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TESTING THE PSYCHOMETRIC PROPERTIES OF GENERIC HEALTH-RELATED QUALITY OF LIFE MEASURES IN CHRONIC SKIN DISEASES AND THE GENERAL POPULATION IN HUNGARY

PhD thesis

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List of Abbreviations

AD – anxiety/depression dimension of EQ-5D
AQOL – Assessment of Quality of Life
BMI – body mass index
CFI – comparative fit index
CO – self-confidence dimension of EQ-PSO
COVID-19 – Coronavirus disease 2019
CTT – classical test theory
DIF – differential item functioning
DLQI – Dermatology Life Quality Index
ECV – explained common variance
EQ-5D-3L – three-level EQ-5D
EQ-5D-5L – five-level EQ-5D
EQ-5D-Y – EQ-5D youth questionnaire
EQ-PSO – EQ-5D-5L with psoriasis-specific bolt-ons
EQ VAS – EuroQol Visual Analogue Scale
ES – effect size
EU – European Union
GMH – Global Mental Health
GPH – Global Physical Health
H' – Shannon's index
H&H$_i$ – Mokken scale analysis coefficients
HRQoL – health-related quality of life
HS – hidradenitis suppurativa
HS-PGA – Physicians' Global Assessment of hidradenitis suppurativa severity
IQR – interquartile range
IRT – item response theory
J' – Shannon's evenness index
MO – mobility dimension of EQ-5D
PD – pain/discomfort dimension of EQ-5D
PROM – patient-reported outcome measure
PROMIS – Patient-Reported Outcomes Measurement Information System
PROMIS-29+2 – Patient-Reported Outcomes Measurement Information System 29+2
PROMIS-GH – Patient-Reported Outcomes Measurement Information System Global Health
PtGA VAS – Patient's Global Assessment of disease severity visual analogue scale
QALY – quality-adjusted life year
QoL – quality of life
RE – relative efficiency
RMSEA – root mean square error of approximation
S-χ2 – item fit index
SC – self-care dimension of EQ-5D
SD – standard deviation
SE – standard error
SF-12 – 12-Item Short Form
SF-36 – 36-Item Short Form
SF-6D – Short form 6 dimensions
SI – skin irritation dimension of EQ-PSO
SRMR – standardized root mean squared residual
TLI – Tucker-Lewis index
UA – usual activities dimension of EQ-5D
US – United States
VAS – visual analogue scale

1. Introduction

1.1 Concept of quality of life

Quality of life (QoL) is a widely used term in everyday life, often without an explicit definition (1, 2). Several conceptualisations of QoL exist, frequently associated with the concepts of health and health-related quality of life (HRQoL) (3). The World Health Organization defines QoL as "*an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns"* (4). This multidimensional concept encompasses several domains of QoL, such as physical health, psychological state, level of independence, social relationships, environment and personal beliefs (4). As reported by the National Healthcare Service Center in Hungary: "*In general terms, it is a measure of an individual's (or population's or population group's) perception of well-being, along the various physical and mental aspects that are important to them, taking into account both objective and subjective aspects of quality of life*" (5). Subjectivity highlights that QoL can only be assessed from an individual's (e.g., patient) perspective. However, someone else can also evaluate QoL, such as a parent assessing their child's QoL (6). According to the Food and Drug Administration in the United States (US), QoL is "*a general concept that implies an evaluation of the impact of all aspects of life on general well-being. Because this term implies the evaluation of nonhealth-related aspects of life, it is too broad to be considered appropriate for a medical product claim"* (7). Due to the several definitions, distinguishing between QoL, health and HRQoL remained a subject of continuous discourse (3).

1.1.1 Health and health-related quality of life

Although QoL affects many facets of life, healthcare professionals are primarily concerned with the one that covers the health-related aspects of life (e.g., mental health, physical functioning, social functioning), consequently positioning health at the centre (8). In the literature, the health-related phrase is often used to complement the definition of QoL to provide a more accurate understanding (9). The literature presents at least four distinct delineations of HRQoL. The first defines HRQoL as an individual's perceived well-being in the physical, mental, and social domains of health and functioning; the second one directly associates it with QoL and encompasses only factors that belong to

an individual's health; the third interpretation of HRQoL focuses on the elements of QoL that are influenced by an individual's health; ultimately there is a definition that connects HRQoL with the value of health (3).

1.2 Utility

In the case of measuring the value of health, the concepts of utility and preference need to be introduced. Preference shows the value an individual assigns to a certain health state under conditions of uncertainty (10). Utilities are anchored at 0 and 1, where 0 is dead, and 1 is equal to full health. Of note, health states may be valued as being worse than dead. In those cases, the utilities are negative values. Multiple methods are available to quantify utilities. Utilities may be measured either directly or indirectly. Direct methods include standard gamble and time trade-off, among others. In contrast, indirect methods involve generic HRQoL measures such as EQ-5D, Short form 6 dimensions (SF-6D), Assessment of Quality of Life (AQOL) and Patient-Reported Outcomes Measurement Information System 29+2 (PROMIS-29+2) (11-13).

1.3 Quality-adjusted life year

Utilities are essential for health economic appraisal, evaluations and overall health technology assessment, as pharmaceutical and medical device reimbursement processes worldwide usually require such analyses (10). In these cases, utilities are used to compute quality-adjusted life years (QALYs), and the analysis is referred to as cost-utility analysis (13). In cost-utility analysis, the typical focus is on comparing the differences in the cost of different health interventions to the QALY gained. In other words, QALYs enable to quantify the effectiveness of health interventions.

QALY is a single measure that combines quantity (life years) and quality (utility) of life. QALY shows the time spent in a certain health state, for example, three years spent in a health state with a utility of 0.5 equals 1.5 QALYs (14, 15). QALY has been in use for a long time and its advantages and drawbacks are therefore well-known. One of the criticisms is that QALY may undervalue the lives of those with disabilities. Limitations of QALY also include ethical considerations (one QALY is one QALY, regardless of the individual) and the lack of recognition of non-health effects (16). Ultimately, a key benefit is its ability to facilitate the comparison of a broad range of health interventions to support resource allocation decisions in healthcare (14).

1.4 HRQoL measures

The development and use of HRQoL measures is a highly relevant area for clinicians, health economists, the industry, policymakers in healthcare and health outcomes researchers. To date, a wide range of measures have been developed to support decision-making in those fields. HRQoL measures may be classified into the following categories: generic vs. condition-specific and preference-based vs. non-preference-based (17, 18). Generic measures capture overall health, whereas condition-specific measures are tailored to specific patient populations. Preference-based measures allow to assign preferences or utilities to health states, whereas non-preference-based measures lack this capacity. Based on the categories, there are four combinations, illustrated by the following measures: generic preference-based measures (e.g., EQ-5D), generic non-preference-based measures (e.g., Patient-Reported Outcomes Measurement Information System Global Health), condition-specific preference-based measures (e.g., NEWQOL-6D), and condition-specific non-preference-based measures (e.g., Psoriasis Index of Quality of Life) (19-22).

HRQoL measures can be used as patient-reported outcome measures (PROMs). It is important to note that PROMs can be used to assess any aspect of patients' lives, not exclusively HRQoL, for example, symptoms, disease severity, well-being, and work productivity. PROMs are gaining popularity due to their patient-centered approach. PROMs may help in the assessment of patient satisfaction or facilitate patient-physician communication (23). The value of PROMs is significant since clinicians may face challenges in fully understanding the treatment's effects from the patient's perspective (24).

1.5 Description of the HRQoL measures used in this thesis

This thesis focuses on two HRQoL measures, the EQ-5D in patients with dermatological diseases and the Patient-Reported Outcomes Measurement Information System Global Health (PROMIS-GH) in the general population.

1.5.1 EQ-5D-3L and EQ-5D-5L

The EQ-5D is a generic preference-based HRQoL measure designed to provide a simple measure for economic evaluations (19, 25). The EQ-5D consists of a descriptive system and a visual analogue scale (EQ VAS). Both ask about the respondent's health on the day

of completion (i.e., ‘your health today’). The EQ VAS measures self-rated health using a 20-centimeter vertical health thermometer. The endpoints are at 0 and 100, representing ‘the worst health you can imagine’ and ‘the best health you can imagine’, respectively. The descriptive system covers five health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Two adult versions of the EQ-5D have been developed: the EQ-5D-3L (hereafter referred to as 3L) and the more recent EQ-5D-5L (hereafter referred to as 5L) (19, 26). The former has three response levels in each dimension, while the latter has five. A single-digit number may be attached to the responses on each dimension, indicating the selected level on each dimension. For example, the profile ‘11111’, indicating the best possible health status, can be obtained by marking the best health state on all five dimensions. The advantages of the EQ-5D include its shortness and good psychometric properties across a wide range of populations (27). However, the EQ-5D may not capture all important HRQoL areas in specific patient populations (28-30). The EQ-5D is the most commonly used HRQoL measure in estimating QALYs and is endorsed by more than 20 health technology assessment bodies globally, including Hungary (31-33).

Using the 3L, respondents have three response options in each dimension to describe their health status: no problem, some/moderate problems, and extreme problems/unable to/confined to bed. With the 3L, 243 different health states can be described. The 5L is available in more than 150 languages and has five severity-type response levels: no problems, slight problems, moderate problems, severe problems, and extreme problems/unable to (34). The 5L allows to describe 3125 health states (26). There are two substantial differences between the 3L and 5L in addition to the number of levels, and both are related to the wording. First, in the 5L, the term ‘some’ has been replaced by ‘moderate’ in the dimensions of mobility, self-care, and usual activities. Second, in the mobility dimension, the 3L uses ‘confined to bed’ to indicate the worst possible answer, while the 5L uses ‘unable to walk about’ (25, 26).

In 2020, the Hungarian 3L and 5L value sets were published in a general population-based valuation study (35). There is an additional smaller difference in the wording between the Hungarian 3L and 5L versions, as the ‘anxiety/depression’ dimension is translated to Hungarian as ‘anxiety/feeling down’ in the 3L, but as ‘anxiety/depression’ in the 5L (35). The utilities range from –0.865 to 1 for the 3L and from –0.848 to 1 for

the 5L. With the development of the Hungarian value sets, Hungary has joined regional countries such as Poland (3L and 5L) and Slovenia (3L and 5L), which also developed their own national value sets (32, 36). In addition to the 3L and 5L value sets, another form of the EQ-5D is available in Hungary, the EQ-5D-Y, which was designed for younger populations (children and adolescents aged 8-15 years) (37). Of note, according to the latest Hungarian health technology assessment guideline, the preferred method for measuring HRQoL in adults for QALYs is the 5L using the Hungarian value set, with the 3L being the secondary choice (38).

1.5.2 EQ-PSO

Bolt-ons are additional dimensions of HRQoL or well-being and are used to supplement the five core dimensions of the EQ-5D (39). So far, several bolt-on items have been developed, for example, cognition, social relationships, hearing, vision, breathing and tiredness (40). Two bolt-ons (skin irritation and self-confidence) have been developed for the EQ-5D-5L, targeting patients with psoriasis, which, together with the five core dimensions, are often referred to as EQ-PSO. Based on a literature review and interviews, four potential bolt-on dimensions were initially identified (skin irritation, self-confidence, skin appearance, and social/relationship difficulties). However, only two dimensions were retained after thorough qualitative and quantitative analyses (41).

1.5.3 PROMIS-GH

Unlike many other PROMs developed decades ago, the Patient-Reported Outcomes Measurement Information System (PROMIS) items and instruments were developed using item response theory (IRT) (42). Over the past decades, the PROMIS initiative has created approximately 100 item banks and a few fixed-length short-forms to measure health outcomes (43, 44). PROMIS-GH is the shortest PROMIS short-form that measures five generic domains of health (physical functioning, pain, fatigue, emotional distress, social health) using ten global health items (20). It has two subscales: Global Mental Health (GMH) and Global Physical Health (GPH). The items have different recall periods: some refer to ‘in general’, others to the ‘past seven days’, and some are unspecified. Each item is rated on a five-point scale. For Global01, Global02, Global03, Global04, Global05, and Global09 items, the response options range from excellent (5) as the best to poor (1) as the worst. For Global06, options range from completely (5) to

not at all (1), for Global10 from never (5) to always (1) and for Global08 from none (5) to very severe (1). However, Global07 is an exception, as it is rated on a scale from 0 to 10, where 0 means no pain, and 10 represents the worst imaginable pain (20).

1.6 Frameworks used to conduct psychometric analyses in this thesis

The concept of psychometrics is concerned with the theory and techniques of large-scale cognitive assessments (45). From a psychometric perspective, classical test theory (CTT) and item response theory (IRT) are two fundamental approaches for constructing and testing HRQoL measures (46). In CTT, an individual's observed score is the result of the combination of the true score, which represents the individual's level of the trait being measured by the instrument, and random measurement error. Shortcomings of CTT include sample dependency, assumption of equivalence between items, standard error of measurement and equating tests (46). IRT focuses on connecting the abilities of individuals with the probability of endorsing an item (47). IRT offers several advantages over CTT methods, including the estimation of the respondents' location on an underlying 'latent' trait (e.g., health status) using any subset of items that do not vary depending on the characteristics of the population, as well as the possibility to perform computer adaptive testing for assessing health status (48). One limitation of IRT is that the properties of test items are independent of the specific group of individuals from which they were initially obtained (46).

1.7 Psychometric properties and methods

Psychometric properties refer to the wide range of properties, including reliability, validity, and responsiveness of measures (49). Several other psychometric properties are usually the subject of evaluations, however, in this thesis, the focus was on the following properties: content validity, measurement agreement, ceiling and floor effects, informativity, convergent and known-groups validity, internal consistency, structural validity and differential item functioning (DIF) (50-52). HRQoL instruments are evaluated by many characteristics, but the most common are validity and reliability (53).

1.7.1 Reliability

Reliability (or, in some cases, reproducibility) refers to the consistency of a measure. In other words, a highly reliable measure produces similar results for the same individual in the same circumstances. Reliability can be tested by using a different set of similar items

from the same instrument, evaluating test-retest reliability over time, and assessing reliability through different individuals on the same or other occasions. The reliability analysis often includes the analysis of agreement (51, 54). When evaluating reliability, the following properties are most often assessed:

1. Consistency refers to the degree of correlation (homogeneity) among items within a measure (sub)scale. The underlying idea is that items assessing the same concept (e.g., physical function) exhibit correlation. For example, measuring internal consistency is possible for the PROMIS-GH measure but irrelevant for the EQ-5D, as its items are intended to be independent (50, 52). In this thesis, internal consistency is referred to as unidimensionality in the case of PROMIS-GH.
2. Parallel-forms reliability reflects both the degree of correlation and agreement between measures, and the intraclass correlation coefficient is the indicator to express this. Bland-Altman plot and other correlation coefficients, such as Pearson's, are often used to assess parallel-forms reliability (55).
3. Measurement error refers to the combination of systematic and random errors in the respondent's score that are not associated with true changes in the measured construct (54).
4. Test-retest reliability indicates the measure's performance over time, thus being able to assess the instrument's stability. In other words, it is the observation of respondents on two occasions at two different times (54).
5. Measurement error and test-retest reliability can be assessed by different individuals on different occasions. Inter-rater reliability refers to the level of agreement among different raters' assessments when evaluating the same individual. Intra-rater reliability refers to the consistency of the rater's assessment across different occasions for the same person (54).

1.7.2 Validity

Validity is associated with the accuracy of a measure, or in other words, the instrument captures what it is intended to measure. It usually focuses on the following areas: content validity, criterion validity, and construct validity (54).

1. Content validity examines whether the instrument contains the appropriate items it seeks to capture. Content validity focuses on three aspects: relevance,

comprehensiveness, and comprehensibility. To determine content validity for qualitative research, the Consensus-based Standards for the selection of health Measurement Instruments methodology provides a 10-point list to ensure good content validity. It is worth mentioning that content validity often includes face and social validity (51, 54).

2. Criterion validity tests the performance of an instrument against a 'gold standard' measure. Analysis of variance tests and correlations are used to determine criterion validity. Criterion validity is not commonly analysed for HRQoL measures as no 'gold standard' measure exists for such analyses (52, 54).
3. Construct validity concerns the observed and the hypothesised performance of the measure and includes three measurement properties: hypotheses testing, structural validity, and cross-cultural validity. Hypotheses testing includes convergent, discriminant and known-groups validity. Convergent and discriminant validity involves the comparison with other HRQoL measures or their domains or subscales, while known-groups validity refers to the ability to differentiate between relevant subgroups of respondents (52, 54). Structural validity refers to the extent to which the instrument scores adequately reflect the underlying dimensionality of the construct being measured. Cross-cultural validity focuses on the adaptations of measures and the differences between translations of measures (54).

Alongside reliability and validity, responsiveness is another frequently evaluated psychometric property. Responsiveness refers to the ability of a measure to detect clinically important changes over time. In other words, responsiveness is considered as longitudinal validity (50, 52, 54).

1.7.3 Other psychometric properties

In addition to reliability, validity, and responsiveness, various measurement properties are usually assessed as well. The ceiling and floor effect examines the extent to which responses to a given item, domain or (sub)scale are grouped around the highest and lowest possible scores, respectively (50). Informativity is used to reflect discriminatory power, often measured by Shannon's (H') and Shannon's evenness (J') indices (56, 57). Lastly, DIF analysis is used to assess measurement invariances. DIF analysis enables testing

whether item responses differ between subgroups when controlling the latent trait (e.g., physical health). There are two types of DIF: uniform DIF is a constant systematic difference in item response across the entire latent trait continuum among respondent subgroups. Meanwhile, non-uniform DIF involves varying differences between subgroups along the latent trait continuum (48).

1.8 Skin conditions relevant to this thesis

1.8.1 Hidradenitis suppurativa

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic inflammatory skin disease that predominantly affects the apocrine gland-bearing areas of the body and is characterised by painful, deep-seated lesions (58, 59). It mostly affects young working-age adults, and women nearly three times more often have HS than men (60). In Europe, it has been reported that the average prevalence is up to 1%, and the mean incidence is 6.0 per 100,000 person-years (59, 61-64). Treatments include several medical interventions: topical, conventional systemic, biological and surgical (e.g., laser) treatments (65). There are several types of comorbidities associated with HS, such as inflammatory and autoimmune diseases, psychiatric illnesses, cardiovascular diseases and hormone-related disorders (66, 67). In addition, HS imposes a significant economic burden not only on patients but also on their families and overall, the healthcare system (68). One of the greatest challenges for both the patient and the healthcare system is the typically long diagnostic delay, which may range up to 7.2 years in HS patients, or the complete lack of formal diagnosis (69). Various measurement tools are available to assess changes in HRQoL in HS patients (70). The EQ-5D is particularly notable for its measurement performance, which has been demonstrated in several studies in patients with skin diseases, including HS (71-74). However, evidence concerning the performance of 5L in a sample of HS patients is limited, especially compared to 3L.

1.8.2 Psoriasis

Psoriasis is an immune-mediated, chronic inflammatory skin disease. Clinical manifestations include red patches and silvery scales on the skin’s surface, usually on the scalp, knees, elbows, and lower back (75, 76). It can appear at any age, but most often with advancing age (77). The prevalence of psoriasis in adults is estimated at 1.83% in central Europe, and globally, it ranges from 0.51% to 11.43%. The incidence of psoriasis

in Europe varies from 31.4 to 521.1 per 100,000 person-years (77, 78). Treatments include topical drugs, ultraviolet-A light, systemic non-biological (e.g., methotrexate) and systemic biologic drugs (79). Psoriasis may be associated with various comorbidities, including psoriatic arthritis, malignancies, diabetes, depression as well as cardiovascular diseases (80). Psoriasis can be severely debilitating and stigmatising, significantly impacting individuals' HRQoL as well as work productivity (80, 81). The burden of psoriasis extends beyond the psychological and social aspects, with high costs to patients and healthcare systems (82). Just as in the case of HS, the EQ-5D is one of the most used generic HRQoL measures among patients with psoriasis, appearing in various observational studies and clinical trials (71, 83, 84). Two bolt-ons have been developed for the EQ-5D-5L to better capture the HRQoL effects of psoriasis: skin irritation and self-confidence (EQ-PSO) (41, 85).

2. Objectives

1. EQ-5D-3L and 5L study

Several studies have applied and validated the 3L and 5L in HS patients (86-91). However, no head-to-head comparison studies have been conducted to compare the psychometric performance of the 3L and 5L in HS patients.

- The aim of the study was to compare the psychometric performance of the 3L and 5L descriptive systems and utilities of the EQ-5D in a sample of patients with HS along the following measurement properties: feasibility, agreement, ceiling effects, redistribution properties, inconsistency in responses, informativity, convergent and known-groups validity.

2. EQ-PSO study

The content validity of the EQ-PSO has only been established in the development study and in English language (41). In addition, it is unclear whether there are any conceptual overlaps between the skin irritation and self-confidence bolt-on dimensions and the five core dimensions of the EQ-5D. Therefore, this study aimed:

- To investigate and compare the relevance of the content, comprehensiveness, and comprehensibility of EQ-5D-5L and EQ-PSO in Hungarian psoriasis patients.
- To explore the potential conceptual overlaps between the existing five dimensions and the two bolt-ons.

3. PROMIS-GH study

To ensure consistent psychometric performance across languages, standardised HRQoL measures need to demonstrate robust psychometric properties across language versions. Although the PROMIS-GH measure is available in Hungarian, its psychometric properties have never been investigated. Furthermore, only the Netherlands and the US developed general population reference values for the PROMIS-GH (92, 93). Our objectives were the following:

- To evaluate the psychometric performance of the Hungarian PROMIS-GH.
- To develop general population reference values for the two subscales in Hungary.

3. Results

This chapter relies on the findings of the three publications of the candidate:

1. **Bató A,** Brodszky V, Gergely LH, Gáspár K, Wikonkál N, Kinyó Á, Szabó Á, Beretzky Z, Szegedi A, Remenyik É, Kiss N, Sárdy M, Rencz F. The measurement performance of the EQ-5D-5L versus EQ-5D-3L in patients with hidradenitis suppurativa. Qual Life Res. 2021;30(5):1477-90.
2. Rencz F, Mukuria C, **Bató A,** Poór AK, Finch AP. A qualitative investigation of the relevance of skin irritation and self-confidence bolt-ons and their conceptual overlap with the EQ-5D in patients with psoriasis. Qual Life Res. 2022;31(10):3049-60.
3. **Bató A,** Brodszky V, Mitev AZ, Jenei B, Rencz F. Psychometric properties and general population reference values for PROMIS Global Health in Hungary. Eur J Health Econ. 2023 [Epub ahead of print: 10.1007/s10198-023-01610-w].

All HRQoL measures used in this thesis were administered in Hungarian. Ethics approval was obtained for each study separately:

1. The EQ-5D-3L and 5L study protocol was approved by the Scientific and Ethical Committee of the Medical Research Council in Hungary (Reference No. 40579-2/2017/EKU).
2. Ethical approval of the EQ-PSO study was obtained from the Research Ethics Committee of the Corvinus University of Budapest (no. KRH/342/2020).
3. The PROMIS-GH study was approved by the Research Ethics Committee of the Corvinus University of Budapest (no. KRH/343/2020).

3.1 EQ-5D-3L and 5L study

3.1.1 Sample characteristics

A total of 200 consecutive patients with HS participated in the survey (Table 1). The majority of the patients were male (61.5%), and the mean age was 37.13 ± 12.43 years. The mean disease duration was 4.76 ± 6.72 years. Overall, 46.0% of the patients had at least one comorbidity, with cardiovascular disease (16.5%), acne vulgaris (7.0%), inflammatory bowel disease (7.0%), diabetes (6.0%) and psychiatric illness (6.0%) being the most commonly reported. Altogether, 80.7% of the patients were overweight or obese (body mass index ≥ 25). Almost half of the patients had Hurley III stage disease (48.5%). According to Physicians' Global Assessment of hidradenitis suppurativa severity (HS-PGA) scores, over one-third of the patients had severe or very severe HS.

Table 1 Characteristics of patients with HS (94)

Variables	Mean (SD) or n (%)
Age (years)	37.13 (12.43)
Sex – Female	77 (38.5%)
Sex – Male	123 (61.5%)
Disease duration (years)	4.76 (6.72)
Disease severity	
Hurley staging – Hurley I (missing n=4)	22 (11.2%)
Hurley staging – Hurley II (missing n=4)	79 (40.3%)
Hurley staging – Hurley III (missing n=4)	95 (48.5%)
HS-PGA – Clear (missing n=7)	6 (3.1%)
HS-PGA – Minimal (missing n=7)	7 (3.6%)
HS-PGA – Mild (missing n=7)	37 (19.3%)
HS-PGA – Moderate (missing n=7)	69 (35.9%)
HS-PGA – Severe (missing n=7)	40 (20.7%)
HS-PGA – Very severe (missing n=7)	34 (17.7%)
Modified Sartorius Score[a] *(missing n=2)*	60.69 (50.24)
PtGA VAS (0-100) *(missing n=1)*	69.62 (22.22)
Current pain intensity VAS (0-10) *(missing n=1)*	4.70 (2.99)
Worst pain intensity[b] VAS (0-10) *(missing n=1)*	6.28 (3.04)
Health-related quality of life	
EQ-5D-3L index (-0.865 to 1) *(missing n=2)*	0.78 (0.21)
EQ-5D-5L index (-0.848 to 1) *(missing n=2)*	0.76 (0.30)
EQ VAS (0-100) *(missing n=2)*	64.29 (22.68)
DLQI (0-30) *(missing n=2)*	11.75 (8.11)
Skindex-16 Symptoms subscale (0-100) (missing n=2)	46.74 (29.36)
Skindex-16 Emotions subscale (0-100) (missing n=2)	64.55 (29.28)
Skindex-16 Functioning subscale (0-100) (missing n=2)	49.40 (34.70)

For EQ-5D-5L and EQ VAS higher scores refer to better health status. For all other measures higher scores represent worse health status. a: The measure has no upper limit, b: For the past one month. DLQI = Dermatology Life Quality Index; HS = hidradenitis suppurativa; HS-PGA = Physicians' Global Assessment of hidradenitis suppurativa severity; PtGA VAS = Patient's Global Assessment of disease severity visual analogue scale; SD = standard deviation

3.1.2 Psychometric performance

3.1.2.1 Feasibility

One patient did not complete the 5L measure, and there were two partially incomplete 3L and one 5L descriptive systems. There were two missing values on the EQ VAS. For 3L, 43 distinct health state states were observed versus 101 for the 5L. There was a great dispersion of both 3L and 5L health states among HS patients, with few clustering. One and ten patients had negative index values in the 3L and 5L, respectively. There were more patients between index values of 0.2 to 0.6 and 0.7 to 0.8 with the 3L, whereas the 5L allowed more observations for mild (index value 0.9-1) and very severe health states (index value < 0.2) (Figure 1).

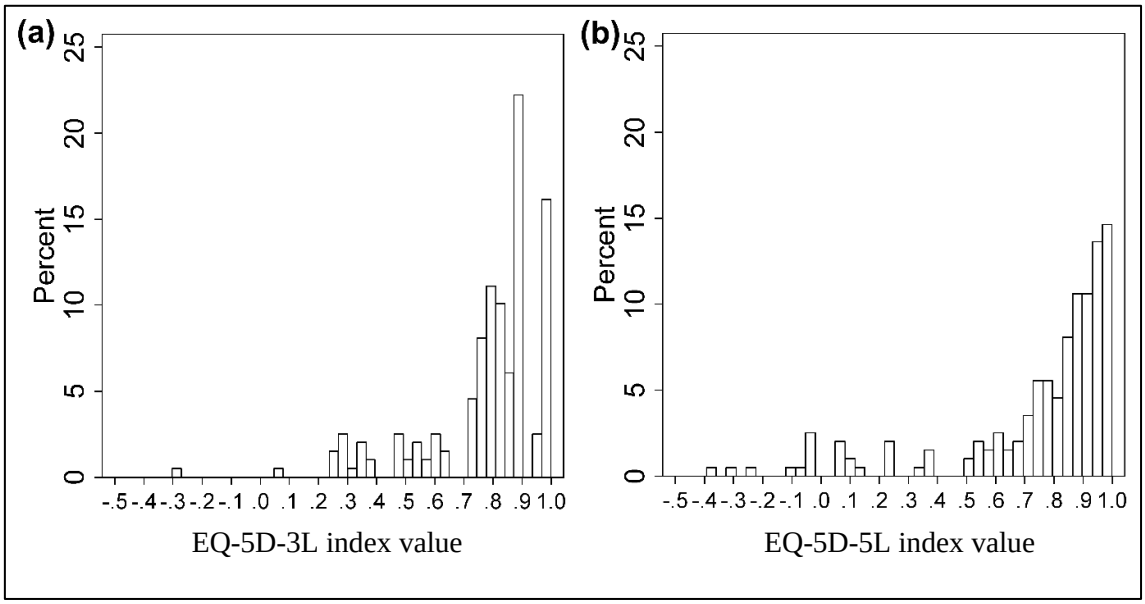

Figure 1 Distribution of EQ-5D-3L and EQ-5D-5L index values (94)

3.1.2.2 Ceiling effects

Patients reported the most problems with pain/discomfort ('any problems': 75.4% in 3L and 77.4% in 5L), while the least problems occurred with self-care ('no problems': 19.5% in 3L and 28.3% in 5L) (Table 2). Absolute reduction in ceiling effects was the highest for self-care (8.8%), whereas relative reduction was the highest for usual activities (15.5%). We found increased ceiling effects for the 5L in the dimension of anxiety/depression with absolute and relative increases of 5.0% and 11.4%, respectively. Ceiling effect reduction was statistically significant for the mobility, self-care and usual

activities dimensions. The proportion of ‘11111’ health states decreased from 16.0% on the 3L to 14.6% on the 5L. The absolute and relative ceiling effect reductions in the proportion of full health (‘11111’) responses were 1.4% and 9.4%, respectively. There were four (2.0%) ‘the best health you can imagine’ (= 100) and no ‘the worst health you can imagine’ (= 0) responses on the EQ VAS.

Table 2 Ceiling effects, inconsistencies and informativity (94)

Dimensions	Ceiling effects							Inconsistencies		Informativity			
	EQ-5D-3L		EQ-5D-5L		Ceiling effect reduction		McNemar's test *p*-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	199	121 (60.8)	199	107 (53.8)	7.0	11.6	0.003	7 (3.5)	1.14	0.93	0.59	1.65	0.71
Self-care	200	161 (80.5)	198	142 (71.7)	8.8	11.8	<0.001	7 (3.5)	1.14	0.71	0.45	1.25	0.54
Usual activities	200	103 (51.5)	198	87 (43.9)	7.6	15.5	0.024	20 (10.0)	1.00	1.22	0.77	1.88	0.81
Pain/discomfort	199	49 (24.6)	199	45 (22.6)	2.0	8.2	0.503	15 (7.5)	1.00	1.32	0.83	2.06	0.89
Anxiety/depression	199	88 (44.2)	199	98 (49.2)	-5.0	-11.4	0.163	30 (15.1)	1.20	1.38	0.87	1.79	0.77
Overall (11111) or mean	200	32 (16.0)	199	29 (14.6)	1.40	9.38	0.607	79 (8.0)	1.10	1.11	0.70	1.73	0.74

H' = Shannon's index; J' = Shannon's evenness index. a: The total number of pairs is 198 for all dimensions.

3.1.2.3 Agreement

A good agreement was established between the 3L and 5L with an intraclass correlation coefficient of 0.872 (95% confidence interval 0.830–0.903; $p < 0.001$). This finding was supported by the Bland-Altman plot (Figure 2). The mean 3L index values of HS patients were higher than those of the 5L (0.78 ± 0.21 and 0.76 ± 0.30; $p < 0.031$). Differences between 3L and 5L index values tended to increase at lower mean index values. Below the index value of 0.5, a higher 3L index value was found for almost all 3L-5L index value pairs falling out of the 95% limits of agreement.

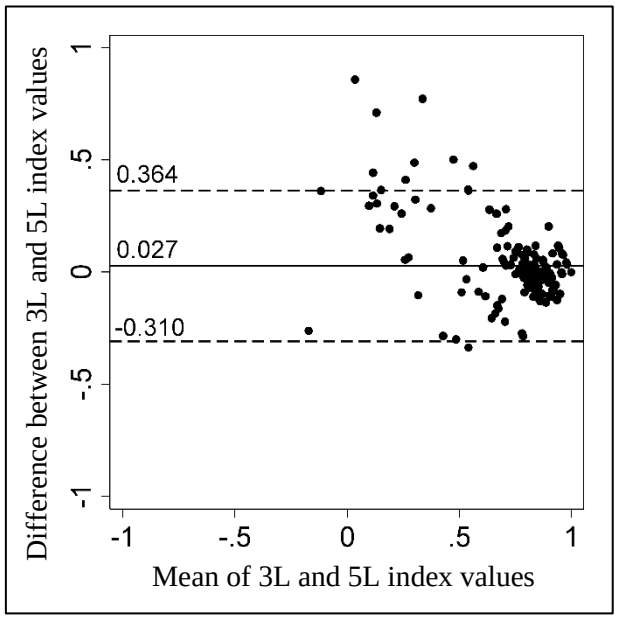

Figure 2 Bland-Altman plot of the EQ-5D-3L and EQ-5D-5L index values in HS (94)

The horizontal line represents the mean of the differences (d) between 3L and 5L index values, while the 95% limits of agreement, obtained as d ± 1.96 * SD of d, are indicated by dashed lines.

3.1.2.4 Redistribution properties and inconsistencies

Responses covered nearly all levels for both EQ-5D versions (Table 3). There were 79 (8.0%) inconsistent response pairs provided by 21 (10.5%) patients. The size of inconsistency was generally low, ranging from 1.00 (usual activities and pain/discomfort) to 1.2 (anxiety/depression). The rate of inconsistent 3L-5L response pairs varied between 3.5% (mobility and self-care) and 15.1% (anxiety/depression) (Table 2).

Table 3 Redistribution properties: cross-tabulation of EQ-5D-3L and EQ-5D-5L responses (94)

3L	5L				
Dimensions	Level 1	Level 2	Level 3	Level 4	Level 5
Mobility, n (%)					
Level 1	104 (86.0)	13 (10.7)	3 (2.5)	1 (0.8)	0 (0.0)
Level 2	3 (3.9)	28 (36.8)	36 (47.4)	9 (11.8)	0 (0.0)
Level 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)
Self-care, n (%)					
Level 1	141 (88.1)	13 (8.1)	5 (3.1)	1 (0.6)	0 (0.0)
Level 2	1 (2.6)	16 (42.1)	15 (39.5)	6 (15.8)	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	75 (73.5)	22 (21.6)	5 (4.9)	0 (0.0)	0 (0.0)
Level 2	12 (13.6)	35 (39.8)	25 (28.4)	15 (17.0)	1 (1.1)
Level 3	0 (0.0)	0 (0.0)	2 (25.0)	4 (50.0)	2 (25.0)
Pain/discomfort, n (%)					
Level 1	37 (75.5)	9 (18.4)	3 (6.1)	0 (0.0)	0 (0.0)
Level 2	8 (6.6)	58 (47.5)	49 (40.2)	7 (5.7)	0 (0.0)
Level 3	0 (0.0)	0 (0.0)	4 (14.8)	16 (59.3)	7 (25.9)
Anxiety/depression, n (%)					
Level 1	76 (86.4)	12 (13.6)	0 (0.0)	0 (0.0)	0 (0.0)
Level 2	20 (22.5)	38 (42.7)	25 (28.1)	6 (6.7)	0 (0.0)
Level 3	1 (4.8)	4 (19.0)	5 (23.8)	7 (33.3)	4 (19.0)

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.

3.1.2.5 Informativity

The 5L improved the absolute discriminatory power (H') of the measure in all dimensions (3L: 0.71 to 1.38 vs. 5L: 1.25 to 2.06), indicating that the two extra levels of the 5L were effectively used (Table 2). Similarly, the relative discriminatory power (J') increased for all dimensions (3L: 0.45 to 0.87 vs. 5L: 0.54 to 0.89) with the exception of anxiety/depression (3L: 0.87 vs. 5L: 0.77). The average H' and J' values improved when moving from the 3L (H' = 1.11 and J' = 0.70) to the 5L (H' = 1.73 and J' = 0.74).

3.1.2.6 Convergent validity

The results supported the majority of our hypotheses, with some interesting exceptions; for instance, the EQ-5D pain/discomfort dimensions and index values correlated strongly

with the Dermatology Life Quality Index (DLQI) and the functioning subscale of Skindex-16 (Table 4). Furthermore, the self-care and mobility dimensions of the EQ-5D demonstrated weak correlations with the symptoms and emotions subscales of Skindex-16.

When comparing the 3L and 5L, the index values of both measures showed moderate correlations with EQ VAS (0.535 vs. 0.592). The 5L exhibited stronger correlations with EQ VAS for all dimensions except for anxiety/depression (range of coefficients: –0.449 to –0.350 for the 3L and –0.505 to –0.385 for the 5L). The 5L produced stronger correlations in mobility, self-care and pain/discomfort dimensions with DLQI and all Skindex-16 subscale scores. However, 3L index values correlated stronger with DLQI and all Skindex-16 subscale scores, except for the symptoms subscale. Considering disease severity scales, the 5L resulted in a stronger correlation with Patient's Global Assessment of disease severity visual analogue scale (PtGA VAS) (5/5 dimensions), Modified Sartorius Score (3/5 dimensions) and HS-PGA (2/5 dimensions). The 5L demonstrated a better convergent validity with current pain intensity visual analogue scale (VAS) for four dimensions, including the pain/discomfort dimension (3L: 0.534 vs. 5L: 0.591). Three dimensions of the 3L, including pain/discomfort, were better correlated with the worst pain intensity VAS scores than those of the 5L. The correlations between index values and pain scales revealed an improved performance of the 3L and 5L with worst and current pain intensities, respectively.

Table 4 Convergent validity: Spearman's correlation coefficients (94)

HRQoL measures		EQ-5D					
	Version	**Mobility**	**Self-care**	**Usual activities**	**Pain/ discomfort**	**Anxiety/ depression**	**Index value**
EQ VAS (0-100)	**3L**	–0.406	–0.365	–0.350	–0.414	–0.449	0.535
	5L	–0.473	–0.399	–0.422	–0.505	***–0.385***	0.592
Skindex-16 symptoms (0-100)	**3L**	0.331	0.287	0.420	0.523	0.422	–0.561
	5L	0.396	0.334	***0.396***	0.595	***0.401***	–0.573
Skindex-16 emotions (0-100)	**3L**	0.261	0.274	0.358	0.471	0.513	–0.535
	5L	0.289	0.282	***0.302***	0.473	***0.511***	***–0.500***
Skindex-16 functioning (0-100)	**3L**	0.403	0.434	0.538	0.610	0.566	–0.708
	5L	0.467	0.457	***0.501***	0.625	***0.530***	***–0.674***
DLQI (0-30)	**3L**	0.396	0.409	0.547	0.628	0.564	–0.722
	5L	0.426	0.469	***0.541***	0.671	***0.560***	***–0.697***
PtGA VAS (0-100)	**3L**	0.264	0.334	0.316	0.337	0.296	–0.395
	5L	0.340	0.347	0.363	0.391	0.315	–0.434
HS-PGA (0-5)	**3L**	0.291	0.348	0.371	0.230	0.205	–0.337
	5L	0.349	***0.343***	***0.354***	0.290	***0.173***	–0.350
Modified Sartorius Score (0-)[a]	**3L**	0.266	0.335	0.319	0.243	0.212	–0.332
	5L	0.325	***0.301***	0.333	0.302	***0.166***	–0.334
Current pain intensity (0-10)	**3L**	0.286	*0.306*	0.314	0.534	0.374	–0.540
	5L	0.384	*0.310*	0.337	0.591	***0.315***	–0.544
Worst average pain in the past 1 month (0-10)	**3L**	0.315	0.328	0.368	0.553	0.263	–0.499
	5L	0.328	***0.299***	***0.353***	***0.529***	0.285	***–0.473***

$p < 0.05$ for all correlation coefficients.

a: The measure has no upper limit. Bold and italic values indicate a lower correlation coefficient for the 5L compared to the 3L. DLQI = Dermatology Life Quality Index; HS = hidradenitis suppurativa; HS-PGA = Physicians' Global Assessment of hidradenitis suppurativa severity; PtGA VAS = Patient's Global Assessment of disease severity visual analogue scale

3.1.2.7 Known-groups validity

Comparisons across known groups of patients provided consistent evidence for most of our hypotheses apart from the impact of perianal localisation on HRQoL. Contrasting the 3L and 5L, in almost every subgroup of patients, the mean 5L index values were lower, while the medians were higher than their respective mean and median 3L index values (Table 5). Patients with gluteal or inguinal localisation or more severe disease, as assessed by the Hurley classification system or HS-PGA, had more impaired HRQoL on both the 3L and 5L. In addition, the 5L detected significantly lower index values in patients with

more comorbidities. Effect sizes were primarily small or moderate. Known-groups validity analysis resulted in insignificant differences between groups defined by the majority of localisations both with the 3L and 5L versions. Overall, the 5L was able to better discriminate between known-groups of patients based on the number of comorbidities, HS-PGA groups, and inguinal localisation (relative efficiency (RE) > 1), whereas the 3L exhibited a better known-groups validity for body mass index, Hurley stages and gluteal localisation (RE < 1).

Table 5 Known-groups validity (94)

	EQ-5D-5L					EQ-5D-3L					RE[b]
	n	**Mean (SD)**	**Median (IQR)**	***p*-value[a]**	**ES**	**n**	**Mean (SD)**	**Median (IQR)**	***p*-value[a]**	**ES**	
Total sample	198	0.76 (0.30)	0.86 (0.71-0.96)	–	–	198	0.78 (0.21)	0.82 (0.75-0.90)	-	-	-
Body mass index (BMI) *(missing n=3)*											
Normal or underweight (<24.9)	38	0.81 (0.20)	0.86 (0.76-0.93)	0.235	0.005	38	0.81 (0.14)	0.81 (0.78-0.90)	0.046	0.022	0.216
Overweight (25.0-29.9)	65	0.78 (0.28)	0.89 (0.71-0.96)			65	0.83 (0.21)	0.88 (0.79-0.98)			
Obese (≥30)	92	0.72 (0.33)	0.85 (0.64-0.96)			92	0.75 (0.22)	0.82 (0.60-0.90)			
Comorbidities											
None	106	0.79 (0.27)	0.89 (0.75-0.96)	0.003	0.050	106	0.81 (0.17)	0.85 (0.78-0.90)	0.160	0.032	1.539
1	55	0.80 (0.22)	0.86 (0.76-0.96)			55	0.82 (0.15)	0.82 (0.78-0.90)			
≥2	37	0.59 (0.41)	0.74 (0.39-0.88)			37	0.64 (0.31)	0.80 (0.36-0.88)			
Hurley staging *(missing n=4)*											
Hurley I	22	0.83 (0.23)	0.89 (0.77-0.97)	0.001	0.068	22	0.83 (0.18)	0.89 (0.78-0.93)	<0.001	0.071	0.960
Hurley II	79	0.83 (0.21)	0.92 (0.76-0.96)			79	0.83 (0.17)	0.88 (0.80-0.90)			
Hurley III	93	0.67 (0.35)	0.80 (0.57-0.92)			93	0.73 (0.24)	0.80 (0.64-0.88)			
HS-PGA *(missing n=7)*											
Clear-minimal	13	0.91 (0.12)	1.00 (0.83-1.00)	<0.001	0.116	13	0.90 (0.14)	1.00 (0.81-1.00)	<0.001	0.112	1.036
Mild	37	0.85 (0.17)	0.92 (0.81-0.96)			37	0.84 (0.15)	0.82 (0.80-0.90)			
Moderate	69	0.79 (0.27)	0.88 (0.75-0.96)			69	0.80 (0.19)	0.85 (0.79-0.90)			
Severe	40	0.73 (0.31)	0.81 (0.69-0.92)			39	0.79 (0.16)	0.82 (0.72-0.90)			
Very severe	32	0.53 (0.40)	0.64 (0.20-0.86)			33	0.62 (0.30)	0.72 (0.42-0.81)			
Localisation											
Axillary											
No	44	0.78 (0.25)	0.85 (0.73-0.92)	0.771	0.000	43	0.80 (0.17)	0.80 (0.78-0.90)	0.850	0.000	2.371
Yes	154	0.75 (0.31)	0.87 (0.71-0.96)			155	0.78 (0.22)	0.82 (0.75-0.90)			
Genital											
No	147	0.77 (0.29)	0.88 (0.75-0.96)	0.079	0.016	147	0.79 (0.19)	0.82 (0.75-0.90)	0.491	0.002	6.518
Yes	51	0.71 (0.33)	0.80 (0.60-0.92)			51	0.76 (0.26)	0.82 (0.72-0.90)			

	EQ-5D-5L					EQ-5D-3L					RE[b]
	n	Mean (SD)	Median (IQR)	*p*-value[a]	ES	n	Mean (SD)	Median (IQR)	*p*-value[a]	ES	
Gluteal											
No	140	0.80 (0.25)	0.88 (0.75-0.96)	<0.001	0.061	141	0.82 (0.16)	0.85 (0.80-0.90)	<0.001	0.062	0.986
Yes	58	0.64 (0.36)	0.77 (0.37-0.90)			57	0.68 (0.28)	0.78 (0.54-0.90)			
Inguinal											
No	72	0.85 (0.18)	0.89 (0.79-0.96)	0.004	0.041	72	0.84 (0.14)	0.86 (0.80-0.90)	0.013	0.031	1.314
Yes	126	0.70 (0.34)	0.84 (0.60-0.96)			126	0.75 (0.23)	0.82 (0.64-0.90)			
Perianal											
No	176	0.76 (0.30)	0.87 (0.71-0.96)	0.509	0.002	176	0.79 (0.19)	0.82 (0.78-0.90)	0.140	0.011	0.200
Yes	22	0.73 (0.32)	0.85 (0.70-0.90)			22	0.70 (0.31)	0.79 (0.58-0.88)			
Submammary											
No	174	0.77 (0.28)	0.87 (0.71-0.96)	0.655	0.001	174	0.79 (0.19)	0.82 (0.77-0.90)	0.746	0.001	1.903
Yes	24	0.68 (0.42)	0.82 (0.66-0.96)			24	0.71 (0.33)	0.82 (0.60-0.90)			

a: Mann-Whitney test or Kruskal Wallis test, where a $p < 0.05$ was considered statistically significant. b: Relative efficiency compared to the EQ-5D-3L. ES = effect size; HS = hidradenitis suppurativa; RE = relative efficiency; SD = standard deviation; IQR = interquartile range

3.2 EQ-PSO study

3.2.1 Sample characteristics

A total of 21 patients with psoriasis were recruited, three of whom withdrew. Two participants did not show up, resulting in a final sample of 16 patients. For 15 of them, we conducted the interview face-to-face. The mean interview duration was 59 minutes (range 41–91 minutes). No important new themes emerged after the eleventh interview, confirming that data saturation was attained. The sample had a good spread of age groups, was balanced in terms of gender, was well-educated and had heterogeneous clinical characteristics. Detailed characteristics of the participants are presented in Table 6.

Table 6 Characteristics of psoriasis patients (n = 16) (85)

Variables	Median (range) or n (%)
Age (years)	54 (22-72)
Gender	
Female	9 (56%)
Male	7 (44%)
Education	
Primary	1 (6%)
Secondary	4 (25%)
College/university	11 (69%)
Employment	
Employed full-time	8 (50%)
Employed part-time	1 (6%)
Unemployed	1 (6%)
Retired	6 (38%)
Disease duration (years)	23 (3-48)
Number of body regions affected	
1-2	2 (13%)
3-4	6 (38%)
≥ 5	8 (50%)
Body regions affected	
Scalp	12 (75%)
Face	5 (31%)
Auditory canals	2 (13%)
Arms	7 (44%)
Hands	3 (19%)
Fingernails	6 (38%)
Chest	5 (31%)
Back	6 (38%)
Abdomen	4 (25%)
Buttocks	7 (44%)
Genitals	2 (13%)
Thighs	9 (56%)
Legs	5 (31%)
Feet	5 (31%)
Toenails	1 (6%)
Self-reported severity VAS (0-10)*	5.3 (1-10)

Variables	Median (range) or n (%)
Comorbidities	13 (81%)
Anxiety	7 (44%)
Cardiovascular disease	4 (25%)
Chronic tinnitus	1 (6%)
Depression	2 (13%)
Diabetes	1 (6%)
Gastroesophageal reflux disease	1 (6%)
Liver cirrhosis	1 (6%)
Musculoskeletal disease**	6 (38%)
Psoriatic arthritis	5 (31%)
Thyroid disease	2 (13%)
Current treatment	
Topical therapy	11 (69%)
Combination of topical and photo- and/or systemic non-biological therapy	4 (25%)
Biological therapy	1 (7%)
EQ VAS (0-100)	70 (30-100)

Figures may not total 100% due to rounding. VAS = visual analogue scale

*Endpoints: not severe at all = 0, extremely severe = 10

**Other than psoriatic arthritis

3.2.2 Impact of psoriasis on patients' lives

Patients reported 35 aspects of how psoriasis impacted their lives, which were grouped into six concepts: triggers, physical symptoms, mental health consequences, HRQoL consequences, searching for a cure and coping (Figure 3). Skin scaling was the most mentioned troubling symptom of psoriasis, followed by itching and scratching. A few patients experienced painful cracking and bleeding of the skin. Among adverse physical consequences of psoriasis, patients frequently reported problems with their social relationships, leisure activities, mobility and limitations in clothing choices due to their visible skin symptoms. These were connected to mental health consequences, such as feeling unattractive, being stared at by others and having to frequently inform others that psoriasis is not contagious or caused by poor hygiene.

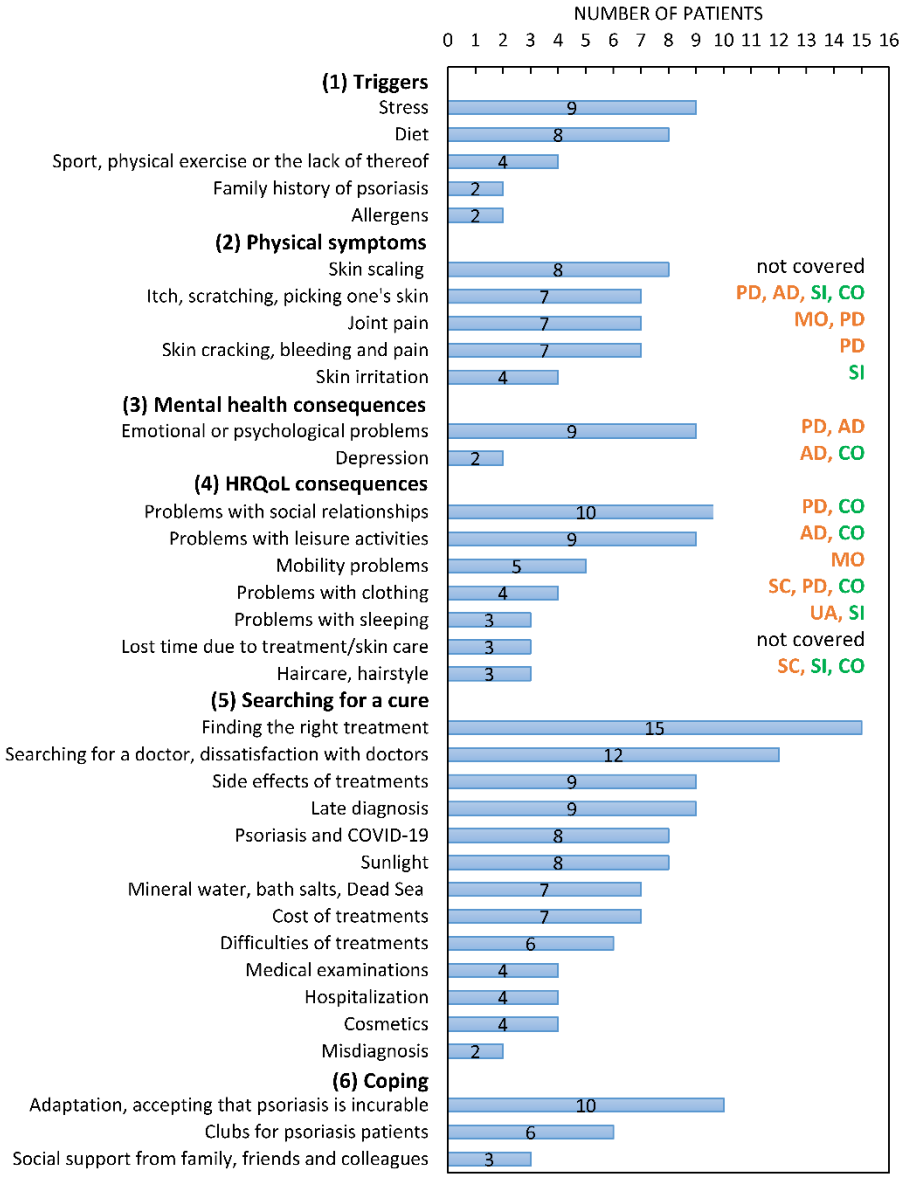

Figure 3 Concept map of the impact of psoriasis on patients' lives and EQ-5D-5L and EQ-PSO content coverage (85)

AD = anxiety/depression, CO = self-confidence, HRQoL = health-related quality of life, MO = mobility, PD = pain/discomfort, SC = self-care, SI = skin irritation, UA = usual activities. Orange dimensions refer to the EQ-5D-5L and green to the two psoriasis-specific bolt-ons.

3.2.3 Psychometric performance of the EQ-5D-5L and EQ-PSO

Results of the thematic analysis were summarized under the following themes: content of dimensions, overall relevance, missing concepts, ranking of dimensions, overlap of dimensions, suggested changes, response levels, EQ VAS and recall period.

3.2.3.1 Content of the EQ-5D and EQ-PSO

Generally, patients interpreted the five dimensions as intended. However, three patients (19%) interpreted 'dressing myself' not as an ability to dress but rather as psoriasis influencing the clothes they can wear, e.g., *"My scalp is scaling so I cannot really wear black tops, and this is very bad especially that I have to wear black at one of my workplaces and I continuously keep on shaking my top as it looks like I have dandruff".* Another patient said that *"I also have a problem with washing myself because I have to pay attention to what cosmetics I use".* There was considerable agreement about the meaning of skin irritation since all patients responded to this dimension, taking into account their perceived level of itch. However, four patients mentioned skin irritation being independent from itch, and one patient emphasized the difference between these two: *"Well, it is also possible that a skin irritation hurts but does not itch. It is like all bugs are insects, but not all insects are bugs".* For most patients, self-confidence covered their problems with social relationships due to psoriasis; over one-third of patients interpreted this dimension as a belief in oneself or being a valued person.

3.2.3.2 Relevance of the EQ-5D-5L and the EQ-PSO

The instructions in the descriptive systems were clear and easily understandable for all patients. In total, 38% of the patients considered the EQ-5D-5L covered important aspects of HRQoL: *"Overall, I find the questionnaire good because this is what a human being is made of, and these are the most important ones [dimensions] in my opinion, too".* Other patients expressed concerns about the questionnaire, such as the irrelevance of some dimensions in the context of psoriasis: *"Well, I cannot connect these first four topics to psoriasis and myself".* Two patients noticed that the EQ-5D-5L is relevant for detecting the impact of severe psoriasis on patients and recognized the generic nature of the questionnaire. For example, *"It is much more relevant for those patients that have joint symptoms or whose condition is more severe"* and *"here, many of the questions are not related to psoriasis, but to the problems of an elderly person in general"*.

Sixteen (100%) and fifteen (94%) patients considered skin irritation and self-confidence bolt-ons important areas in psoriasis, respectively. All patients rated the EQ-PSO better than the EQ-5D-5L to describe their problems with health-related quality of life, e.g., *"the*

topics of the skin irritation and self-confidence which are, can be said, the two most important aspects of this problem or disease".

Figure 3 shows that the EQ-PSO was well aligned with nearly all important impacts of psoriasis raised by patients, except skin scaling and lost time due to psoriasis.

3.2.3.3 Missing concepts

Overall, 11 (69%) patients indicated 16 missing themes for the EQ-5D-5L, and 12 (75%) patients indicated 11 missing themes for the EQ-PSO. These missing concepts were summarized under three large categories: general health-related, psoriasis-related, and non-health-related concepts. In the EQ-5D-5L, the most commonly reported missing concepts were social relationships (n = 8), with several other concepts highlighted by three or fewer participants. Itching as a missing concept was raised by only one patient. Limitations in clothing (i.e., preference for covering visible skin symptoms or avoidance of wearing dark colours to hide flaking skin) were considered missing by two patients. There were fewer missing concepts identified in the EQ-PSO with social relationships identified by five participants (Appendix Table 1). The majority of the remaining themes were suggestions for other background information to solicit in a more general measure designed for psoriasis patients, e.g., the presence of psoriatic arthritis, activities given up since having been diagnosed with psoriasis or how patients' eating choices affect their psoriasis.

3.2.3.4 Ranking and overlap between dimensions

In the EQ-5D-5L, over one-third of patients considered usual activities and anxiety/depression the most relevant dimensions, whereas half of the patients indicated self-care as being the least relevant one (Table 7). The relevance of dimensions substantially changed when the two bolt-ons were added to the EQ-5D-5L. In the EQ-PSO, skin irritation was identified as the most relevant dimension, followed by self-confidence, whereas self-care and anxiety/depression were the least relevant.

Table 7 Most and least relevant dimensions (85)

Dimension*	EQ-5D-5L				EQ-PSO			
	Most relevant		Least relevant		Most relevant		Least relevant	
	n	%	n	%	n	%	n	%
Mobility	2	14	3	21	1	7	2	14
Self-care	0	0	7	50	1	7	4	29
Usual activities	5	36	1	7	0	0	3	21
Pain/discomfort	1	7	2	14	3	21	2	14
Anxiety/depression	5	36	2	14	2	14	4	29
Skin irritation	n/a	n/a	n/a	n/a	5	36	0	0
Self-confidence	n/a	n/a	n/a	n/a	4	29	1	7
All are relevant	1	7	0	0	1	7	0	0

*Only asked in 14 interviews and not in the pilot. One patient may have indicated none or multiple dimensions as most and least relevant. n/a = not applicable

Several minor conceptual overlaps were identified between the seven dimensions (Table 8). Two patients described washing oneself as part of both self-care and usual activities, and two patients reported a potential overlap between anxiety and discomfort and one patient reported an overlap between depression and discomfort. For the two bolt-on dimensions, three patients considered 'itch' a form of discomfort, and thus, pointed out a potential overlap between pain/discomfort and skin irritation: *"I rather have a moderate discomfort, I do not have much pain in my joints, the patches do not hurt either, they rather itch".* Self-confidence showed an overlap with anxiety/depression (anxiety n = 1, depression n = 1 and both n = 1) according to three patients.

Table 8 Overlapping dimensions (85)

(Sub) dimension	Overlap	n	%	Example quote
Self-care (washing)	Usual activities	2	13	010: Washing myself is a usual activity, I don't have any problem with it
Anxiety	Discomfort	2	13	003: That is right, these [anxiety and discomfort] are the same since anxiety is a kind of discomfort when one cannot relax because of what the others may say…
Depression	Discomfort	1	6	005: The weather also affects the depression a bit, because when it is so ugly, foggy and gloomy weather this is so depressing for me
Skin irritation*	Pain	1	6	011: It is painful since it [my scalp] has been stretching
	Discomfort	3	19	004: I rather have a moderate discomfort, I do not have much pain in my joints, the patches do not hurt either, they rather itch
Self-confidence*	Anxiety	2	13	003: Anxiety could also belong to the self-confidence, because whoever does not have self-confidence they are probably anxious
	Depression	2	13	009: Self-confidence overlaps a bit with depression. It might be possible to rephrase 'depression' to ask if it causes lack of self-confidence

*In total, three patients reported an overlap between skin irritation and pain/discomfort and three patients between self-confidence and anxiety/depression

3.2.3.5 Suggested changes

Ten patients suggested changes in the EQ-5D-5L or EQ-PSO dimensions (Appendix Table 2). Changes included the use of wider descriptors for mobility to include other motor abilities and for skin irritation, by extending the range of symptoms described beyond itching (e.g., skin scaling, skin cracking or skin flaking). Few patients suggested adding further supporting examples to other dimensions, e.g., 'flaking skin' to usual activities, 'frustration' to pain/discomfort, 'stress' to anxiety/depression and 'self-esteem' to self-confidence. The self-care, pain/discomfort and anxiety/depression dimensions were sometimes suggested to be separated. Three wording changes were proposed: the replacement of 'washing' with 'skincare', 'anxiety' with 'stress' and 'depression' with 'mood disorder'.

3.2.3.6 Response levels

Six patients (38%) reframed the response levels when completing the EQ-5D-5L or EQ-PSO (Appendix Table 3). Of these, five patients used the response levels as a 'frequency scale' and one patient considered 'level of bother' for at least one dimension. This reframing most commonly occurred for mobility, pain/discomfort and skin irritation. Five patients reported problems with the level modifiers, including difficulty differentiating between levels 1 and 2 (for mobility) and levels 4 and 5 (for pain/discomfort, anxiety/depression and skin irritation).

3.2.3.7 EQ VAS

Patients provided a wide range of interpretations of the endpoint labels 'the best health you can imagine' (= 100) and 'the worst health you can imagine' (= 0) (Appendix Table 4). Most patients interpreted EQ VAS as generic, and only a few used it as a psoriasis-specific scale. For example, when interpreting '0' two patients referred to *"when one's whole body is covered with psoriasis".* The instructions of EQ VAS were clear for the majority of patients; however, two patients mixed up the endpoints '0' and '100'.

3.2.3.8 Recall period

Several participants did not use the stated recall period but intended it as in general for the EQ-5D-5L (62%), EQ VAS (25%) and EQ-PSO (31%). Six participants reported that they would have provided identical answers if a different recall period had been asked: *"There is no difference between today and the other days of the week or other days of the*

month". Eleven patients reported that the recall period of the EQ-5D-5L and EQ-PSO might be subject to bias because of the daily or within-day fluctuations of their symptoms: *"in fact, this is changing as dynamically if we had done this an hour ago, I would have answered certain questions differently than now".*

3.2.3.9 Focus group

Eight patients were invited to the focus group, five of whom attended (three women and two men). The discussions lasted 94 minutes (excluding the introduction of each patient). Three of the five patients considered itching a form of discomfort and responded to the EQ-PSO accordingly, whereas two patients reported their level of itching only in the skin irritation dimension. Of note, during the interviews, these three patients did not mention itching as discomfort. All patients agreed that skin irritation is a broader category than itching, which consists of other symptoms, such as skin scaling and plaquing. Although patients welcomed adding these two symptoms as supportive examples to the skin irritation dimension, two patients cautioned against creating a double-barrelled question and reported that their levels of itch and scaling are often not identical (e.g., slight itch and moderate scaling). Two patients described 'skin cracking' as a form of pain/discomfort, while two other patients considered to belong to skin irritation. One patient said she would report skin cracking both on pain/discomfort and skin irritation. Patients came to a consensus that although self-confidence and anxiety/depression are related constructs, there is no overlap between these two dimensions. Of note, one patient in the focus group was among the three patients who had suggested an overlap between self-confidence and anxiety/depression in the individual interviews.

3.3 PROMIS-GH study

3.3.1 Sample characteristics (unweighted)

Overall, 2502 respondents initiated the survey, 2079 of whom consented, and 379 quit before the end of the questionnaire. A total of 1700 respondents completed the survey. The mean age was 47.9 ± 16.3 years, and 56.3% of the respondents were female. Nearly one-third (32.4%) of the sample had tertiary education. Half (50.9%) of the respondents were employed, 23.5% were retired, and 4.4% were students. Overall, 22.4% lived in the capital, 48.2% in other towns and 29.4% in villages. The geographical distribution of the sample was as follows: Western Hungary 29.0%, Central Hungary 33.6%, and Eastern

Hungary 37.4%. Overall, 67.4% of the sample reported to have any chronic disease. The overall sample showed good representativeness for the general population in Hungary; however, respondents with secondary education were slightly underrepresented, and those who lived in the capital were somewhat overrepresented (Appendix Table 5).

3.3.2 Psychometric performance of PROMIS-GH

3.3.2.1 Floor and ceiling effect

The distributions of GPH and GMH raw scores are presented in Figure 4. We found almost no floor and low ceiling effect for both GPH (0.4% and 4.1%) and GMH subscales (0.5% and 4.8%) (Table 9). Among the items, Global07 demonstrated the highest floor (29.8%). Global06 showed the highest ceiling (58.2%), followed by Global10 (38.3%), Global08 (23.9%) and Global09 (15.8%).

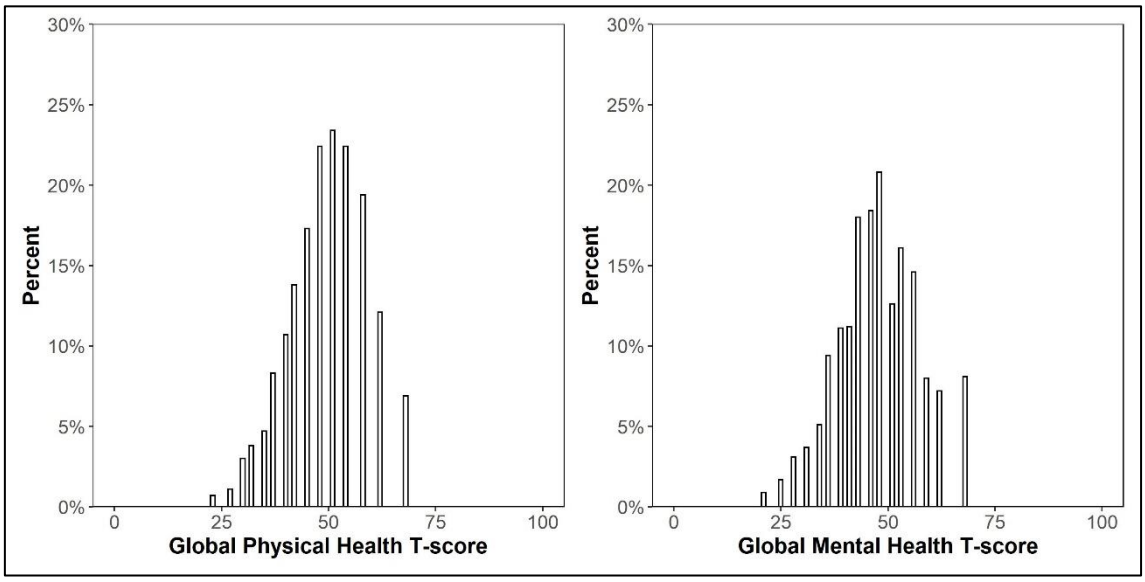

Figure 4 Distribution of Global Physical Health and Global Mental Health T-scores (unweighted) (95)

Table 9 Floor and ceiling of PROMIS Global Health items and subscales (95)

Items and subscales	Floor[a]		Ceiling[b]	
	n	%	n	%
Global01 (general health)	89	5.24	175	10.29
Global02 (quality of life)	81	4.76	162	9.53
Global03 (physical health)	107	6.29	156	9.18
Global04 (mental health)	95	5.59	252	14.82
Global05 (satisfaction with discretionary social activities)	107	6.29	245	14.41
Global06 (physical function)	27	1.59	990	58.24
Global07 (0-10 pain intensity numeric rating scale)[c]	507	29.82	5	0.29
Global08 (fatigue)	17	1.00	407	23.94
Global09 (social roles)	67	3.94	269	15.82
Global10 (emotional problems)	40	2.35	651	38.29
Global Physical Health (GPH)	7	0.41	69	4.06
Global Mental Health (GMH)	9	0.53	81	4.76

a: Worst health status for all items except for Global07

b: Best health status for all except for Global07

c: Not reverse coded item

3.3.2.2 Factor and IRT analysis

1. Unidimensionality

Fit indices confirmed the unidimensionality of both GPH (comparative fit index (CFI) = 0.993, Tucker-Lewis index (TLI) = 0.978, standardized root mean squared residual (SRMR) = 0.039) and GMH (CFI = 0.999, TLI = 0.997, SRMR = 0.025), except for root mean square error of approximation (RMSEA) (GPH 0.114 and GMH 0.071). The bifactor models supported the hypotheses, resulting in explained common variance (ECV) values higher than the tentative benchmark for both subscales (GPH 0.72 and GMH 0.78). Omega Hierarchical was above the tentative benchmark only for GMH (0.73) but not for GPH (0.66) (Table 10).

2. Local independence

We found no local dependence between item pairs (Appendix Table 6). Eight item pairs had negative residual correlations, but all values were above –0.20.

3. Monotonicity

The Mokken scale analysis resulted in coefficients (*H*) higher than the cut-off value for both subscales ($H = 0.531$ and 0.638 for GPH and GMH, respectively) and items, ranging from $H_i = 0.480$ (Global08) to 0.717 (Global04) supporting monotonicity (Table 10).

4. Model fit

Given that unidimensionality, local independence and monotonicity were supported for both subscales, graded response models were fitted. Acceptable fit indices were found for both subscales (GPH: RMSEA = 0.008, SRMR = 0.045, TLI = 0.905, CFI = 0.968 and GMH: RMSEA = 0.012, SRMR = 0.031, TLI = 0.969, CFI = 0.990). A few items showed misfits to the graded response model, namely Global03, Global06, Global02, Global05 and Global10 ($p < 0.001$) (Table 10). Item difficulties (*b*) ranged from –3.7 (Global08) to 1.7 (Global03) for GPH and from –2.9 (Global10) to 1.7 (Global02) for GMH. Item discrimination (*a*) values ranged from 1.6 (Global08) to 2.3 (Global07) and from 1.7 (Global10) to 8.0 (Global04) for GPH and GMH, respectively. Item characteristic curves for the two subscales are displayed in Figure 5.

Table 10 Psychometric properties of PROMIS Global Health items and subscales (95)

	Uni-dimensionality		Monotonicity		Graded response model Item discrimination, difficulties, and model fit indices											
	Omega hierarchical	**ECV**	H_i **(SE)**	H **(SE)**	***a***	***b*1**	***b*2**	***b*3**	***b*4**	**Average *b***	**S-χ2**	***p*-value**	**RMSEA**	**SRMR**	**TLI**	**CFI**
Global Physical Health (GPH)	0.66	0.72	-	0.531 (0.016)	-	-	-	-	-	-	-	-	0.008	0.045	0.905	0.968
Global03	-	-	0.541 (0.017)	-	2.045	–2.053	–0.697	0.646	1.740	–0.091	88.703	<0.001	-	-	-	-
Global06	-	-	0.552 (0.019)	-	2.143	–2.879	–2.177	–1.071	–0.252	–1.595	52.425	<0.001	-	-	-	-
Global07[c]	-	-	0.550 (0.017)	-	2.322	–3.616	–1.747	–0.716	0.663	–1.354	31.494	0.086	-	-	-	-
Global08	-	-	0.480 (0.019)	-	1.577	–3.693	–2.257	–0.525	1.044	–1.358	17.520	0.353	-	-	-	-
Global Mental Health (GMH)	0.73	0.78	-	0.638 (0.012)	-	-	-	-	-	-	-	-	0.012	0.031	0.969	0.990
Global02	-	-	0.600 (0.016)	-	2.059	–2.179	–0.885	0.544	1.721	–0.200	74.081	<0.001	-	-	-	-
Global04	-	-	0.717 (0.011)	-	8.005	–1.601	–0.697	0.193	1.066	–0.260	32.060	0.002	-	-	-	-
Global05	-	-	0.657 (0.013)	-	2.898	–1.771	–0.799	0.299	1.242	–0.257	69.617	<0.001	-	-	-	-
Global10	-	-	0.571 (0.017)	-	1.721	–2.925	–1.628	–0.655	0.420	–1.197	116.608	<0.001	-	-	-	-

a = Item discrimination (slope), *b* = Item difficulty (threshold), c = reverse coded item, CFI = comparative fit index, ECV = explained common variance, H_i&H = Mokken scale analysis coefficients, RMSEA = root mean square error of approximation, SE = standard error, SRMR = standardized root mean squared residual, S-χ2 = item fit index, TLI = Tucker-Lewis index, Global02 = quality of life, Global03 = physical health, Global04 = mental health, Global05 = satisfaction with discretionary social activities, Global06 = physical function, Global07 = pain (reverse coded 5-level item), Global08 = fatigue, Global10 = emotional problems

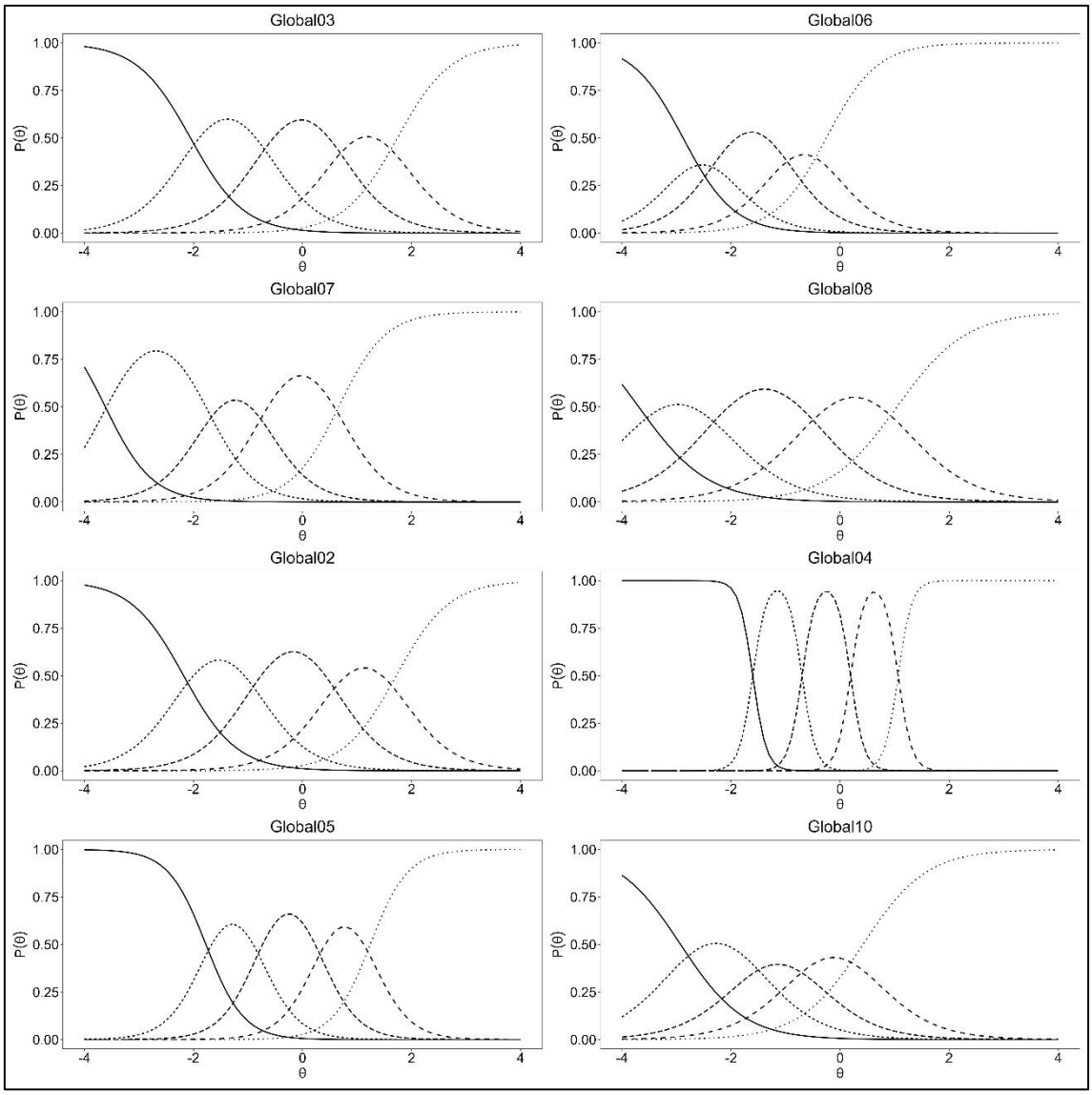

Figure 5 Item characteristic curves of items of the Global Physical Health and Global Mental Health subscales (95)

Global02 = quality of life, Global03 = physical health, Global04 = mental health, Global05 = satisfaction with discretionary social activities, Global06 = physical function, Global07 = pain (reverse coded 5-level item), Global08 = fatigue, Global10 = emotional problems

Global Physical Health items: Global03, Global06, Global07, Global08; Global Mental Health items: Global02, Global04, Global05, Global10; theta = latent trait; *p* = probability

3.3.2.3 Measurement invariance

After the first step (without anchors), one item (Global07) was flagged for DIF based on age groups, and two items (Global02 and Global10) were flagged for DIF by gender. After the second step (with anchors), DIF was no longer detected for age group and

gender, as the Pseudo R^2 change was < 0.02 for each analysis. No DIF was detected for education, region, employment, place of residence, marital status or income at all.

3.3.2.4 Convergent validity

GMH T-score showed a strong correlation with the mental health composite score of 36-Item Short Form (SF-36) ($r_s = 0.708$) and GPH T-score with the physical health composite score ($r_s = 0.829$) (Figure 6). Among the SF-36 subscales, the GPH T-score had the highest correlation with general health ($r_s = 0.740$) and bodily pain ($r_s = 0.738$), while the GMH T-score showed the strongest correlation with mental health ($r_s = 0.699$) and vitality ($r_s = 0.657$).

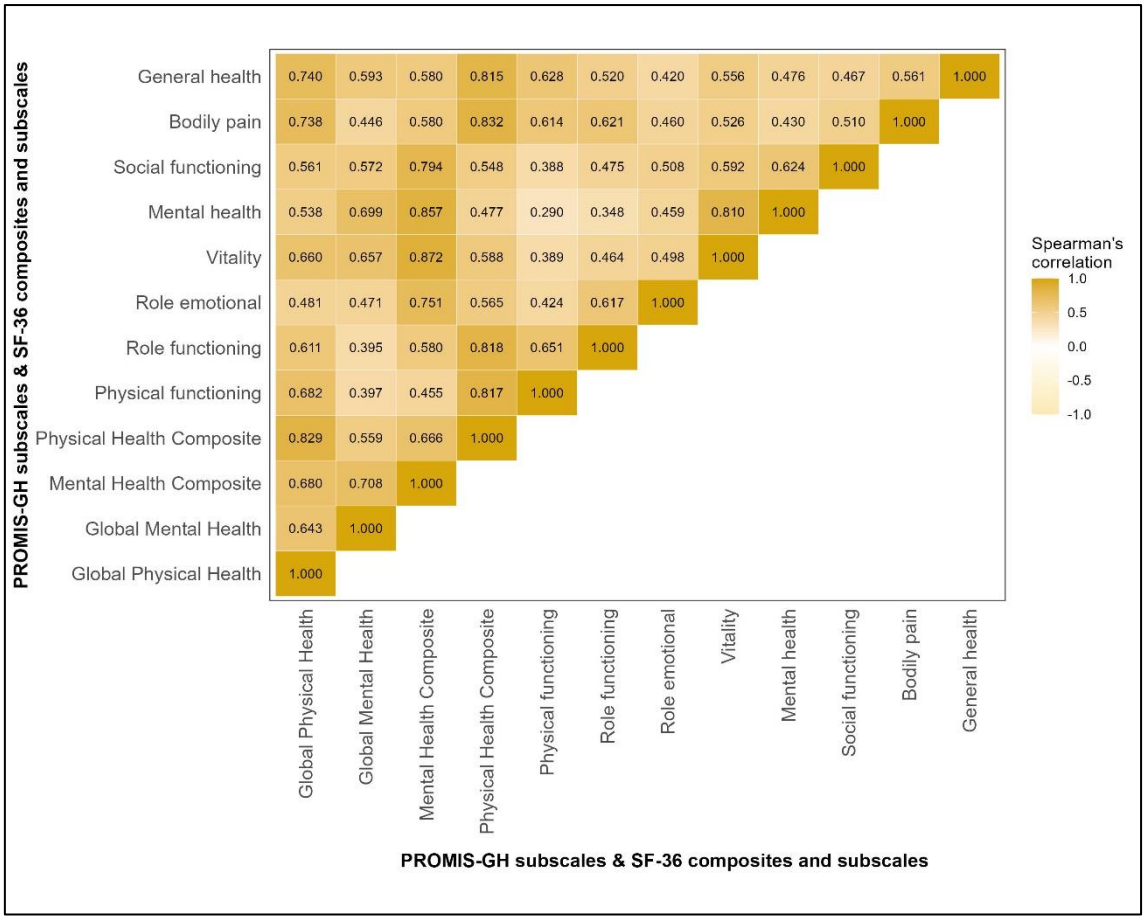

Figure 6 Convergent validity of PROMIS Global Health subscales with SF-36 composites and subscales (95)

$p < 0.001$ for all correlation coefficients (Spearman's).

PROMIS-GH = Patient-Reported Outcomes Measurement Information System Global Health, SF-36 = 36-Item Short Form

3.3.3 Reference values for PROMIS-GH in Hungary

The mean total T-scores for GPH and GMH were 49.0 and 47.7, respectively (Appendix Table 5). The mean GPH and GMH T-scores of females were lower (47.8 and 46.4) compared to males (50.5 and 49.3) ($p < 0.001$). We found the highest mean T-scores for GPH and GMH in the 18–24 age group (GPH: 52.3 and GMH: 49.9). Mean GPH and GMH T-scores showed a decreasing trend with age ($p < 0.05$). Those with higher levels of education, living in towns, being students, having higher income and without chronic disease had higher mean T-score for both GPH and GMH ($p < 0.001$). Concerning BMI, mean GPH T-scores were higher in respondents with normal weight compared to those underweight or overweight/obese ($p < 0.001$). Those who reported ‘excellent’ health on the first question of the SF-36 had the highest, while those who reported ‘poor’ had the lowest mean GPH and GMH T-scores ($p < 0.001$).

4. Discussion

4.1 EQ-5D-3L and 5L study

The objective of this study was to compare the psychometric performance of two adult versions (3L and 5L) of the EQ-5D questionnaire in a sample of patients diagnosed with HS. A considerable proportion of HS patients were able to report more problems on the 5L than on the 3L, particularly for mobility, self-care and usual activities dimensions. We found reduced ceiling effects, improved informativity and better known-groups validity for many relevant clinical characteristics for the 5L.

Both acute and chronic pain are common problems reported in HS, often necessitating pain medication to improve health outcomes in these patients (96). Among the five dimensions, the most problems occurred in pain/discomfort, whereby 75.4% (3L) to 77.4% (5L) reported to have 'any problems'. The pain/discomfort dimension of both the 3L and 5L showed a moderate or moderate-to-strong correlation with current and the worst pain VAS scores, suggesting that the pain/discomfort domain of the EQ-5D well captures pain. This corroborates with the literature in patients with skin burn, arthritis and Crohn's disease (97-99).

Ceiling effects were smaller on the 5L across all dimensions except for anxiety/depression, whereby ceiling effects increased by 5.0%. This result corresponds to the findings of two 3L-5L head-to-head comparison studies in Hungarian patients with psoriasis and atopic dermatitis (74, 83). Furthermore, the anxiety/depression (AD) dimension of the 3L showed a stronger correlation with most other outcome measures than that of the 5L. This may be attributable to the different wording used in the descriptor of AD in the Hungarian 3L (3L: 'anxiety/feeling down' vs. 5L: 'anxiety/depression'). This finding is in line with the results from a 3L-5L comparison study with psoriasis patients in Hungary, whereby the AD dimension of the 3L correlated stronger with both the EQ VAS and DLQI (83).

The 5L exhibited lower mean index values compared to the 3L. As the two Hungarian value sets were developed in a parallel valuation study from a common sample using the same preference elicitation technique (i.e. composite time trade-off) and modelling approach, the majority of the differences between index values are attributable to the differences in wording between the two descriptive systems (35). This difference between

3L and 5L index values tended to increase at lower values (Figure 2). For instance, we observed a substantial difference between the average 3L and 5L index values in patients with ‘severe’ and ‘very severe’ HS-PGA (0.79 vs. 0.73 and 0.62 vs. 0.53), whereas mean index values were nearly identical with the two questionnaire versions for the milder severity groups. This suggests that an estimated health gain from an improvement from a ‘very severe’ to ’mild’ HS-PGA health state is considerably larger with the 5L (0.32) than the 3L (0.22), possibly leading to more favourable cost-effectiveness estimates for HS treatments.

A particular added value of this study is that the Hungarian EQ-5D value sets were applied that had been developed in a parallel valuation study from the same respondents. Using these value sets to generate index values allowed to explore the ‘true’ difference between the 3L and 5L index values by ruling out the impact of different population samples, study years, valuation protocol and statistical modelling (35). Further strengths of the study include the multicentre design, the diverse patient population, and the large number of measures available to assess disease severity, pain and HRQoL in HS.

Limitations of this study include the lack of HS-specific HRQoL measures available in Hungarian language and the relatively small proportion of patients with lower EQ-5D index values. Additionally, a notable proportion of patients in the sample had severe HS. On the one hand, we believe that the distribution of the sample across severity groups well represents the treated HS population at large in Hungary, since this was a multicentre study carried out at three academic dermatology clinics. HS patients are almost exclusively treated at these institutions, as systemic and surgical treatments are only available here. On the other hand, the precise epidemiology of HS in Hungary is currently unknown. Compared to the baseline characteristics of HS patients in large international registries (100-103), the proportion of patients with severe HS is higher in our sample, which might somewhat limit the external generalizability of the results. A further constraint concerns the positioning of the 3L and 5L within the wider questionnaire causing an ordering effect. The last limitation is that we could not compare the responsiveness and test-retest reliability of the 3L and 5L due to the cross-sectional nature of the study.

4.2 EQ-PSO study

Qualitative methodologies were used to investigate the content validity of the EQ-5D-5L and EQ-PSO among Hungarian psoriasis patients, focusing on potential conceptual overlap across dimensions. The results showed that while the EQ-5D-5L is considered relevant in psoriasis, its descriptive system may still be missing some important aspects of HRQoL for this population. Examples include general physical or mental health (e.g., stress, sex life) and psoriasis-specific health (e.g., itching, social relationships, dietary awareness). These findings extend the existing literature on important aspects of health and HRQoL that the EQ-5D does not adequately capture in specific populations (104, 105). Furthermore, some of the missing concepts identified by psoriasis patients are covered by already existing EQ-5D bolt-on dimensions, such as stress, social relationships or sexual activity (106-108).

The patient sample confirmed nearly unanimously the relevance of the skin irritation and self-confidence bolt-on dimensions to their experience with psoriasis. Most patients with psoriasis described these as the two most important aspects of HRQoL. In most cases, patients interpreted the EQ-5D-5L or EQ-PSO dimensions as generic and unrelated to any specific condition. However, there were a few instances where certain words or phrases were interpreted as related to psoriasis. The most prominent example was seen in the self-care dimension, whereby one-fifth of patients interpreted ‘dressing myself’ not as an ability to dress but rather as psoriasis influencing the clothes they can wear. Similarly, a small number of patients used the EQ VAS as a scale that measures the proportion of body surface area affected by psoriasis. We believe that the mode of administration and the study context may be, at least in part, responsible for this effect. Patients were aware of participating in a psoriasis-related interview, which might have led them to overly focus on their skin problems when completing the questionnaires.

We observed a conceptual overlap between the pain/discomfort and skin irritation dimensions, and some patients reported itching on both dimensions. Yet other patients thought differently and reported itching only in the skin irritation dimension. These disagreements may be attributable to the multifaceted nature of psoriasis. Due to the large variability of skin and joint symptoms, including different clinical manifestations, localisations and symptoms, no two patients experience psoriasis the same way. For

example, the focus group discussion highlighted that some patients experience itch, while others only report skin scaling, and for others, joint symptoms are more bothersome than those of the skin. Based on our results, the skin irritation dimension seems to be a useful bolt-on in this population that might cause some (minor) overlap with pain/discomfort. Conversely, the focus group members agreed that the self-confidence bolt-on dimension is independent of the other dimensions of the EQ-5D-5L and represents a standalone value.

While patients pointed out various limitations of the EQ-PSO, one should also consider that adding two condition-specific items to the EQ-5D-5L cannot be expected to reflect all the important facets of psoriasis. Considerations related to scale development and valuation implications, such as keeping the number, length, and wording of the new dimensions reasonable, should also be considered. It is possible, therefore, that what patients consider missing or suggest improving may confront the researchers' aims, and a judgement has to be made as to whether those limitations are sufficient to warrant changing or adding to the measure. For example, during the concept elicitation phase of our study, the problems caused by skin scaling were raised by more patients than itching. In agreement with this, several patients proposed an extension of this dimension by adding other frequent psoriasis skin symptoms beyond itching. However, by doing so, one may risk of creating a double-barrelled question in the skin irritation dimension. Moreover, when valuing health states, general population members may easily imagine itching, while imagining other skin symptoms, such as skin scaling that they most likely have never experienced, could be challenging.

Considering that the EQ-PSO has a value set developed in the United Kingdom (41), our findings are of direct relevance to cost-utility analyses and subsequent reimbursement decisions by providing supporting evidence on the usefulness of the two bolt-on dimensions in psoriasis. Health technology assessment bodies, such as the National Institute for Health and Care Excellence (109) in the United Kingdom and the Canadian Agency for Drugs & Technologies in Health, have already accepted the EQ-PSO in recent submissions for psoriasis treatments' appraisals as a sensitivity analysis of the EQ-5D-5L (110). Moreover, a recent Hungarian study established the content validity of the two bolt-on dimensions in patients with atopic dermatitis, which suggests the possibility of extending the use of the two bolt-ons to other chronic skin conditions (111).

Some limitations of the study need to be mentioned. Convenience sampling was used, and the overwhelming majority of patients were related to a patient association. Self-selection bias may also be present as patients voluntarily applied to the study. It is possible, for example, that willingness to participate in such an interview or being a member of a patient association is not independent of one's self-reported health or self-confidence. Data were collected through two different modes of administration (face-to-face and video-interviewing), which could be a source of potential influence on responses, but the majority used one mode, and there were no differences in what was reported across the modes. An additional limitation is that as a substantially large pool of experimental bolt-on dimensions is available for the EQ-5D, it could have been possible to include further bolt-ons in our study, especially those that one may anticipate being relevant for psoriasis patients (e.g., social relationships, sleep). Lastly, there may be minor differences in semantics between the Hungarian and other language versions of the EQ-5D-5L and EQ-PSO, which may prevent the generalizability of these findings to other countries.

4.3 PROMIS-GH study

This study provided a psychometric assessment of the Hungarian version of PROMIS-GH and developed population reference values for its physical and mental health subscales in Hungary. We used both classical test theory and IRT methods to establish the psychometric properties of the measure. PROMIS-GH subscales showed no ceiling and floor effects. All assumptions of IRT (unidimensionality, local independence and monotonicity) were met. Although the Omega Hierarchical value was below the tentative benchmark for GPH, it is important to emphasize that PROMIS-GH is inherently a multidimensional measure, and therefore, individual subscale values within the range of 0.6 and 0.8 seem appropriate both for Omega Hierarchical and ECV (112, 113). The goodness of fit to the graded response model was acceptable, with a few items misfitting. No evidence of measurement invariance was observed across various sociodemographic characteristics. Strong correlations were found between corresponding PROMIS-GH subscales and SF-36 physical and mental health composite scores. The Hungarian general population's mean GPH and GMH T-scores were 49.0 and 47.7, respectively.

It is worthwhile to compare our findings about the psychometric performance of PROMIS-GH to those of earlier psychometric studies among members of the general

population in the Netherlands and the US (20, 114). Unidimensionality was supported with negligible deviations in each study. Neither the Hungarian nor the Dutch general population samples demonstrated any evidence of local dependence. The coefficients of the Mokken scale analysis showed that monotonicity was supported in the Hungarian and Dutch samples, and an interesting similarity occurred that in both studies the Global06 item had the smallest distance between the item difficulty (*b*) thresholds (Hungarian: –2.879 to –0.252; Dutch: –2.668 to –0.055). The range of item difficulty (*b*) values was very similar in all three general population studies with minor differences at both ends (US: –3.9 to 1.5, Hungarian: –3.7 to 1.7, Dutch: –3.7 to 2.2) (20, 114). Ranges of item discrimination parameters (*a*) were similar for both subscales, with slight differences between the US and Dutch studies (20, 114). While the item discrimination parameters of the Hungarian GPH were in the same range (from 1.6 to 2.3) as the previous two, the Hungarian GMH was somewhat biased due to Global04 (from 1.7 to 8.0), as it usually ranges between 0.5 and 2.5 (115). The validity, reliability, and responsiveness of PROMIS-GH have been confirmed in several countries and patient groups, including dermatological populations, such as atopic dermatitis, vulvar inflammatory dermatoses, psoriatic arthritis and patients with a history of acute or chronic itch (116-119).

Regarding the general population reference values, the Hungarian overall mean GPH and GMH T-scores (49.0 and 47.7) were slightly lower than those of the US reference population values (GPH: 50.0, GMH: 50.0) and higher than the Dutch values (GPH: 45.2, GMH: 44.7), suggesting that the Hungarian general population is in a better health status than the Dutch (Appendix Table 7). In contrast, the standardised Dutch SF-36 physical (49.7) and mental health composite scores (52.1) outperformed the Hungarian standardised scores (48.3 and 48.2), implying that the Dutch general population is in a better health status (120). However, the Dutch population norm data were collected using the 12-Item Short Form (SF-12) and in 1996, which may limit the comparison (121). A similar pattern was observed for GPH and GMH in the Hungarian general population as in the US and Dutch samples, with a decreasing mean T-score with age and males reporting better health status than females (93, 122). However, it should be noted that the US sample (data collected in 2006–2007) and the Dutch sample (data collected in 2016) were obtained considerably earlier than this study. Additionally, the US calibration sample may not represent the European populations. Ultimately, the following

characteristics were associated with better physical and mental health in the Hungarian sample: younger age, male gender, higher level of education, living in towns, student status, higher income level, having no chronic diseases and reporting better self-perceived health on the first question of the SF-36. A notable finding of this study is that the Hungarian general population reported better overall health status than the Dutch general population. Life expectancy in the Netherlands is almost one year higher (81.5) than the weighted European Union (EU) average (80.6), while life expectancy in Hungary is almost five years (75.7) behind the weighted EU average (123). Regarding government funding, compulsory and voluntary health insurance and out-of-pocket payments, the Netherlands has one of the highest per capita spending on healthcare in the EU. At the same time, Hungary continues to fall behind the EU average in this regard. The most striking contrast might be that in 2019, 75% of the Dutch general public reported that they were in good health, and this figure did not reach 60% in Hungary in the same year (123). However, the comparability of PROMIS-GH scores between these two countries is restricted by the fact that the Dutch sample was not representative of some important sociodemographic and health-related characteristics of the general population, such as employment and marital status, income and the prevalence of chronic diseases (93).

In Hungary, a number of population norm studies have been conducted using various generic HRQoL measures, including the SF-36, EQ-5D-3L and 15D (124-126). The SF-36 and EQ-5D-3L population norm studies were developed decades ago, limiting their comparability with the PROMIS-GH results. This limitation arises from the structural changes in factors related to the economy, society, culture and the availability of health technologies (124, 125). Additionally, major events, such as an economic crisis and the Coronavirus disease 2019 (COVID-19) pandemic over these two decades, may have also contributed to the observed changes. Consequently, comparing the PROMIS-GH results with more recently published studies is of greater relevance. The results of the 15D study are more comparable with those of PROMIS-GH results due to the data collection dates (15D: August 2021; PROMIS-GH: November 2020). The results of the 15D study are consistent with the PROMIS-GH results in that respondents with higher educational attainment, student status, higher income, and the absence of chronic diseases reported better health status (126).

This study has a few limitations. Our data were collected during the pandemic, which might have influenced the general population's health status. However, a recent study has shown that the COVID-19 pandemic had a negligible impact on the health status of US patients measured by PROMIS-GH (127). Furthermore, self-reported health status on the first question of SF-36 in our study was very similar to what had been reported in a pre-COVID-19 online general population survey in Hungary in 2019 (128). Selection bias might have occurred as online panel data collections may be subject to possible self-selection and underrepresentation of certain groups (e.g., those without internet access) (129). Another limitation is the cross-sectional nature of this study which prevented us from assessing test–retest reliability and responsiveness of PROMIS-GH.

5. Conclusions

1. EQ-5D-3L and 5L study

In conclusion, our work indicates that the 5L outperforms the 3L version of the EQ-5D in most psychometric properties in HS patients. We recommend using the 5L in HS patients across various settings, including clinical care, research and economic evaluations. Future research is recommended to focus on other psychometric properties, such as responsiveness, test-retest reliability and comparing the acceptability of the two descriptive systems in terms of ease of understanding and better reflection of health status in this patient population.

2. EQ-PSO study

In summary, the skin irritation and self-confidence bolt-on dimensions are particularly pertinent and contribute to improving the content validity of the EQ-5D-5L in patients with psoriasis. Although there is a slight conceptual overlap between pain/discomfort and skin irritation dimensions, this does not seem to diminish the added value of the bolt-on item. The qualitative approach taken in this study expands the existing methodological framework for developing and testing the validity of bolt-ons for the EQ-5D.

3. PROMIS-GH study

This study provided a comprehensive psychometric evaluation of the Hungarian PROMIS-GH in a large general population sample and established general population reference values for Hungary. Data were collected during the COVID-19 pandemic; therefore, future research is recommended to replicate this general population study and further test psychometric properties of the Hungarian PROMIS-GH in paper-and-pencil surveys, longitudinal studies and in various patient populations.

6. Summary

This thesis investigated the psychometric properties of generic health-related quality of life (HRQoL) measures (EQ-5D-3L, EQ-5D-5L and PROMIS-GH) and their modifications (EQ-PSO) in chronic dermatological patients and the general population. The thesis is based on three separate studies conducted between 2017 and 2021. The first study compared the psychometric performance of the EQ-5D-3L (3L) and EQ-5D-5L (5L) in 200 hidradenitis suppurativa patients. Overall, the 5L outperformed the 3L in feasibility, ceiling effects, informativity, and convergent and known-groups validity for several clinically relevant subgroups of patients. In the second study, we conducted 16 qualitative one-on-one interviews and a focus group with psoriasis patients to establish the content validity of the Hungarian versions of the EQ-5D-5L and its modified version (EQ-PSO). The EQ-PSO consists of the 5L descriptive system and two psoriasis-specific bolt-ons: skin irritation and self-confidence. Our results showed that 16 and 15 patients considered skin irritation and self-confidence as relevant areas to describe psoriasis problems, respectively. Patients reported fewer missing themes for the EQ-PSO, of which social relationships were the most frequently mentioned. Overall, all patients rated the EQ-PSO better than the 5L for describing their problems with HRQoL. In the third study, we tested the psychometric properties of the Hungarian version of PROMIS-GH using classical test theory and item response theory (IRT) methods on a sample of 1700 general population members. All IRT assumptions (unidimensionality, local independence, monotonicity) were met. We observed acceptable model fit for both subscales, no measurement invariance, no or negligible ceiling and floor effects, and strong correlations between corresponding PROMIS-GH and SF-36 subscales. As part of this study, we developed the Hungarian general population reference values for the PROMIS-GH. Overall, the following attributes were associated with better physical and mental health: younger age, male gender, higher level of education, living in towns, student status, higher income level, and the absence of chronic diseases. In conclusion, our results provide new evidence on the psychometric performance of the Hungarian versions of commonly used generic HRQoL measures in chronic skin diseases and the general population. Our findings are intended to support decision-makers, clinicians, researchers, and health economic analysts in evaluating treatment benefits in terms of HRQoL improvement to inform both clinical and financial decisions.

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8. Bibliography of the candidate's publications

Σ IF: 29.806

8.1 Publications related to this thesis Σ IF: 11.340

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- **Bató A,** Brodszky V, Gergely LH, Gáspár K, Wikonkál N, Kinyó Á, Szabó Á, Beretzky Z, Szegedi A, Remenyik É, Kiss N, Sárdy M, Rencz F. The measurement performance of the EQ-5D-5L versus EQ-5D-3L in patients with hidradenitis suppurativa. Qual Life Res. 2021;30(5):1477-90. **IF: 3.440 (Q1)**
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- **Bató A**, Brodszky V, Gergely LH, Gáspár K, Wikonkál N, Kinyó Á, Beretzky Z, Szegedi A, Remenyik É, Kiss N, Sárdy M, Bánvölgyi A, Rencz F. PSY30 The Measurement Performance of the EQ-5D-5L Versus EQ-5D-3L in Patients with Hidradenitis Suppurativa. Value Health. 2020;23: Suppl. 2 pp. S748-S748. (International Society For Pharmacoeconomics and Outcomes Research Annual European Congress, 19 November - 31 December 2020, Virtual)
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10. Appendices

Appendix Table 1 – Missing concepts from the EQ-5D-5L and EQ-PSO (85)

Concepts	EQ-5D-5L		EQ-PSO		Example quote
	n	%	n	%	
GENERAL HEALTH-RELATED					
Sex life	3	19	1	6	014: Certainly, I would include how this affects, for instance, sex life
Stress and conflict management	1	6	1	6	006: In my opinion, [the questionnaire] did not ask about stress and conflict management
PSORIASIS-RELATED					
Physical symptoms					
Itching	1	6	0	0	010: These symptoms at the beginning, e.g., itching, there was horribly itchy and painful…. maybe this is missing, too
Psoriatic arthritis	0	0	1	6	P001: I might still miss that it [psoriasis] extends to the joints and it would be possible to ask if it has already reached that stage at all or not
Skin oozing	0	0	1	6	013: Well, yes, this oozing, it is not listed here
Assessment of psoriasis by others					
Social relationships	8	50	5	31	004: [Psoriasis] makes dating harder anyway, let's say, I go to a party, I tie my hair up and when someone notices it, then obviously their first thought is not 'wow how nice is that', so yes, people cannot really deal with this for the first time
Clothing	2	13	0	0	010: In summer I put on my thin knee-length pants made of canvas or a knee-length skirt no matter that I am full of patches and I do not care, but others may be bothered even by this
Hairstyle	2	13	0	0	001: It is a continuously recurring thing for me to try fixing my hair that it [my psoriasis] should not be visible
Searching for a cure					
Finding the right treatment	2	13	5	31	004: Perhaps I might add which lotions, solutions or medicines did you try up till now and which of these did you find effective?
What I do to feel better	1	6	2	13	002: What steps I have done to improve the already lost of function or to maintain health that is the most important part in quality of life
Doctors' attitude	0	0	1	6	010: How doctors handle this thing [psoriasis], let's say, how much attention they pay to this
Life changes					
Changing workplace/profession	0	0	1	6	008: Perhaps one might have to change workplace/profession
Giving up leisure activities	2	13	1	6	010: [What is missing] if I dare to go to the swimming pool or how do I look like there?

Concepts	EQ-5D-5L		EQ-PSO		Example quote
	n	%	n	%	
Dietary awareness	3	19	3	19	001: I would ask who and to what extent is consciousness about nutrition
NON-HEALTH-RELATED					
Education and being connected to the arts	1	6	0	0	005: The education level or connectedness to the arts, to what extent a person's way of life is influenced by these, for example, theatre, a book, or cinema, or it may even be a sport event
Financial situation	1	6	0	0	009: I would say 'background and financial situation' as a headline… marital status or housing conditions also belong here
Family situation	1	6	0	0	
Housing conditions	1	6	0	0	
Workplace	1	6	0	0	009: What has a great impact on quality of life is what one works
Travelling	1	6	0	0	001: …in addition to the things which to be done compulsory, it also includes things that improve quality of life very much, for example, leisure... not what I have to do, or I am anxious about it or not because I do it. My quality of life is good because I go on a summer vacation once a year or go skiing so these really-really improve my quality of life

Appendix Table 2 – Suggested changes in EQ-5D-5L and two bolt-on dimensions (85)

Themes	n	%	Example quote
Mobility			
'Walking about' is too narrow, replace it by 'Moving (and sports)'	4	25	001: I would not limit mobility only to walking about; a healthy physique involves not only being able to walk about itself but other movements, such as if I can bend down, if it does not cramp or does not stretch anywhere
Need to define mobility in terms of both quantity and quality	1	6	006: The amount of time [you spend moving] or what kind of physical activity causes a limitation to you
Self-care			
Split it into 2 questions	1	6	012: Now what do I have a mild problem with, washing myself or getting dressed?... It should have been taken apart, at least
Replace 'washing yourself' by skincare	1	6	P002: For patients with psoriasis, another definition would be needed; suddenly 'skin care' comes to my mind which, of course, is equivalent to 'washing myself' but still is somehow different
Usual activities			
Add 'flaking skin'	1	6	013: When someone has many plaques, almost covered from head to toe, when they move, it [skin] falls down to the floor, you know, this silvery thing and after it should be vacuumed or swept
Pain/discomfort			
Split it into 2 questions	1	6	006: I don't know how I should answer that. I don't have any pain, but in the meantime, there is discomfort, so I don't feel this is an appropriate response... I would separate it, yes, I would
Add 'frustration'	1	6	004: I would still add frustration here next to pain/discomfort
Anxiety/depression			
Split it into 2 questions	3	19	P002: Well, I would absolutely exclude depression, so I would not even put them [anxiety and depression] in the same [dimension]
Replace 'anxiety' with stress	1	6	P002: When I think of anxiety it reminds me something which makes me constantly anxious, some problem, something which is there all the time, but stress comes as if I may be stressed about something today but maybe I will be stressed again only on Saturday or Sunday... Well, I would not really call stress as anxiety... I would rather put 'stress' or 'everyday problems' here [instead of anxiety]

'Depression' is a too strong word, replace it with 'mood disorder'	2	13	002: Respondent: The word depression may be a bit too strong… Because of the stigma, so one knows that this is the problem, but it is still quite bad to face this… *Interviewer: And what would you use instead?* Respondent: Let's say, mood disorder
Add 'stress'	1	6	006: I think stress would be more easy to understand for people, I might write stress next to depression
Skin irritation			
'Skin irritation' is too narrow	1	6	006: I see this [itching] as small as walking in mobility, the other topics are much bigger and more comprehensive... it is like, let's say, a little toe hurts or the middle and I take that out of pain, so I feel that this itch is just one thing in this whole problem...
Add 'skin scaling' and 'skin cracking'	3	19	004: I would add skin scaling and cracking to the irritation because, for me, when it is worse then it cracks
Add 'flaking skin'	1	6	P001: Psoriasis comes together with an excessive skin production, and it is extremely horrible when one sweeps 200 g of skin from everywhere, everywhere... by the morning the skin gets dry and scaly, it is like snowing. Well, this may be added to skin irritation because it is a form [of skin irritation] too
Add ‘skin symptoms of bad smell’	1	6	002: I have a strong sense of smell… and in connection to skin irritation that it is not only irritation, for example, itch, but I specifically feel like my skin is rotting
Self-confidence			
Add 'self-esteem', 'self-identity', 'self-love'	1	6	006: Well, before self-confidence I would add self-esteem because this is a broad concept, or I would still add self-identity and self-love

Appendix Table 3 – Comments on response levels (85)

Themes	Dimension	n	%	Example quote
REFRAMED THE RESPONSE LEVELS				
Reframed as a frequency scale	MO	3	19	010: Mostly I marked 'slight problems' because this replaces rare for me. 014: I think 'severe problems' means daily, nearly permanent.
	PD	3	19	010: Because it is very rare and that is rather mild.
	SI	2	13	006: I know the phases, when it is moderate and when severe. I take it as 'severe' when it itches more often.
Reframed as 'level of bother'	MO, SC, UA	1	6	011: I felt from the questionnaire that the first part is about [activities] that you can or cannot do, you can or cannot get dressed ... but obviously we [psoriasis patients] can do it, so am I, but if it bothers me in any activity there is a lot more here, it bothers me very-very much in a lot, lot of activities.
REPORTED PROBLEMS WITH LEVEL MODIFIERS				
Too difficult to differentiate between levels 1 and 2	MO	2	13	P002: Here I can mark more than one, because it does not limit so much to say 'slight'.
Too difficult to differentiate between levels 4 and 5	PD	1	6	001: Concerning such subjective topics as discomfort… it is hard for me to make a difference [between levels 4 and 5] ... for me both answers are equal so they would have the same weight.
	AD	1	6	001: I am very anxious, I am extremely anxious, so where are the differences between the levels? I am severely depressed or extremely depressed, it would be hard for me to make any difference.
	SI	2	13	011: For me, between extreme and severe, it is really interesting, but severe comes last [instead of extreme].
Mild depression is a clinical diagnosis	AD	1	6	002: According to my clinical condition, I have a mild depressive episode and mixed anxiety-depressive disorder.
'Moderate' or 'medium' [Hungarian-specific]	PD, AD	1	6	001: It [the questionnaire] uses similar words everywhere and here earlier I wondered a little for a moment why it did not put it that way that 'I am medium-anxious' or 'I am medium-depressed' there is no such thing as being 'moderately depressed'?
SUGGESTED A CHANGE				
Increase the number of response levels	MO	1	6	010: It suddenly came to my mind that sometimes a sort of 10-point scale is used in certain situations, perhaps that might be better.
More information next to the response levels	PD	1	6	004: I would explain it a bit in parentheses what slight, moderate, and severe mean.

AD = anxiety/depression, CO = self-confidence, MO = mobility, PD = pain/discomfort, SC = self-care, SI = skin irritation, UA = usual activities.

Appendix Table 4 – Content of the EQ VAS (85)

Theme	n	%	Example quote
THE BEST HEALTH YOU CAN IMAGINE			
In general			
Lack of pain	4	25	004: Yes, it would be 100 if I did not have any pain
Healthy lifestyle (e.g., sport, diet)	3	19	P002: One does sport regularly, eats properly and is happy.
Youth	3	19	005: Well, the best imaginable health, you know, has many components, one of them is having a very good health, for that you have to be a bit younger
Lack of illness (in general)	2	13	007: I would not have any problem not even age-related diseases
Free of symptoms/free of health complaints	2	13	002: I am completely free of symptoms, and I have already forgotten that I had an experience like that with a disease
Unachievable	2	13	012: There is no man on earth who is fit as a fiddle who was born lucky and 100% virus-free, disease-free, there is nothing wrong with him, has never been sick… 80-85 let's agree, I think that's the normal health of an average person
Happiness	1	6	P002: The best, who is obviously young, does sport regularly, eats properly and is happy.
Health or well-being of my family	1	6	009: My health today is 100… Since everything was fine, my child is in a good place, I talked with the other two [children]
No need for using healthcare	1	6	013: One does not need to visit the doctor or hospital
No discomfort, harmony	1	6	005: If someone feels good and is balanced that is a very good thing
Lack of anxiety	1	6	006: I have nothing to be anxious about…
Physical health, vitality	1	6	001: When one feels so well in one's skin, and feels vital, that the word 'health' does not even go through their mind.
Physical and mental health	1	6	014: As long as someone is young and does not even know how good it is because they do not feel what it is like to always have pain somewhere. I don't know if mental health belongs here because that is the other side
In relation to psoriasis			
I have no skin symptoms	3	19	004: It would be 100 if, on the one hand, I did not have any pain, I were free of symptoms, so my scalp was not flaking regardless of having it [psoriasis], it did itch in every hour and were not painful or cracking
I do not have psoriasis	2	13	003: Not to have psoriasis, so to get rid of this problem
THE WORST HEALTH YOU CAN IMAGINE			
In general			
Unable to take care oneself	6	38	013: Complete dependency on others, when one is unconscious, they have to wear a diaper, have to be fed and washed
Paralyzed/disabled	3	19	004: Well, when I am not even able to stand up…
Extreme pain	3	19	001: When someone thinks 'shoot me in the head', because even existence means a problem, there is that level of pain…
Severe/deadly disease	3	19	P001: If someone has a deadly disease e.g., cancer or after having a stroke or heart attack
Dying	2	13	003: Shall I say now if someone is dying?
Poor mental health	2	13	009: It is an anxiety because of something ... I would rather say it for a mental state, there I could mark a 0.
Depression, panic disorder	1	6	010: If I had a bad depression because of this, that would be the worst
Grief	1	6	009: on the day of my father's funeral... that morning, yes, if I had to answer to something like this then for sure [would have marked 0]
Dead	1	6	007: When someone is already in the coffin.
Worse than dead	1	6	P001: For example, to be physically paralyzed, not able to walk or anything, this is worse than dead, in my opinion.
In relation to psoriasis			
My whole body would be covered with psoriasis	2	13	011: If one's whole body was covered [with psoriasis]

Appendix Table 5 – Characteristics of the study population and PROMIS Global Health reference values in Hungary (95)

Variables	General population (130)	Un-weighted sample	Weighted sample	Global Physical Health (GPH) T-score					Global Mental Health (GMH) T-score				
	%	n (%)	n (%)	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]
Total	–	1700	1700	49.04	48.60-49.49	47.7	42.3-54.1	–	47.7	47.27-48.22	48.3	41.1-53.3	–
Gender													
Female	53.1	957 (56.3)	902 (53.1)	47.75	47.14-48.35	47.7	42.3-54.1	<0.001	46.41	45.79-47.02	45.8	41.1-53.3	<0.001
Male	46.9	743 (43.7)	798 (46.9)	50.50	49.85-51.16	50.8	44.9-57.7		49.26	48.51-50.00	48.3	43.5-56.0	
Age groups (years)													
18-24	10.0	148 (8.7)	169 (9.9)	52.28	50.63-53.92	50.8	47.7-57.7	<0.001	49.87	47.84-51.90	48.3	43.5-56.0	0.011
25-34	15.2	293 (17.2)	259 (15.2)	50.93	49.91-51.94	50.8	44.9-57.7		49.26	47.98-50.54	48.3	43.5-56.0	
35-44	19.5	309 (18.2)	331 (19.5)	49.96	48.99-50.92	50.8	44.9-54.1		48.20	47.07-49.32	48.3	41.1-56.0	
45-54	16.0	304 (17.9)	272 (16.0)	48.71	47.69-49.73	50.8	42.3-54.1		47.23	46.18-48.28	48.3	41.1-53.3	
55-64	16.8	296 (17.4)	286 (16.8)	47.68	46.59-48.77	47.7	42.3-54.1		46.34	45.33-47.34	45.8	41.1-53.3	
65+	22.5	350 (20.6)	383 (22.5)	46.80	45.79-47.81	47.7	39.8-54.1		46.80	45.86-47.73	45.8	41.1-53.3	
Highest level of education													
Primary school or less	23.8	468 (27.5)	464 (27.3)	47.05	46.00-48.09	47.7	39.8-54.1	<0.001	46.37	45.33-47.41	45.8	38.8-53.3	<0.001
Secondary school	55.0	682 (40.1)	692 (40.7)	49.09	48.43-49.76	47.7	44.9-54.1		47.34	46.59-48.09	45.8	41.1-53.3	
College/university degree	21.2	550 (32.4)	544 (32.0)	50.68	49.97-51.38	50.8	44.9-57.7		49.42	48.67-50.18	48.3	43.5-56.0	
Place of residence													
Capital	17.9	380 (22.4)	384 (22.6)	49.53	48.65-50.41	50.8	44.9-54.1	<0.001	47.99	47.08-48.90	48.3	43.5-53.3	<0.001
Other town	52.6	820 (48.2)	814 (47.9)	49.89	49.23-50.56	50.8	44.9-57.7		48.54	47.83-49.26	48.3	43.5-56.0	
Village	29.5	500 (29.4)	503 (29.6)	47.29	46.44-48.13	47.7	39.8-54.1		46.26	45.38-47.14	45.8	38.8-53.3	
Geographical region													
Central Hungary	30.4	572 (33.6)	581 (34.2)	49.38	48.65-50.11	50.8	42.3-54.1	0.203	47.87	47.09-48.64	48.3	43.5-43.3	0.175

Variables	General population (130)	Un-weighted sample	Weighted sample	Global Physical Health (GPH) T-score					Global Mental Health (GMH) T-score				
	%	n (%)	n (%)	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]
Western Hungary	30.2	493 (29.0)	480 (28.2)	48.61	47.83-49.40	47.7	42.3-54.1		47.29	46.43-48.15	45.8	41.1-53.3	
Eastern Hungary	39.5	635 (37.4)	640 (37.6)	49.20	48.33-50.06	50.8	42.3-54.1		48.20	47.33-49.07	48.3	43.5-56.0	
Employment status													
Employed	53.1	865 (50.9)	858 (50.5)	50.28	49.71-50.85	50.8	44.9-54.1	<0.001	48.77	48.12-49.41	48.3	43.5-56.0	<0.001
Retired	26.1	399 (23.5)	427 (25.1)	46.87	45.91-47.83	47.7	39.8-54.1		46.89	46.03-47.76	45.8	41.1-53.3	
Disability pensioner	3.1	67 (3.9)	64 (3.8)	39.79	37.44-42.14	39.8	32.4-47.7		41.04	38.49-43.59	38.8	33.8-48.3	
Student	3.1	74 (4.4)	87 (5.1)	53.59	51.60-55.58	54.1	47.7-57.7		50.17	47.19-53.16	48.3	43.5-56.0	
Unemployed	4.7	129 (7.6)	125 (7.4)	49.88	47.81-51.94	50.8	42.3-57.7		46.43	44.25-48.61	45.8	38.8-56.0	
Homemaker/housewife	1.0	99 (5.8)	80 (4.7)	48.86	47.38-50.33	47.7	44.9-54.1		47.18	45.19-49.17	48.3	41.1-53.3	
Other	0.0	67 (3.9)	60 (3.5)	48.62	46.30-50.95	47.7	42.3-57.7		46.26	43.65-48.88	45.8	41.1-53.3	
Household net monthly income per person (HUF)[b]													
First quintile (0 - 66,779)	n/a	224 (13.2)	217 (12.8)	46.22	44.72-47.72	44.9	39.8-54.1	<0.001	43.60	42.06-45.14	43.5	36.3-50.8	<0.001
Second quintile (66,780 – 99,511)		252 (14.8)	255 (15.0)	46.66	45.37-47.94	47.7	39.8-54.1		45.92	44.55-47.29	45.8	38.8-53.3	
Third quintile (99,512–126,924)		229 (13.5)	234 (13.8)	49.59	48.26-50.93	50.8	42.3-57.7		48.44	47.09-49.78	48.3	43.5-56.0	
Fourth quintile (126,925-164,049)		207 (12.2)	207 (12.2)	48.89	47.72-50.06	47.7	42.3-54.1		48.11	46.84-49.39	48.3	43.5-53.3	
Fifth quintile (164,050-)		423 (24.9)	425 (25.0)	50.47	49.67-51.27	50.8	44.9-54.1		49.55	48.73-50.37	48.3	43.5-56.0	
Do not know		69 (4.1)	74 (4.4)	51.56	49.25-53.87	50.8	44.9-57.7		50.05	47.40-52.69	48.3	43.5-56.0	
Do not want to answer		296 (17.4)	288 (16.9)	50.19	49.21-51.17	50.8	44.9-54.1		48.39	47.33-49.45	48.3	43.5-53.3	
Marital status													
Married	45.6	718 (42.2)	691 (40.6)	48.74	48.05-49.43	50.8	42.3-54.1	0.038	48.40	47.67-49.13	48.3	43.5-53.3	0.221
Domestic partnership	13.4	360 (21.2)	348 (20.5)	49.02	48.12-49.92	47.7	42.3-54.1		47.75	46.77-48.73	48.3	41.1-53.3	
Single	18.5	336 (19.8)	350 (20.6)	50.58	49.51-51.64	50.8	44.9-57.7		47.12	45.88-48.36	45.8	41.1-53.3	

Variables	General population (130)	Un-weighted sample	Weighted sample	Global Physical Health (GPH) T-score					Global Mental Health (GMH) T-score				
	%	n (%)	n (%)	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]	Mean	Confidence interval (95%)	Median	IQR	*p*-value[a]
Widowed	11.4	98 (5.8)	115 (6.8)	47.23	45.27-49.18	44.9	39.8-54.1		46.94	45.26-48.61	45.8	43.5-53.3	
Divorced	11.1	156 (9.2)	163 (9.6)	48.52	46.96-50.07	47.7	39.8-57.7		46.70	45.13-48.27	48.3	38.8-53.3	
Other	n/a	32 (1.9)	33 (1.9)	48.20	44.70-51.70	50.8	42.3-57.7		48.43	44.38-52.48	45.8	43.5-56.0	
Self-perceived health status (first question of SF-36)													
Excellent	n/a	139 (8.2)	145 (8.5)	60.47	58.99-61.95	61.9	57.7-67.7	<0.001	59.40	57.62-61.18	62.5	56.0-67.6	<0.001
Very good		401 (23.6)	412 (24.2)	55.33	54.68-55.98	54.1	50.8-57.7		53.39	52.60-54.18	53.3	48.3-56.0	
Good		682 (40.1)	668 (39.3)	49.13	48.68-49.57	47.7	44.9-54.1		46.80	46.27-47.34	45.8	43.5-50.8	
Fair		388 (22.8)	386 (22.7)	41.76	41.20-42.33	42.3	37.4-44.9		42.21	41.45-42.97	41.1	36.3-45.8	
Poor		90 (5.3)	90 (5.3)	32.51	31.34-33.68	32.4	29.6-34.9		33.91	32.32-35.50	33.8	28.4-38.8	
BMI groups													
Underweight (under 18.5)	n/a	56 (3.3)	49 (2.9)	49.71	47.27-52.15	50.8	44.9-54.1	<0.001	47.09	44.30-49.87	45.8	41.1-53.3	0.075
Normal weight (between 18.5 and 24.9)		497 (29.2)	500 (29.4)	51.01	50.16-51.86	50.8	44.9-57.7		48.27	47.33-49.21	48.3	43.5-56.0	
Overweight (between 25.0 and 29.9)		535 (31.5)	539 (31.7)	49.58	48.80-50.36	50.8	42.3-54.1		48.21	47.37-49.06	48.3	41.1-53.3	
Obese (between 30.0 and 39.9)		374 (22.0)	375 (22.1)	46.61	45.70-47.52	47.7	39.8-54.1		46.79	45.83-47.74	45.8	41.1-53.3	
Chronic disease[c]													
Yes	48.0	1146 (67.4)	1127 (66.3)	46.72	46.20-47.24	47.7	39.8-54.1	<0.001	45.91	45.35-46.47	45.8	38.8-53.3	<0.001
No	52.0	410 (24.1)	423 (24.9)	54.66	53.81-55.50	54.1	50.8-61.9		52.38	51.44-53.32	53.3	45.8-59.0	
Do not know/want to answer	–	144 (8.5)	150 (8.8)	50.65	49.20-52.11	50.8	44.9-57.7		48.48	56.71-50.24	48.3	43.5-56.0	

BMI = body mass index (n=238 were missing, *p*-value was computed without these respondents), HUF = Hungarian forint, IQR = interquartile range, n/a = not available

a: Computed by Mann-Whitney and Kruskal-Wallis tests

b: *p*-values were calculated after excluding the 'I do not know' and 'I do not want to answer' responses

c: Hungarian Central Statistical Office, Health at a Glance 2019

Appendix Table 6 – Residual correlations from the confirmatory factor analysis (95)

Global Physical Health items				
Items	Global03	Global06	Global07	Global08
Global03	0.000	-	-	-
Global06	0.058	0.000	-	-
Global07	–0.033	–0.021	0.000	-
Global08	–0.029	–0.071	0.066	0.000
Global Mental Health items				
Items	Global02	Global04	Global05	Global10
Global02	0.000	-	-	-
Global04	–0.004	0.000	-	-
Global05	0.026	–0.006	0.000	-
Global10	–0.067	0.029	–0.013	0.000

Global02 = quality of life, Global03 = physical health, Global04 = mental health, Global05 = satisfaction with discretionary social activities, Global06 = physical function, Global07 = pain (reverse coded 5-level item), Global08 = fatigue, Global10 = emotional problems

Appendix Table 7 – Comparison of PROMIS Global Physical Health and Global Mental Health mean T-scores across the Hungarian, Dutch and US general population (95)

	Weighted Hungarian population (n, %)	**Dutch population (n, %) (93)**	**Global Physical Health**				**Global Mental Health**			
			US population (n, %) (122)	**Hungarian mean T-score (SD)**	**Dutch mean T-score (SD)**	**US mean T-score (SD)**	**US population (n, %)**	**Hungarian mean T-score (SD)**	**Dutch mean T-score (SD)**	**US mean T-score (SD)**
Total	1700 (100)	4370 (100)	5228 (100)	49.0 (9.1)	45.2 (9.2)	50.0 (10.0)	5215 (100)	47.7 (9.5)	44.7 (8.0)	50.0 (10.0)
Gender										
Female	902 (53)	2301 (53)	3015 (58)	47.8 (9.2)	44.5 (9.1)	49.1 (10.1)	3008 (58)	46.4 (9.4)	44.1 (8.0)	49.4 (10.0)
Male	798 (47)	2069 (47)	2212 (42)	50.5 (8.8)	46.1 (9.2)	51.2 (9.8)	2206 (42)	49.3 (9.4)	45.5 (8.0)	50.8 (10.0)
Age groups (years)										
18-34	428 (25.2)	891 (20)	1182 (23)	51.5 (8.2)	47.8 (8.0)	51.6 (8.4)	1183 (23)	49.5 (10.2)	45.6 (8.0)	48.5 (9.7)
35-44	331 (19.5)	753 (17)	865 (17)	50.0 (8.7)	45.2 (8.2)	50.1 (9.8)	863 (17)	48.2 (10.0)	43.8 (8.3)	48.4 (10.4)
45-54	272 (16.0)	646 (15)	910 (17)	48.7 (9.2)	44.6 (9.3)	48.2 (10.9)	902 (17)	47.2 (9.4)	43.6 (8.1)	48.2 (10.3)
55-64	286 (16.8)	918 (21)	875 (17)	47.7 (9.6)	43.4 (9.7)	48.8 (11.3)	873 (17)	46.3 (8.9)	43.6 (8.0)	50.3 (10.5)
65-74	329 (19.4)	893 (20)	713 (14)	47.1 (9.3)	45.1 (9.5)	51.0 (9.9)	715 (14)	46.8 (8.4)	45.9 (7.4)	53.1 (8.8)
75+	54 (3.2)	269 (6)	683 (13)	45.2 (7.7)	44.9 (9.8)	49.9 (9.2)	679 (13)	46.8 (8.4)	47.3 (7.7)	53.4 (8.4)

Hungarian mean T-scores were age- and gender-weighted. SD = standard deviation

Percentages may not total 100% due to rounding