

TÁJÉKOZTATÓ SZEMÉLYES ADATOK GYŰJTÉSÉRŐL

„Atopiás dermatitisben (atopiás ekzemában) szenvedő felnőtt betegek betegségteher felmérése Magyarországon”; kérdőíves felmérés

Tisztelt Betegünk!

Önnek atopiás dermatitis nevű gyulladással járó bőrbetegsége van, amely tüneteket, panaszokat okoz vagy okozott. Az Önt kezelő klinikus szeretne adatokat gyűjteni minden betegről, akinél ez a megbetegedés fennáll. Az adatgyűjtés célja, hogy elemezni tudják az atopiás dermatitis megbetegedés klinikai és egészség-gazdaságtani jellemzőit. Ezzel közvetve sokat segíthet saját és betegársai sorsán, mert az eredmények később állami vagy egészségbiztosítási döntések (pl. adókedvezmény, gyógyszer támogatás) alapját képezhetik. A kutatásban 2018 januárjától kezdődően a Semmelweis Egyetem, Bőr-, Nemikórtani és Bőronkológiai Klinika és a Debreceni Egyetem, Bőrgyógyászati Klinika, Bőrgyógyászati Tanszék várhatóan 200 betege vesz részt.

Az Ön esetéből származó információk, adatok az Önt ellátó orvos adatállományába kerülnek. Az adatok statisztikai elemzését, kiértékelését a Budapesti Corvinus Egyetem Egészségügyi Közgazdaságtan Tanszék végzi (1093 Budapest, Fővám tér 8., kutatásvezető: Dr. Brodszky Valentin).

A Tanszéknek eljuttatott adatok nem tartalmazzák az Ön nevét és egyéb személyes adatait, mely lehetővé tenné az Ön azonosítását, s így kerülnek feldolgozásra, elemzésre. Az adatok tudományos közzétételre is kerülnek, de mindig a személy azonosítási adatai nélkül.

Az Ön ellátását orvosa mindenben a szokásos gyakorlatnak megfelelően végzi, a részvétel nem befolyásolja kivizsgálását és kezelését. Amennyiben úgy dönt, hogy részt vesz a felmérésünkben, ennek a kérdéssornak a kitöltésére kérjük. A kérdőív kitöltése egyszeri és nagyjából 30 percet vesz igénybe.

Kérdezze orvosát bármiről, amit nem ért pontosan. Amennyiben egyetért a részvétellel, kérjük, írja alá a beleegyezési nyilatkozatot a 4. oldalon, ezzel jelezve, hogy megértette az információkat és egyetért a nyilvántartásban való részvétellel.

Önkéntes részvétel

Az Ön önkéntes döntése részt venni a felmérésben. Önnek joga van megtagadni a részvételt vagy visszalépni bármikor, bármilyen okból. Amennyiben nem a részvétel mellett dönt, vagy visszalép, ez a tény nem befolyásolja a gyógyítás minőségét, sem a kapcsolatot orvosával és az ápolókkal. Ön a felmérésben való részvételért semmiféle ellenszolgáltatásra nem jogosult.

Köszönettel: Az Önt kezelő orvos és a Budapesti Corvinus Egyetem Egészségügyi Közgazdaságtan Tanszéke

Budapest, 2021. hónap nap

Beteg neve: _____ anyja neve: _____

TAJ: _____ születési hely, idő: _____

lakcím: _____

A tájékoztatást végző személy neve: _____

Dátum: 2021. _____

beteg aláírása

tájékoztatást végző aláírása

Ez az oldal a vizsgáló centrumban marad!

BELEEGYZŐ NYILATKOZAT SZEMÉLYES ADATOK GYŰJTÉSÉHEZ**Atopiás dermatitisben (atopiás ekzemában) szenvedő felnőtt betegek betegségteher felmérése Magyarországon**

Alulírott, beleegyezem, hogy részt vegyek az „**Atopiás dermatitisben (atopiás ekzemában) szenvedő felnőtt betegek betegségteher felmérése Magyarországon**”; című magyarországi kérdőíves felmérésben. Hozzájárulok a kérdőív kitöltésével szolgáltatott adatok tudományos kutatás céljára való felhasználásához. Az adatok kezelését az Önt ellátó intézmény végzi, az adatok feldolgozását a Budapesti Corvinus Egyetem Egészségügyi Közgazdaságtan Tanszék (1093 Budapest, Fővám tér 8., kutatásvezető: Dr. Brodszky Valentin) végzi. Az Ön önkéntes döntése részt venni a felmérésben. Önnek joga van megtagadni a részvételt vagy visszalépni bármikor, bármilyen okból. Amennyiben nem a részvétel mellett dönt, vagy visszalép, ez a tény nem befolyásolja a gyógyítás minőségét, sem a kapcsolatot orvosával és az ápolókkal.

Kijelentem, hogy elolvastam a Tájékoztatót és kezelőorvosom megválaszolta a felméréssel kapcsolatban felmerült kérdéseimet. Kijelentem, hogy beleegyezésemet önként, befolyástól mentesen adtam, annak tudatában, hogy azt bármikor, szóban vagy írásban, indoklás nélkül visszavonhatom.

Beteg neve: _____

Születési hely, idő: _____

Az egészségügyi intézmény neve: _____

A tájékoztatást végző személy neve: _____

Beosztása, munkaköre: _____

Dátum: 2021. _____

beteg aláírása

tájékoztatót végző aláírása

Ez az oldal a vizsgáló centrumban marad!

I. Általános és demográfiai adatok

A kitöltés dátuma: év hónap nap

1. Neme: férfi
nő

2. Mikor született? (évszám)

3. Testsúly: /kg/

4. Legmagasabb iskolai végzettsége: Jelölje X-szel!

Általános iskola

Középiskola, szakközépiskola, technikum

Főiskola, egyetem

5. Dolgozik jelenleg? Kérjük, jelölje X-szel a megfelelőt! Több választ is megjelölhet!

Teljes munkaidőben dolgozom

Részmunkaidőben dolgozom

Nyugdíjas vagyok

Rokkantsnyugdíjas vagyok Ha IGEN, bőrbetegsége miatt?

Munkanélküli vagyok Ha IGEN, bőrbetegsége miatt?

Tanuló

Egyéb:.....

6. Önt is beleszámítva hányan laknak egy háztartásban? fő

Ebből hány fő 18 éves vagy idősebb?

18 éven aluli?

II. Bőrtünetek

7. Mikor jelentkeztek először az atopiás dermatitis tünetei? Kérjük, írja be az évszámot!

				év
--	--	--	--	----

8. Mikor diagnosztizálták Önnél először az atopiás dermatitis betegséget?

				év
--	--	--	--	----

9. Családjában (a vérrokonai között) előfordultak-e valakinél az alábbi betegségek? Kérem, jelölje X-szel! Több válasz is megjelölhető!

Atopiás dermatitis	<input type="checkbox"/>
Asztma	<input type="checkbox"/>
Szénanátha	<input type="checkbox"/>
Nem fordult elő egyik sem	<input type="checkbox"/>

10. Kérjük, jelölje meg az alábbi skálán, hogy atopiás dermatitis betegsége jelenleg milyen súlyos panaszt okoz Önnek. A 0 azt jelenti, hogy „nincs panasz”, a 10 pedig azt, hogy „elképzelhető legsúlyosabb panasz”.



11. Kérjük, jelölje meg az alábbi skálán, hogy milyen erős viszketést okozott atopiás dermatitis betegsége az elmúlt 1 hónapban Önnek? A 0 azt jelenti, hogy „nem volt viszketés”, a 10 pedig azt, hogy „elképzelhető legerősebb viszketés”.



17. Hány alkalommal járt családorvosánál bőrbetegsége miatt az elmúlt 1 hónapban?

Összesen alkalommal Egyszer sem

18. Hány alkalommal járt járóbeteg szakorvosi rendelésen bőrbetegsége és szövődményei miatt az elmúlt 3 hónapban?

Szakorvosi rendelés	Alkalmak száma az elmúlt 3 hónapban
Bőrgyógyász	_ _ alkalommal
Fül-orr-gégész	_ _ alkalommal
Tüdőgyógyász	_ _ alkalommal
Szemész	_ _ alkalommal
Pszichiáter vagy pszichológus	_ _ alkalommal
_____	_ _ alkalommal

19. Hány alkalommal került bőrbetegsége vagy szövődményei miatt kórházi felvételre az elmúlt 12 hónapban? (Kérjük, írja be a felvételek számát!)

Osztály	Alkalmak száma az elmúlt 12 hónapban
Bőrgyógyászat	_ _ alkalommal
Fül-orr-gégészlet	_ _ alkalommal
Tüdőgyógyászat	_ _ alkalommal
Szemészet	_ _ alkalommal
Pszichiátria	_ _ alkalommal
_____	_ _ alkalommal

20. A mai napon hogyan jött a szakrendelésre? Jelölje X-szel!**Kivel utazott?****Mivel utazott?**

Egyedül utaztam

Tömegközlekedési eszközzel

Elkísért rokon/segítő

Távolsági busszal

Vonattal

Autóval

Taxival

Mentővel

Kerékpárral

Gyalog

21. Milyen távolságra lakik kb. a klinikától? km**22. Hányszor vett igénybe mentőszállítást bőrbetegsége miatt az elmúlt 12 hónapban? (Ha oda és vissza is mentővel utazott, azt 2-nek számolja!)**

mentőszállítást

alkalommal

Nem vettem igénybe

23. Használt-e az elmúlt 1 hónapban bőrbetegsége miatt valamilyen külső kezelést vagy gyógyhatású készítményt, mint például fürdőolajak, nem szárító detergenssek, antiszeptikumok, emolliensek (zsírozók és hidratálók)?

igen

nem

Ha igen, adja meg a készítmény nevét és az elmúlt hónapban ráfordított összeget!

A készítmény megnevezése	A teljes ráfordított összeg az elmúlt 1 hónapban Ft-ban
Nem szárító detergens (visszazsírozó szappan vagy mosakodó krém)	
Testápoló, zsírozó vagy hidratáló készítmények	
Antiszeptikum (bőrfertőtlenítő készítmény)	

24. Hány alkalommal vett igénybe bőrbetegsége miatt társadalombiztosítás által nem térített ellátást (magánorvos, természetgyógyász, klímaterápia) az elmúlt 3 hónapban, és mennyit költött összesen ezekre az ellátásokra?

Kérjük, írja be az alkalmak számát és az elköltött összeget!

Az ellátás	Alkalmak száma	A teljes ráfordított összeg az elmúlt 3 hónapban Ft-ban
Magánorvosi vizsgálat	_ _ alkalommal	
Természetgyógyászati rendelés	_ _ alkalommal	
Klímaterápia	_ _ alkalommal	
Sóbarlang	_ _ alkalommal	
_____	_ _ alkalommal	
_____	_ _ alkalommal	

25. Kérjük, adja meg, hogy bőrbetegsége miatt milyen, nem az egészségügyi ellátáshoz kapcsolódó költségei jelentkeztek az elmúlt 12 hónapban. A lenti táblázatban példákat talál, de bármilyen szolgáltatást vagy eszközt megadhat, amiről úgy érzi, kapcsolatban van a betegségével! **Kérjük, írja be az elköltött összeget, és hogy mire fordította!**

Eszköz vagy szolgáltatás megnevezése	A teljes ráfordított összeg az elmúlt 12 hónapban Ft-ban
Speciális porszívó	
Pollenzűrő autóba	
Cérnakesztyű	
Speciális ágynemű vagy egyéb textília	
Lakásátalakítás (pl. padlószőnyeg lecserélése)	
Átképzés költsége munkahelyváltás miatt	

IV. Bőrgyógyászati Életminőség Index

DLQI

Pontszám:

A kérdőívvel azt mérjük, hogy bőrével kapcsolatos problémája mennyire befolyásolta az Ön életét AZ ELMÚLT HÉT SORÁN. Kérjük, egy négyzetet jelöljön be a válasznál!

- | | | | |
|-----|---|---|--|
| 1. | Az elmúlt hét során mennyire volt viszketős, sebes, fájdalmas vagy égetően fájdalmas a bőre? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | |
| 2. | Az elmúlt hét során mennyire volt veszélyezett , vagy volt zavarban a bőre miatt? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | |
| 3. | Az elmúlt hét során mennyire akadályozta bőre, hogy elmenjen vásárolni , rendben tartsa otthonát vagy kertjét ? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 4. | Az elmúlt hét során mennyire befolyásolta bőre, hogy milyen ruhát visel? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 5. | Az elmúlt hét során mennyire befolyásolta bőre társasági életét vagy szabadidős tevékenységét? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 6. | Az elmúlt hét során mennyire nehezítette meg bőre a sportolást ? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 7. | Az elmúlt hét során meggátolta bőre abban, hogy dolgozzon vagy tanuljon ? | Igen <input type="checkbox"/>
Nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| | Ha válasza "Nem": az elmúlt hét során mennyire jelentett problémát bőre a munkában vagy a tanulásban ? | Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | |
| 8. | Az elmúlt hét során mennyire okozott bőre problémákat partnerével , bármelyik közeli barátjával vagy rokonaival kapcsolatosan? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 9. | Az elmúlt hét során mennyire okozott bőre bármilyen szexuális nehézséget ? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |
| 10. | Az elmúlt hét során mennyire okozott problémát bőre kezelése : például bepiszkitotta lakását, vagy sok időt vett igénybe? | Nagyon <input type="checkbox"/>
Meglehetősen <input type="checkbox"/>
Kissé <input type="checkbox"/>
Egyáltalán nem <input type="checkbox"/> | Nem vonatkozik Önre <input type="checkbox"/> |

Kérjük ellenőrizze, hogy MINDEN kérdésre válaszolt-e! Köszönjük.



Egészségi kérdőív

magyar verzió Magyarország részére

Az egyes címsorok alatt kérjük, jelölje be azt az EGY négyzetet, amely a legjobban jellemzi az Ön MAI egészségi állapotát.

MOZGÉKONYSÁG

- Nincs problémám a járással
- Enyhe problémám van a járással
- Mérsékelt problémám van a járással
- Súlyos problémám van a járással
- Képtelen vagyok járni

ÖNELLÁTÁS

- Nincs problémám a tisztálkodással vagy az öltözködéssel
- Enyhe problémám van a tisztálkodással vagy az öltözködéssel
- Mérsékelt problémám van a tisztálkodással vagy az öltözködéssel
- Súlyos problémám van a tisztálkodással vagy az öltözködéssel
- Képtelen vagyok önállóan tisztálkodni vagy öltözködni

SZOKÁSOS TEVÉKENYSÉGEK (pl. munka, tanulás, házimunka, családi vagy szabadidős tevékenységek)

- Nincs problémám a szokásos tevékenységeim elvégzésével
- Enyhe problémám van szokásos tevékenységeim elvégzésével
- Mérsékelt problémám van szokásos tevékenységeim elvégzésével
- Súlyos problémám van szokásos tevékenységeim elvégzésével
- Képtelen vagyok elvégezni szokásos tevékenységeimet

FÁJDALOM / ROSSZ KÖZÉRZET

- Nincs fájdalmam vagy rossz közérzetem
- Enyhe fájdalmam vagy kissé rossz közérzetem van
- Mérsékelt fájdalmam vagy közepesen rossz közérzetem van
- Súlyos fájdalmam vagy nagyon rossz közérzetem van
- Rendkívül erős fájdalmam vagy rendkívül rossz közérzetem van

SZORONGÁS / DEPRESSZIÓ

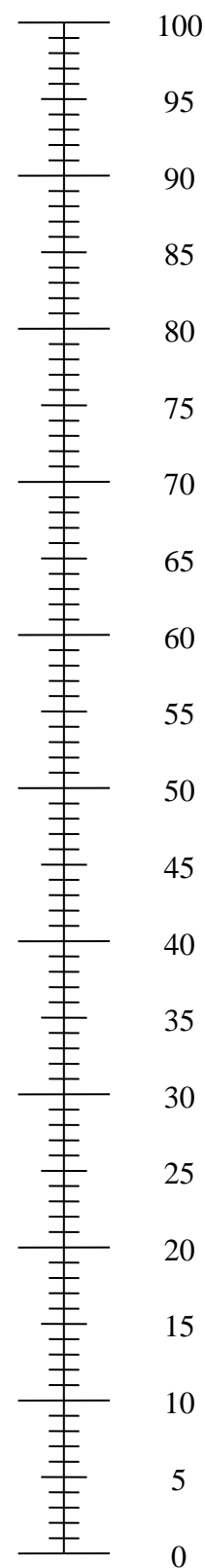
- Nem szorongok vagy nem vagyok depressziós
- Enyhén szorongok vagy enyhén depressziós vagyok
- Mérsékelt szorongok vagy közepesen depressziós vagyok
- Nagyon szorongok vagy súlyosan depressziós vagyok
- Rendkívül erősen szorongok vagy rendkívül depressziós vagyok

Szeretnénk megtudni, hogy MA milyen jó vagy rossz az Ön egészségi állapota.

- Ez a skála 0-tól 100-ig számozott.
- Az elképzeltető legjobb egészségi állapotot „100”, míg az elképzeltető legrosszabb egészségi állapotot „0” jelöli.
- Kérjük, jelölje X-szel a skálán azt a pontot, amely megmutatja, hogy milyen az Ön MAI egészségi állapota.
- Ezután az alábbi rubrikába írja be azt a számot, amelyet a skálán megjelölt.

AZ ÖN MAI EGÉSZSÉGI ÁLLAPOTA =

Az elképzeltető legjobb
egészségi állapot



Az elképzeltető
legrosszabb egészségi
állapot

V. SKINDEX-16 kérdőív

AZ ALÁBBI KÉRDÉSEK ARRRA A BŐRPROBLÉMÁJÁRA VONATKOZNAK, AMI ÖNT A LEGJOBBAN ZAVARTA AZ ELMÚLT 7 NAPBAN.

Az elmúlt 7 napban milyen gyakran zavarták Önt az alábbiak?	Egyszer sem zavart ↓	●	Állandóan zavart ↓				
1. Viszketés a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
2. Égő vagy szúró érzet a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
3. Fájdalom a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
4. Irritáció a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
5. A bőrproblémája nem szűnik meg, kiújul	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
6. Aggódik a bőrproblémája miatt (<u>például</u> hogy tovább terjed, rosszabbodik, hegesedik vagy kiszámíthatatlanná válik stb.)	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
7. A bőr külső megjelenése a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
8. Tehetetlen düh a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
9. Szégyenérzet a bőrproblémája miatt.	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
10. Bosszúság a bőrproblémája	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
11. Lehangeltség a bőrproblémája miatt	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
12. A bőrproblémája hatásai társas kapcsolataira (<u>például</u> családi, baráti, intim kapcsolatok stb.)	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
13. A bőrproblémája hatásai a másokkal való együttlét iránti igényére	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
14. A bőrproblémája megnehezíti a gyengédség fizikai kifejezését	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
15. A bőrproblémája hatásai mindennapos tevékenységeire	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6
16. A bőrproblémája megnehezíti a munkáját vagy hogy azt tegye, amit szeret	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6

Minden kérdésre válaszolt? Igen Nem

26. Kérjük, értékelje 1-től 5-ig terjedő skálán, hogy mennyire tartja fontosnak az előző oldalakon kitöltött bőrgyógyászati életminőség indexek kérdései alapján megfogalmazott állításokat. Válaszát minden sorban karikázza be! (ahol 1 = egyáltalán nem fontos, 5 = nagyon fontos)

Tevékenység	Fontosság				
Viszketős, sebes, fájdalmas vagy égetően fájdalmas a bőre	1	2	3	4	5
Feszélyezett, vagy zavarban van a bőre	1	2	3	4	5
Bőre akadályozza, hogy elmenjen vásárolni, rendben tartsa otthonát vagy kertjét.	1	2	3	4	5
Bőre befolyásolja, hogy milyen ruhát visel.	1	2	3	4	5
Bőre befolyásolja társasági életét vagy szabadidős tevékenységét.	1	2	3	4	5
Bőre megnehezítette a sportolást	1	2	3	4	5
Bőre meggátolja abban, hogy dolgozzon vagy tanuljon.	1	2	3	4	5
Bőre problémákat okoz partnerével, bármelyik közeli barátjával vagy rokonaival kapcsolatosan	1	2	3	4	5
Bőre szexuális nehézséget okoz.	1	2	3	4	5
Bőre kezelés problémát okoz: például bepiszkítja lakását, vagy sok időt vesz igénybe.	1	2	3	4	5
Szégyenérzete van bőrproblémája miatt	1	2	3	4	5
Lehangolt bőrproblémája miatt.	1	2	3	4	5

VI. Betegséggel kapcsolatos tapasztalatok vizsgálata

27. Kérjük, értékelje az állításokat 1-től 7-ig terjedő skálán. Válaszát minden sorban karikázza be! (ahol 1 = egyáltalán nem értek egyet, 7 = teljes mértékben egyetértek)

1	Sok tekintetben az életem közel van az ideálishoz	1 2 3 4 5 6 7
2	Az életkörülményeim kiválóak.	1 2 3 4 5 6 7
3	Elégedett vagyok az életemmel.	1 2 3 4 5 6 7
4	Már rendelkezem mindazokkal a fontos dolgokkal, amelyeket életemben meg szerettem volna szerezni.	1 2 3 4 5 6 7
5	Ha újraélhetném az életemet, gyakorlatilag semmin sem változtatnék.	1 2 3 4 5 6 7

28. Kérjük, olvassa el az alábbi állításokat figyelmesen és értékelje azokat. Válaszát minden sorban karikázza be!

1	A betegsége milyen hatással van az életére?	0=egyáltalán nincs rá hatással, 10=nagyon komoly hatással van rá 0 1 2 3 4 5 6 7 8 9 10
2	Mit gondol, meddig tart a betegsége?	0 = rendkívül rövid ideig 10 = örökké 0 1 2 3 4 5 6 7 8 9 10
3	Mit gondol, mennyire tudja kontrollálni betegségét?	0 = egyáltalán nem 10= rendkívül nagy mértékben 0 1 2 3 4 5 6 7 8 9 10
4	Mit gondol, a kezelés milyen mértékben tud segíteni a betegségén?	0 = egyáltalán nem 10 = rendkívül nagy mértékben 0 1 2 3 4 5 6 7 8 9 10
5	Milyen mértékben tapasztalja betegsége tüneteit?	1 = egyáltalán nincs tünet 10 = sok komoly tünet 0 1 2 3 4 5 6 7 8 9 10
6	Milyen mértékben zavarja a betegsége?	0= egyáltalán nem 10 = rendkívüli mértékben 0 1 2 3 4 5 6 7 8 9 10
7	Hogy érzi, milyen mértékben érti a betegségét?	0 = egyáltalán nem értem 10 = teljesen világos számomra 0 1 2 3 4 5 6 7 8 9 10
8	Betegsége milyen mértékben hat Önre érzelmileg?	0 = egyáltalán nem, 10 = teljes mértékben 0 1 2 3 4 5 6 7 8 9 10

29. Kérjük, olvassa el az alábbi állításokat figyelmesen és értékelje azokat.

Válaszát minden sorban karikázza be! (7 = annyi van, amennyit szeretnék, 1 = sokkal kevesebb van annál, mint amennyit szeretnék). Nincs jó és rossz válasz.

Az életemben van(nak)...

1	... emberek, akik törődnek azzal, hogy mi van velem	1 2 3 4 5 6 7
2	... szeretet és gyengédség	1 2 3 4 5 6 7
3	... esély, hogy beszéljek valakivel munkahelyi problémáimról	1 2 3 4 5 6 7
4	... esély, hogy olyan valakivel beszéljek személyes és családi problémáimról, akiben megbízom	1 2 3 4 5 6 7
5	... esély, hogy beszéljek pénzügyi problémáimról	1 2 3 4 5 6 7
6	... meghívások, hogy kimozduljak és más emberekkel legyek	1 2 3 4 5 6 7
7	... hasznos tanácsok az élet fontos dolgairól	1 2 3 4 5 6 7
8	... segítség, ha beteg vagyok	1 2 3 4 5 6 7

30. Kérjük, értékelje az állításokat 1-től 7-ig terjedő skálán. Válaszát minden sorban karikázza be! (ahol 1 = egyáltalán nem értek egyet, 7 = teljes mértékben egyetértek)

1	Aggódok, hogy az emberek mit gondolhatnak rólam	1 2 3 4 5 6 7
2	Félek attól, hogy valaki észreveszi hibáimat	1 2 3 4 5 6 7
3	Aggódok, hogy mások nem vélekednek rólam elismerően	1 2 3 4 5 6 7
4	Aggódok, hogy rossz dolgokat mondok vagy teszek.	1 2 3 4 5 6 7
5	Ha valakihez beszélek, nyugtalanít, hogy mit gondol rólam.	1 2 3 4 5 6 7
6	Kényelmetlenül és zavartnak érzem magam, ha a figyelem középpontjába kerülök.	1 2 3 4 5 6 7
7	Nehéznek tartom, hogy másokkal kommunikáljak.	1 2 3 4 5 6 7

VII. EQ-5D-3L kérdőív

31. Az alább szereplő kérdéscsoportok mindegyikébe tegyen X-et azon válasz melletti négyzetbe, amely legjobban jellemzi az Ön mai egészségi állapotát.

Mozgékonyság

- Nincs problémám a járással
- Némi problémám van a járással
- Ágyhoz vagyok kötve

Önellátás

- Nincs problémám önmagam ellátásával
- Némi problémám van a tisztálkodással és az öltözködéssel
- Képtelen vagyok önállóan tisztálkodni vagy öltözködni

Szokásos tevékenységek (pl. munka, tanulás, házimunka, családi vagy szabadidős tevékenységek)

- Nincs problémám a szokásos tevékenységeim elvégzésével
- Némi problémám van szokásos tevékenységeim elvégzésével
- Képtelen vagyok elvégezni szokásos tevékenységeimet

Fájdalom/Rossz közérzet

- Nincs fájdalmam vagy rossz közérzetem
- Mérsékelt fájdalmam vagy kissé rossz közérzetem van
- Nagyon erős fájdalmam vagy rossz közérzetem van

Szorongás/Lehangoltság

- Nem szorongok, vagy nem vagyok lehangolt
- Mérsékelt szorongok, vagy lehangolt vagyok
- Nagyon szorongok, vagy nagyon lehangolt vagyok

VIII. Foglalkoztatottság, munkaképesség

Ha jelenleg NINCS FIZETETT MUNKAVISZONYBAN, kérjük, ugorjon a 100. oldalra!

A következő kérdések azzal foglalkoznak, hogy *börtünetei* milyen hatása vannak munkaképességére és napi tevékenységeire. Egészségügyi gond alatt értünk bármilyen testi vagy lelki panaszt vagy tünetet. *Kérjük, töltsse ki a kérdőívet a megfelelő helyeken vagy karikázza be a megfelelő számot.*

A következő kérdések az **elmúlt hét napra** vonatkoznak, a mai napot nem számítva.

32. Az elmúlt hét nap alatt hány munkaórát mulasztott börtünetei miatt? Számítsa bele azokat az órákat, melyeket betegállományban töltött, amikor későn ért munkába, korábban távozott, stb. egészségügyi gondjai miatt. Ne számítsa bele azt az időt, amelyet azért mulasztott el, mert ebben a klinikai vizsgálatban vesz részt.

órá

33. Az elmúlt hét nap alatt hány munkaórát mulasztott bármilyen egyéb ok miatt, mint például szabadság, ünnepnap, vagy a klinikai vizsgálattal, munkaidőben eltöltött idő?

órá

34. Az elmúlt hét nap alatt hány órát dolgozott ténylegesen?

órá (Ha "0", ugorjon a 36. kérdésre.)

35. Az elmúlt hét nap alatt munkája közben mennyire befolyásolták börtünetei a munkavégzését?

Gondoljon vissza azokra a napokra, amikor kevesebb, illetve kevesebb fajta munkát tudott elvégezni, és azokra a napokra, amikor kevesebbet tudott teljesíteni, mint amennyit szeretett volna, vagy amikor nem tudta munkáját olyan gondosan elvégezni, mint máskor. Ha egészségügyi gondjai csak kismértékben befolyásolták a munkavégzését, akkor válasszon egy kis számot, amennyiben egészségügyi gondjai nagymértékben befolyásolták a munkavégzését, válasszon egy nagy számot az alábbi skálán.

Ennél a kérdésnél csak azt vegye figyelembe, hogy munkavégzés közben börtünetei mennyire befolyásolták a munkavégzését.

Börtüneteim nem		Börtüneteim teljes
befolyásolták a	_____	mértékben
munkavégzésemet.	0 1 2 3 4 5 6 7 8 9 10	megakadályoztak a
		munkavégzésemben.

KARIKÁZZON BE EGY SZÁMOT.

36. Az elmúlt hét nap alatt börtünetei mennyire akadályozták abban, hogy napi rendszeres tevékenységeit elvégezze, melyek nem függenek össze munkahelyi tevékenységével?

A napi rendszeres tevékenységeken azokat értjük, melyeket általában végez, mint például a ház körüli munkát, vásárlást, gyerekek ellátását, testgyakorlást, tanulást, stb. Gondoljon vissza azokra az időkre, amikor kevesebbet, illetve kevesebb félét tudott tenni, és azokra a napokra, amikor kevesebbet tudott elvégezni, mint amennyit szeretett volna. Ha egészségügyi gondjai csak kismértékben befolyásolták napi rendszeres tevékenységét, akkor válasszon egy kis számot, ha egészségügyi gondjai nagymértékben befolyásolták a napi rendszeres tevékenységeit, válasszon egy nagy számot az alábbi skálán.

Ennél a kérdésnél csak azt vegye figyelembe, hogy börtünetei mennyire befolyásolták a munkahelyi feladatain kívüli, napi rendszeres tevékenységeinek végzését.

Börtüneteim nem		Börtüneteim teljes
befolyásolták a	_____	mértékben
napi rendszeres	0 1 2 3 4 5 6 7 8 9 10	megakadályoztak a
tevékenységeimet.		napi rendszeres
		tevékenységeimben.

KARIKÁZZON BE EGY SZÁMOT.

IX. Betegséggel kapcsolatos preferenciák vizsgálata

37. A következőkben az atopiás dermatitis (atopiás ekzema) betegségterhéről fogjuk kérdezni ún. időalku módszer segítségével.

KÉPZELJE el, hogy **az Ön jelenlegi egészségi állapotában** él még pontosan **10 évet**, azután meghal.

VAGY választhat, hogy **ennél rövidebb ideig** él **teljes egészségben**.

Melyiket választaná?

Kérjük, az **alábbi táblázat minden sorában a szürke mezőkben** jelölje meg, hogy az ott feltüntetett két lehetőség közül melyiket választaná.

EGY SORBA mindig 1 db X-et írjon!

AZ ÖN JELENLEGI EGÉSZSÉGI ÁLLAPOTA		TELJES EGÉSZSÉG	
10 ÉV			10 ÉV
10 ÉV			9 ÉV 6 HÓNAP
10 ÉV			9 ÉV
10 ÉV			8 ÉV 6 HÓNAP
10 ÉV			8 ÉV
10 ÉV			7 ÉV 6 HÓNAP
10 ÉV			7 ÉV
10 ÉV			6 ÉV 6 HÓNAP
10 ÉV			6 ÉV
10 ÉV			5 ÉV 6 HÓNAP
10 ÉV			5 ÉV
10 ÉV			4 ÉV 6 HÓNAP
10 ÉV			4 ÉV
10 ÉV			3 ÉV 6 HÓNAP
10 ÉV			3 ÉV
10 ÉV			2 ÉV 6 HÓNAP
10 ÉV			2 ÉV
10 ÉV			1 ÉV 6 HÓNAP
10 ÉV			1 ÉV
10 ÉV			6 HÓNAP
10 ÉV			0 ÉV=azonnali halál

X. MÁSOK GONDOZÁSA

A kérdőívnek ez a része arra a gondozásra vagy segítségre vonatkozik, amit valaki önkéntes alapon nyújt egy olyan családtag, barát vagy más ismerős részére, akinek segítségre van szüksége fizikai vagy mentális egészség-problémák, vagy az idősődéssel kapcsolatos problémák miatt. Az ilyen gondozást vagy segítséget informális gondozásnak nevezik.

Az informális gondozás különböző tevékenységekből állhat, mint például az érzelmi támogatás és felügyelet, utazáshoz nyújtott segítség, háztartási tevékenységek, személyes gondozás, ápolás vagy ügyintézés.

A kérdőívben arra a személyre, akit Ön informális gondozásban részesít, "Ő" néven hivatkozunk.

38. Ön gondoz-e vagy segít-e önkéntes alapon egy olyan családtagot, barátot vagy más ismerőst, akinek segítségre van szüksége fizikális vagy mentális egészség-problémák vagy idősődéssel kapcsolatos problémák miatt?

- Nem **Kérjük, ugorjon a 40. kérdésre!**
- Igen

Ha igen:

Több mint két hete végzi ezt a gondozást vagy segítséget?

- Nem **Kérjük, ugorjon a 40. kérdésre!**
- Igen

Ön mennyi időt töltött az elmúlt héten olyan háztartási tevékenységekkel, amit nem kellett volna elvégezni, ha Ő jó egészségben lenne, vagy ha Ő meg tudta volna csinálni? Például, ételek elkészítése, takarítás, mosás, vasalás, varrás, vigyázzon és játsszon az Ön gyermekeivel, vásárlás, karbantartási munkák, alkalmi munkák, kertészkedés.

_____ órát az elmúlt héten

Ön mennyi időt töltött az elmúlt héten az Ő személyes gondozásával?

Például, öltözködés/vetkőzés, mosakodás, hajápolás, borotválkozás, WC-re kimenni, házon belüli mozgás, evés és ivás, gyógyszerelés.

_____ órát az elmúlt héten

Ön mennyi időt töltött az elmúlt héten olyan gyakorlati segítséggel, amit nem kellett volna elvégezni, ha Ő jó egészségben lenne, vagy ha Ő meg tudta volna csinálni? Például, házon kívüli mozgás beleértve a sétálást vagy kerekesszékekkel való közlekedést, a családtagok és barátok meglátogatását, az egészségügyi ellátásra eljutást (pl. orvosi vizitre), a segítség, fizikai segédeszközök vagy lakásátalakítás megszervezését és az anyagi ügyeket intézését (pl. biztosítást).

_____ órát az elmúlt héten

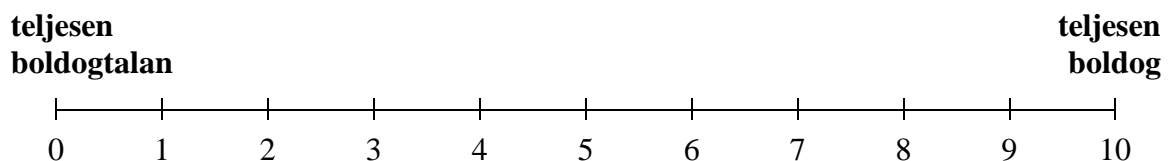
39. Kérjük, jelölje meg azt a négyzetet, amelyik leginkább jellemzi az Ön gondozással kapcsolatos helyzetét jelenleg.

Kérjük, hogy minden egyes állításnál csak egyet jelöljön meg: 'semennyi', 'némi' vagy 'sok'.

- | | semennyi | némi | sok | |
|-------|--------------------------|--------------------------|--------------------------|---|
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | megelégedést okoz a gondozási feladataim elvégzése. |
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | kapcsolati problémám van a gondozottal (pl. Ő nagyon követelőző vagy másképp viselkedik; kommunikációs problémáink vannak). |
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problémám van a saját lelki egészségemmel (pl. stressz, félelem, pesszimizmus, depresszió, a jövővel kapcsolatos aggodalmak). |
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problémám van a gondozási feladataim és a saját napi tevékenységeim összeegyeztetésével (pl. háztartási tevékenységek, munka, tanulás, család, szabadidős tevékenységek). |
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | anyagi problémám van a gondozási feladataim miatt. |
| Én | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | támogatást kapok a gondozási feladataim elvégzéséhez, amikor szükségem van rá (pl. a családtól, barátoktól, szomszédoktól, ismerősöktől). |
| Nekem | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | problémám van a saját testi egészségemmel (pl. gyakrabban vagyok beteg, fáradtság, fizikai stressz). |

40. Mennyire érzi Ön boldognak magát jelenleg?

Kérjük, jelölje be az alábbi skálán, hogy Ön mennyire érzi boldognak magát jelenleg.



A kérdőívnek ezt a részét az Orvos tölti ki!

1. Atopiás dermatitis igazolt diagnózisának dátuma?

év hó

2. Milyen társbetegségek fordulnak elő a betegnél?

Nem fordul elő

Bőrgyógyászati betegségek

Molloscum

Közönséges szemölcs

Condyloma

Folliculitis

Pyoderma

Candida fertőzés

Genitális gyulladás

Egyéb: _____

Nem bőrgyógyászati betegségek

Asthma bronchiale

Depresszió

Szuicid gondolatok

Ételallergia

Pollenallergia

Háziporatka allergia

Fémallergia

Rhinitis allergica

Conjunctivitis allergica

Egyéb allergia

Szorongás

Sinusitis

Otitis

Egyéb: _____

3. Kérjük, jelölje az alábbi skálán, hogy mennyire tartja súlyosnak a beteg atopiás dermatitises bőrtüneteit!

- 0** Tünetmentes (Atopiás dermatitis gyulladásoos tüneteinek teljes hiánya)
- 1** Közel tünetmentes (éppen érzékelhető erythema és papulák/infiltratio)
- 2** Enyhe betegség (enyhe erythema és papulák/infiltratio)
- 3** Közepesen súlyos betegség (közepesen súlyos erythema és papulák/infiltratio)
- 4** Súlyos betegség (súlyos erythema és papulák/infiltratio)
- 5** Nagyon súlyos betegség (súlyos erythema és nedvedző/pörkösödő papulák/infiltratio)

4. EASI (Eczema Area and Severity Index) pontszám:

Testtáj érintettség: Minden testtáj 100%-ban érintett lehet. Az érintett terület nagysága szerint az alábbi pontszámok adhatóak testtájanként:

%-os érintettség	0	1-9%	10-29%	30-49%	50-69%	70-89%	90-100%
Testtáj pontszám	0	1	2	3	4	5	6

A tünetek súlyossága: Minden tünet 0-3-ig terjedő skálán értékelhető, a következő beosztás szerint:

0	Tünetmentes
1	Enyhe
2	Közepesen súlyos
3	Súlyos

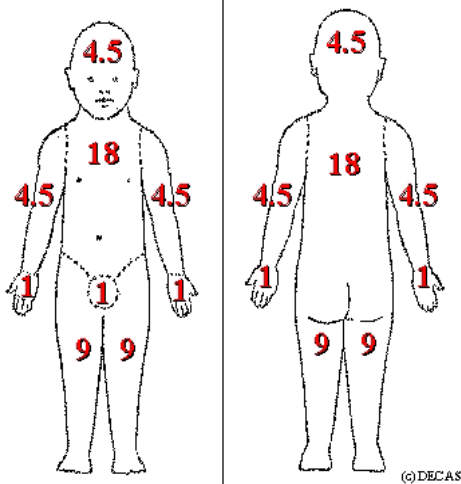
-Több testtáj érintettsége esetén átlagos súlyosságot vegye figyelembe!
 -1,5 és 2,5 pontszám adható, 0,5 nem megengedett.
 Egy tünet jelenléte legalább 1 pont adjon!

Kérem töltsse ki az alábbi pontszámítási táblázatot!

Testtáj	Erythema	Oedema/ papulák	Excoriatio	Lichenificatio	Terület pontszám	Szorzó	Testtáj pontszám
Fej/nyak	(+)	(+)	(+)	()	*	*0,1	
Törzs	(+)	(+)	(+)	()	*	*0,3	
Felső végtag	(+)	(+)	(+)	()	*	*0,2	
Alsó végtag	(+)	(+)	(+)	()	*	*0,4	
A végső EASI pontszám a testtáj pontszámok összege:							<u>(0-72)</u>

5. SCORAD (SCORing Atopic Dermatitis) pontszám:

A. Érintett területek nagyságának meghatározása:



Testtáj	Jobb	Bal	Összesen (jobb + bal)
Kar elől (4,5)			
Kar hátul (4,5)			
Kéz elől (1)			
Kéz hátul (1)			
Láb elől (9)			
Láb hátul (9)			
Nemi szervek (1)			
Törzs hátul (18)			
Törzs elől (18)			
Fej hátul (4,5)			
Fej elől (4,5)			
Összespont (100 max)			

B. Tünetek intenzitásának értékelése:

Az értékelt terület kiválasztása:

- Lokalizált léziók esetében, az a terület, amiatt a beteg jelenleg felkereste a klinikát
- Eltérő súlyosságú területek esetében, válasszon egy átlagos súlyosságú területet

Tünet	0	1	2	3	Pontszám
Erythema					
Ödéma/papula					
Nedvedzés/Pörkösödés					
Excoriatio					
Lichenificatio					
Szárazság					
Összpont (18 max)					

Pontszámítás:

A. Terület= _____ /5= _____ (Max 20)

B. Intenzitás= 7 X _____ = _____ /2= _____ (Max 63)

6. Kapott-e a beteg az elmúlt 1 hónapban bőrbetegsége miatt valamilyen antibiotikumot?

igen nem

Ha igen, adja meg a készítmény nevét, átlagos napi dózisát és kezelés időtartamát napokban!

A készítmény kereskedelmi megnevezése	Napi dózis (mg)	Kezelés időtartama az elmúlt 30 napban (nap)
Zinnat/Cefuroxim	____ ____ ____ mg	____ ____ nap
Augmentin	____ ____ ____ mg	____ ____ nap
Sumetrolim	____ ____ ____ mg	____ ____ nap
Doxycyclin	____ ____ ____ mg	____ ____ nap
Ciprobay/ciprofloxacín	____ ____ ____ mg	____ ____ nap
Ciprofloxacín	____ ____ ____ mg	____ ____ nap
Klarithromycin	____ ____ ____ mg	____ ____ nap
Roxithromycin	____ ____ ____ mg	____ ____ nap
Clindamycin	____ ____ ____ mg	____ ____ nap
_____	____ ____ ____ mg	____ ____ nap

7. Kapott-e a beteg az elmúlt 1 hónapban bőrbetegsége miatt valamilyen antihisztamint?

igen nem

Ha igen, adja meg a készítmény nevét, átlagos napi dózisát és kezelés időtartamát napokban!

A készítmény kereskedelmi megnevezése	Napi dózis (mg)	Kezelés időtartama az elmúlt 30 napban (nap)
Zyrtec/cetirizin	_____ mg	_____ nap
Aerius	_____ mg	_____ nap
Lendin	_____ mg	_____ nap
Xyzal	_____ mg	_____ nap
Claritine	_____ mg	_____ nap
Loratadin	_____ mg	_____ nap
Suprastin	_____ mg	_____ nap
Fenistil	_____ mg	_____ nap
Allegra	_____ mg	_____ nap
Fexgen	_____ mg	_____ nap
Lertazin	_____ mg	_____ nap
Telfast	_____ mg	_____ nap
	_____ mg	_____ nap
	_____ mg	_____ nap

8. Kapott-e a beteg az elmúlt 1 hónapban valamilyen asztma gyógyszert?igen nem Ha igen, adja meg a készítmény nevét, átlagos napi dózisát és kezelés időtartamát napokban!

A készítmény kereskedelmi megnevezése	Napi dózis (mg)	Kezelés időtartama az elmúlt 30 napban (nap)
Berodual	_____ mg	_____ nap
Atrovent	_____ mg	_____ nap
Bricanyl	_____ mg	_____ nap
Budesonid	_____ mg	_____ nap
Pulmicort	_____ mg	_____ nap
Buventol	_____ mg	_____ nap
Flixotide	_____ mg	_____ nap
Montelukast	_____ mg	_____ nap
Singulair	_____ mg	_____ nap
Spiriva	_____ mg	_____ nap
Seretide	_____ mg	_____ nap
Serevent	_____ mg	_____ nap
Symbicort	_____ mg	_____ nap
	_____ mg	_____ nap
	_____ mg	_____ nap

9. Kapott-e a beteg elmúlt 12 hónapban valamilyen szisztémás kezelést?igen nem Ha igen, adja meg a készítmény nevét, átlagos napi dózisát és kezelés időtartamát napokban!

A készítmény kereskedelmi megnevezése	Napi dózis (mg)	Kezelés időtartama az elmúlt évben (nap)	Jelenleg is kapja = X
Cyclosporin A	_ _ _ _ mg	_ _ _ _ nap	<input type="checkbox"/>
Azathioprin	_ _ _ _ mg	_ _ _ _ nap	<input type="checkbox"/>
Szisztémás szteroid	_ _ _ _ mg	_ _ _ _ nap	<input type="checkbox"/>
Methotrexát	_ _ _ _ mg	_ _ _ _ nap	<input type="checkbox"/>
	_ _ _ _ mg	_ _ _ _ nap	<input type="checkbox"/>

10. Kapott-e a beteg elmúlt hónapban valamilyen lokális kezelést?igen nem Ha igen, adja meg a készítmény nevét (ha nincs a felsorolásban) és a felhasznált mennyiséget!

A lokális készítmény megnevezése	Felhasznált mennyiség (tubus, üveg, gramm stb.) az elmúlt 30 napban
Kortikoszteroid	
Tacrolimus	
Pimecrolimus	

11. Kapott-e a beteg az elmúlt hónapban valamilyen fototerápiát?igen nem Ha igen, adja meg a készítmény nevét, az alkalmak számát és kezelés időtartamát napokban!

A készítmény megnevezése	Alkalmak száma az elmúlt 30 napban
UVB	_ _ alkalommal
PUVA	_ _ alkalommal
	_ _ alkalommal
	_ _ alkalommal

Kérdőívet kitöltő kolléga

Neve (és/vagy pecsétje):

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Kedves Kolléga!**Köszönjük, hogy kitöltötte a kérdőívet!**