

# The contribution of health-related quality of life and utility values to decision-making in dermatology

## Outline of PhD Thesis

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# 1 Introduction

The assessment of health-related quality of life (HRQoL) is widely used to explore the burden experienced by patients with chronic skin diseases in everyday clinical settings, as well as in various dermatological researches, including observational and interventional studies. In many dermatological conditions HRQoL does not correlate strongly with disease severity, thus severity scores complement each other in understanding individual patients' health status as a whole. During the management of dermatological issues, several clinical decisions seem to be supported by information on HRQoL: diagnostic criteria, treatment choices, treatment monitoring or hospitalisation decisions.

Besides its role in medical decision-making, assessing improvements in HRQoL with a therapy provides useful information for payers and policymakers about the benefits of certain treatments. The Dermatology Life Quality Index (DLQI) is the most commonly used HRQoL instrument in the field. In many European countries, including Hungary, reimbursement criteria on financing biological therapy for moderate-to-severe psoriasis patients are based on DLQI scores.

There exists a wide range of literature with a number of outcome measures which address HRQoL issues in various chronic skin diseases. Nonetheless, very few studies have been undertaken in this area in Hungary. For reimbursement decisions, though, national guidelines on health technology assessments recommend collecting HRQoL values derived from national-level surveys.

## 2 Objectives

This thesis seeks to investigate HRQoL and utility values in chronic skin diseases in Hungary, with a special focus on issues influencing clinical and financial decision-making in healthcare. The core of the work is formed by three independent, empirical researches carried out between 2012 and 2015 in Hungary.

### 2.1 *Psoriasis study*

1. To evaluate the health status and HRQoL of adult moderate-to-severe psoriasis patients in Hungary, to explore differences in HRQoL among subgroups of patients and to compare EQ-5D results to general population norms in Hungary;
2. The assessment of patients' subjective life expectancy and expected HRQoL for six months ahead and for future ages of 60, 70, 80 and 90, respectively.

### 2.2 *Pemphigus study*

#### **Systematic review and meta-analysis of HRQoL studies**

1. To conduct a systematic review of the existing literature on the impact of pemphigus on HRQoL;
2. To perform a meta-analysis on the outcomes of the most frequently used HRQoL instruments;
3. To identify the possible determinants of HRQoL in pemphigus.

## **Valuation of pemphigus health states by the general population**

1. To elicit utility values for hypothetical pemphigus vulgaris and pemphigus foliaceus health states, using two direct methods, visual analogue scale (VAS) and time trade-off (TTO), in a general population sample.
2. To compare the utilities assigned to different pemphigus health states.

### **2.3 *DLQI study***

1. The estimation of utilities for different health states described by the 10 items of the DLQI by the TTO method;
2. To compare utility values elicited for health states with identical and different DLQI total scores.

## 3 Methods

### 3.1 Psoriasis study

A cross-sectional questionnaire survey of consecutive adult psoriasis patients from two Hungarian university clinics was carried out between September 2012 and May 2013. Patients of 18 years of age or over, who were diagnosed with moderate-to-severe psoriasis (Psoriasis Area and Severity Index, PASI > 10 or DLQI > 10, or being treated by systemic or biological therapy) at least 12 months before the time of the survey, were included in the study. The study protocol was approved by the Scientific and Research Ethics Committee of the Medical Research Council of Hungary (ETT TUKEB), reference No. 35183/2012-EKU.

Patients and their physicians were asked to complete a self-designed questionnaire. The patients' questionnaire consisted of demographic data, the family history of psoriasis, disease duration, affected body sites and HRQoL measures. In the second part of the questionnaire, dermatologists were asked to provide data on the clinical type of psoriasis and treatments in the last 12 months based on medical records. PASI was used to assess the severity of psoriasis.

HRQoL was captured by the validated Hungarian versions of EQ-5D descriptive system and visual analogue scale (EQ VAS) and a dermatology-specific measure, namely the DLQI. To elicit patients' future expectations, we employed a modified version of the descriptive system of the EQ-5D-3L instrument. Patients were asked to indicate the HRQoL they expected to have at six months ahead and at the age of 60, 70, 80, and 90 years, respectively. We measured a point estimate of subjective life expectancy for each patient by asking them, "*To what age do you expect yourself to live?*".

### 3.2 *Pemphigus* study

#### **Systematic review and meta-analysis**

A systematic search was conducted using the following databases from their inception to 6 October, 2014: Ovid Medline, EMBASE, Web of Science, CINAHL, PsycINFO and the Cochrane Library. Titles and abstracts of the identified records were screened by two independent researchers (F.R. and V.B.). Only records meeting the following inclusion criteria were selected for a full-text review: i) the study population included adult pemphigus patients; ii) the study reported HRQoL in pemphigus patients assessed by any instrument and iii) publication type: original article not a review or a conference abstract or proceeding.

Meta-analysis was carried out on total scores or individual domains of HRQoL instruments on which results were reported in at least three separate studies including patients of similar characteristics. Data were pooled by using the inverse-variance weighted method. Heterogeneity across studies was analysed using the Cochran's  $Q$  and the  $I^2$  statistics. Where significant heterogeneity was detected across studies (Cochran's  $Q < 0.01$  or  $I^2 > 50\%$ ), a random-effects meta-analysis (DerSimonian and Laird method) was applied; otherwise, a fixed-effects model was employed.

Determinants of general or dermatology-specific HRQoL were extracted from all studies. We considered significant the relationship between determinants and HRQoL, if a significant unidirectional relationship with HRQoL was justified in  $\geq 2$  studies.

#### **Valuation of pemphigus health states by the general population**

A convenience sample of adults aged  $\geq 18$  years and able to understand the Hungarian language were recruited between December 2014 and May 2015. Data were collected using a paper-based questionnaire in group interviews at the campus of Corvinus University of Budapest. Ethical approval was obtained from the

Semmelweis University Regional and Institutional Committee of Science and Research Ethics (reference No. 275./2014).

Participants evaluated three hypothetical pemphigus health states: uncontrolled pemphigus vulgaris, uncontrolled pemphigus foliaceus and controlled pemphigus. The results of our systematic review, the items of a recently developed blistering skin disease-specific questionnaire, the Autoimmune Bullous Disease Quality of Life and consultations with two dermatologists. The health state vignettes were pilot-tested in four pemphigus patients.

Two direct methods, VAS and TTO, were employed to value health states. To help participants understand the TTO task, we offered a warm-up question that involved a binocular blindness health state. All valuations started with a conventional 10-year TTO. The participants were instructed to choose between 10 years in a pemphigus health state versus a shorter life in perfect health. The top-down titration procedure was used by starting with 10 years in perfect health and descending to 0 years (10, 9.5, 9, 8, 7, etc.). Respondents who preferred 0 years in perfect health (i.e. chose immediate death) over 10 years in a pemphigus health state were given 10 more years spent in perfect health before the 10 years to live in pemphigus (a total of 20 years). The alternative option offered ranged between 10 years and 0 years in perfect health. VAS utilities ranged between 0 and 1, whereas TTO utilities ranged between -1 and 1, where a higher value indicates a better HRQoL.

### **3.3 DLQI study**

The DLQI contains ten questions concerning the patients' perception of the impact of skin disease on their HRQoL, each of which is scored from 0 to 3, where 0 - not at all/not relevant, 1 - a little, 2 - a lot, and 3 - very much. The results of each item are summed into a total score ranging from 0 (best health state) to 30 (worst health state).



A convenience sample of university students and staff was recruited, in order to participate in a cross-sectional survey. The questionnaire was administered through the Internet in March 2015. Inclusion criteria for the study included being able to understand Hungarian and aged 18 years or over. Individuals were invited to participate regardless of having any dermatological condition at the time of the survey. The experiment was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (reference No. 58./2015).

We selected seven different DLQI health states: three of 11 points, three others of six points and one of 16 points. The 11-point health states were chosen, as a DLQI score greater than 10 indicates that the skin disease is having a very large impact on the patient's life, and this is considered to be strong supportive evidence for the need for active patient intervention. The difference between health states was set at 5 points, because this exceeds the minimal clinically important difference (MCID) for general inflammatory skin diseases (4 points). Amongst the 6- and 11-point states, we intended to compile as many different health state profiles as possible in terms of: i) affected items; ii) the total number of negatively affected items and iii) the severity level of impairment (i.e. the scoring of DLQI items from 0 to 3). The descriptions contained neither labels nor names of any specific dermatologic conditions. The TTO task was identical to the utility assessment for better than dead health states in the 'Pemphigus study'.

## 4 Results

### 4.1 Psoriasis study

#### Patient characteristics

A total of 200 patients with moderate-to-severe psoriasis participated in the survey. The mean age was 51 years, and 69% were male. The mean disease duration was 22 years. The following clinical subtypes occurred in the sample: chronic plaque psoriasis (63%), nail psoriasis (36%), scalp psoriasis (35%), psoriatic arthritis (29%), inverse psoriasis (9%), palmoplantar psoriasis (6%), erythrodermic psoriasis (2%) and guttate psoriasis (2%) (combinations are possible). At the time of the survey, 103 (52%) received biological drug in mono- or combination therapy, 61 (31%) systemic non-biological therapy, 30 (15%) only topical treatment and six (3%) were untreated.

#### HRQoL results

Psoriasis patients' mean EQ-5D, EQ VAS, DLQI and PASI scores were  $0.69\pm 0.31$ ,  $64.43\pm 21.34$ ,  $6.29\pm 7.29$  and  $8.01\pm 10.01$ , respectively. Most patients reported problems in the pain/discomfort domain of the EQ-5D descriptive system (60%), followed by mobility (47%), anxiety/depression (47%), usual activities (39%) and self-care (14%), which was found to be worse compared to the age-matched general population in Hungary. Similarly, we found EQ-5D index scores in patients of both females and males with psoriasis lower compared to the general population.

Despite the lack of significant difference in PASI scores between the two genders, female patients showed lower EQ-5D scores compared to males (0.62 vs. 0.73,  $p<0.001$ ). No significant difference was identified between genders in EQ VAS (62.9 and 65.1,  $p=0.461$ ) or DLQI (7.20 and 5.88,  $p=0.535$ ). Among clinical subtypes, patients with palmoplantar psoriasis and psoriatic arthritis reported the

worst health status (mean EQ-5D 0.36 and 0.48, EQ VAS 50.33 and 56.61, DLQI 11.42 and 9.26). Patients treated with biologicals rated their HRQoL significantly better compared to those on either systemic non-biological, topical or no treatment (mean EQ-5D 0.75 vs. 0.63, EQ VAS 70.72 vs. 57.46 and DLQI 2.14 vs. 10.80,  $p < 0.001$  for all).

### **Subjective expectations on HRQoL and life expectancy**

Out of the 200 patients who participated in the survey, answers of 167 were included in the analysis of expectations. Psoriasis patients expected to improve on average by  $0.10 \pm 0.23$  for their EQ-5D score within six months ( $p < 0.001$ ). Overall, 83 (49%) expected no change at all in any of the five dimensions of EQ-5D. Sixty-two (37%) and 22 (13%) patients expected increases and decreases in HRQoL, respectively. The mean EQ-5D score of those who expected better, same or worse HRQoL in six months were 0.52, 0.86 and 0.69, respectively ( $p < 0.001$ ). The most prominent improvement was expected in the dimensions of anxiety/depression and pain/discomfort (16% and 17% expected to reach the level of 'no problems', respectively). Female gender, younger age, non-marital status, psoriatic arthritis, palmoplantar or inverse psoriasis, worse health state (measured by EQ-5D, DLQI or PASI), being at the initiation of first biological therapy were associated more often with optimistic expectations. On the contrary, older patients, those in a better health state (EQ-5D) and those with nail or scalp involvement tended to expect deterioration.

Male and female patients expected to live until  $74.86 \pm 9.54$  and  $80.09 \pm 1.77$  years, respectively. For males we found an overestimation, while for females we uncovered an underestimation of the gender- and age-matched statistical life expectancy. Expected survivors rated their future EQ-5D at ages of 60 to 90:  $0.59 \pm 0.46$ ,  $0.48 \pm 0.41$ ,  $0.42 \pm 0.41$  and  $0.22 \pm 0.47$ . For each decade, the highest decline was expected in mobility and pain/discomfort dimensions of EQ-5D. The

expectations of psoriasis patients are considerably lower than those of the general population in Hungary.

## **4.2 Pemphigus study**

### **Systematic review**

Sixteen studies from eight different countries were identified: Italy (n=5), Iran (n=4), India (n=2), Japan (n=1), Germany (n=1), Poland (n=1), Morocco (n=1) and Brazil (n=1). There were 11 cross-sectional studies, four case-control studies and one prospective cohort with a four-month follow-up period. The patient populations varied between seven and 380 patients, with only five studies enrolling >100 participants. The 16 studies involved a total of 1,465 patients, of whom 966 (66%) had pemphigus vulgaris. Besides pemphigus vulgaris, the following types of pemphigus occurred: 123 foliaceus, 41 seborrheic, eight vegetans, two IgA and two paraneoplastic. The clinical type of 323 (22%) patients was unknown or not specified. The mean age of the included patients ranged between 39 and 62 years (n=12), and the rate of males varied from 37% to 80% (n=13). Two studies recruited only newly diagnosed or untreated patients, five enrolled patients on adjuvant and/or corticosteroid therapy and a small study investigated the impact of physiotherapy on HRQoL.

Four types of HRQoL instruments were used: Short form-36 (SF-36), Activities of Daily Livings (ADLs), World Health Organization Quality of Life-BREF (WHOQOL-BREF), and World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). Four different dermatology- or oral disease-specific measures were applied: Dermatology Life Quality Index (DLQI), Skindex-29, Skindex-17, and Chronic Oral Mucosal Diseases Questionnaire (COMDQ). Among these, SF-36 (n=8), DLQI (n=5) and Skindex-29 (n=4) were the most frequent.

## **Meta-analysis**

Five studies were included in the meta-analysis of SF-36 outcomes, and all reported SF-36 dimension scores on treated and/or hospitalised pemphigus patients. The meta-analysis showed the highest deterioration in the role-physical dimension of SF-36 (38.1, 95% CI 20.4-55.9), followed by role-emotional (47.5, 95% CI 21.9-73.2), vitality (50.7, 95% CI 43.6-57.7) and general health (51.5, 95% CI 45.9-57.0).

Four studies were included in the meta-analysis of DLQI outcomes, all of which enrolled newly diagnosed or untreated pemphigus patients. Newly diagnosed or untreated patients scored on average 12.0 (95% CI 11.1-12.9). Three studies reported the Skindex-29 dimension scores of medically treated and/or hospitalised pemphigus patients. The meta-analysis indicated similar mean scores in the symptoms (35.8, 95% CI 32.7-38.9) and emotions (36.5, 95% CI 33.8-39.2) domains of Skindex-29, whereas they were slightly lower in social functioning (32.8, 95% CI 29.9-35.6).

## **Determinants of HRQoL in pemphigus**

Overall, 41 possible determinants of HRQoL in pemphigus were identified, which we classified into socio-demographic, clinical, treatment-related and psychological factors. HRQoL was clearly associated with higher disease severity, anxiety and depression in at least two separate studies. The impact of several other factors on HRQoL, such as age, sex, type of pemphigus, disease duration, mucocutaneous involvement, itching, or being treated by adjuvant drugs, cannot be stated clearly and should be investigated further.

## **Valuation of pemphigus health states by the general population**

Data from 108 respondents were analysed. The mean age of the subjects was 26, and there were slightly more females (58%) than males. There were no pemphigus patients in the sample, and 97% of the study population had never heard about pemphigus.

The mean estimated VAS scores attached to the pemphigus vulgaris, pemphigus foliaceus and uncontrolled pemphigus health states were as follows:  $0.25\pm 0.15$ ,  $0.37\pm 0.17$  and  $0.63\pm 0.16$ , respectively. Corresponding mean TTO utilities were  $0.34\pm 0.38$ ,  $0.51\pm 0.32$  and  $0.75\pm 0.31$ . Overall, 14% and 6% considered uncontrolled pemphigus vulgaris and foliaceus as being worse than dead. Significant differences were found in both the VAS and TTO utilities for all three health states ( $p<0.001$ ). In each health state, TTO utilities were significantly higher compared to VAS ( $p<0.001$ ).

Male gender and older age were associated with significantly higher utilities for uncontrolled pemphigus foliaceus on VAS, but this was not the case for uncontrolled pemphigus vulgaris or controlled pemphigus. More educated respondents tended to elicit higher utilities in uncontrolled pemphigus foliaceus VAS, TTO and in pemphigus vulgaris VAS. Age or gender had no influence on the TTO responses, and employment status had no impact on either VAS or TTO utilities.

### **4.3 DLQI study**

#### **Study population**

The responses of 308 respondents were judged valid and included in the analyses. The mean age of the study population was 27 (min.-max. 18-75) years, with a female predominance (69%). Almost half of the respondents reported to hold a college or university degree (47%). Overall, 18% of the participants responded to have had a dermatological condition diagnosed by a physician at the time of the survey. Non-atopic dermatitis (4%), acne (3%) and psoriasis (2%) were among the most frequent diagnoses.

### **Utilities for the health states defined by DLQI**

Mean utilities for the six-point health states were as follows:  $0.64\pm 0.32$ ,  $0.75\pm 0.27$  and  $0.62\pm 0.30$ . Mean utilities for the 11-point health states were  $0.66\pm 0.31$ ,  $0.64\pm 0.28$  and  $0.59\pm 0.29$ . The 16-point health state was assessed the most severe with a mean utility of  $0.56\pm 0.29$ .

Overall, 21 pairwise comparisons were made between utilities attached to the seven health states: six and 15 between health states of identical and different DLQI total scores, respectively. In three cases out of the six comparisons significant differences were observed between utilities for health states with identical total DLQI scores. The lack of significant difference was noticed in eight out of the 15 comparisons, where health states for which the DLQI total score differed greater than for the MCID were compared.

The mean utilities elicited from respondents who had no dermatological condition were higher than from those who had no skin problem ( $0.68\pm 0.30$  vs.  $0.63\pm 0.29$ ;  $p=0.029$ ). No difference was observed in mean utilities for binocular blindness between these two groups ( $0.49\pm 0.30$  vs.  $0.50\pm 0.27$ ;  $p=0.796$ ). In a sensitivity analysis, after eliminating the responses of participants with any dermatological conditions, only minor changes occurred in mean utilities and in the significance of the differences between health states.

## 5 Conclusions

### 5.1 *Psoriasis study*

1. This is the first study from Hungary specifically, and more broadly from the whole Central and Eastern Europe, that has used the EQ-5D questionnaire in psoriasis patients. For most age groups, the health status and general HRQoL of moderate-to-severe psoriasis patients is significantly deteriorated compared to the gender- and age-matched EQ-5D population norm in Hungary. Palmoplantar psoriasis and PsA are associated with the largest impairment in HRQoL. Patients receiving biological therapy demonstrate better HRQoL compared with those on any other treatment.
2. We were the first to explore psoriasis patients' expectations regarding their life expectancy and future HRQoL. Male patients expect a longer life, while females expect a shorter life compared to their statistical life expectancy. Patients' short-term expectations regarding their HRQoL are mainly positive, while a great decline is expected for future ages. Expectations are influenced by age, gender, clinical subtype, disease severity, current HRQoL and applied therapy. Our findings illuminate a new dimension of the lifelong burden experienced by psoriasis patients.

### 5.2 *Pemphigus study*

#### **Systematic review and meta-analysis**

1. We conducted the first systematic review summarising HRQoL findings in pemphigus.
2. Pemphigus patients suffer the most problems in the role-physical dimension of HRQoL, followed by role-emotional and vitality.



3. Overall, 41 possible determinants of HRQoL were identified, amongst which clinical severity and associated anxiety or depression were revealed as the most important.
4. There is a need for longitudinal studies in order to explore the disease course of pemphigus with regard to HRQoL.
5. No preference-based HRQoL instruments have yet been applied in pemphigus; thus, input data are missing to calculate quality-adjusted life years in cost-effectiveness analyses of treatments.

### **Valuation of pemphigus health states by the general population**

1. This study provides the first utility values for pemphigus health states. Our utilities may serve as a guide for further utility studies and cost-effectiveness analyses.
2. Pemphigus vulgaris is associated with significantly lower utility values than pemphigus foliaceus.
3. The successful treatment of pemphigus might result in large utility gains, which is very promising for future cost-effectiveness studies involving various treatments for pemphigus patients.

### 5.3 *DLQI study*

Given the discrepancies found between DLQI scores and utilities elicited by the general population:

1. HRQoL (and utilities) may differ a great deal between patients whose DLQI total scores are identical.
2. Patients with DLQI scores differing more than the MCID may have identical HRQoL (and utilities).
3. A reduction in the DLQI score may not be associated with significant (or any) health gains.

As a consequence, the DLQI may distort clinical and financial decisions made during the management of chronic skin diseases.

## 6 List of publications

### 6.1 Publications related to this thesis

#### Peer-reviewed journal articles

1. **Rencz F**, Baji P, Gulácsi L, Kárpáti S, Péntek M, Poór AK, Brodszky V. (2015) Discrepancies between the Dermatology Life Quality Index and utility scores. *Qual Life Res*, 2015 Dec 18. [Epub ahead of print]
2. **Rencz F**, Gulácsi L, Tamási B, Kárpáti S, Péntek M, Baji P, Brodszky V. (2015) Health related quality of life and its determinants in pemphigus: a systematic review and meta-analysis. *Br J Dermatol*, 173: 1076-80.
3. **Rencz F**, Holló P, Kárpáti S, Péntek M, Remenyik E, Szegedi A, Balogh O, Herédi E, Herszényi K, Jókai H, Brodszky V, Gulácsi L. (2015) Moderate to severe psoriasis patients' subjective future expectations regarding health-related quality of life and longevity. *J Eur Acad Dermatol Venereol*, 29: 1398-405.
4. **Rencz F**, Brodszky V, Péntek M, Balogh O, Remenyik E, Szegedi A, Holló P, Kárpáti S, Jókai H, Herszényi K, Herédi E, Szántó S, Gulácsi L. (2014) Disease burden of psoriasis associated with psoriatic arthritis in Hungary. *Orv Hetil*, 155: 1913-21.

#### Published abstracts

5. **Rencz F**, Gulácsi L, Tamási B, Kárpáti S, Brodszky V. (2015) Social Utility Values for Pemphigus Vulgaris and Foliaceus: A Composite Time Trade-Off Study. *Value Health*, 18: A673. (International Society For Pharmacoeconomics and Outcomes Research 18th Annual European Congress, November 7-11, 2015, Milan, Italy)
6. **Rencz F**, Kárpáti S, Baji P, Péntek M, Gulácsi L, Brodszky V. (2015) Valuation of health states defined by Dermatology Life Quality Index using time trade-off. (P1842). (24th European Academy of Dermatology & Venereology (EADV) Annual congress, October 7-11, 2015, Copenhagen, Denmark)
7. **Rencz F**, Gulácsi L, Remenyik É, Szegedi A, Holló P, Kárpáti S, Péntek M, Brodszky V. (2014) Subjective Expectations Regarding Life Expectancy And Health Related Quality Of Life In Moderate To Severe Psoriasis Patients.

Value Health, 17: A611. (International Society For Pharmacoeconomics and Outcomes Research 17th Annual European Congress, November 8-12, 2014, Amsterdam, The Netherlands)

## 6.2 *Publications not related to this thesis*

1. Brodszky V, **Rencz F**, Péntek M, Baji P, Lakatos PL, Gulácsi L. (2016) A budget impact model for biosimilar infliximab in Crohn's disease in Bulgaria, the Czech Republic, Hungary, Poland, Romania and Slovakia. *Expert Rev Pharmacoecon Outcomes Res*, 16: 119-125.
2. Baji P, Gulácsi L, Lovász BD, Golovics PA, Brodszky V, Péntek M, **Rencz F**, Lakatos PL. (2016) Treatment preferences of originator versus biosimilar drugs in Crohn's disease; discrete choice experiment among gastroenterologists. *Scand J Gastroenterol*, 51: 22-7.
3. **Rencz F**, Kemény L, Gajdácsi JZ, Owczarek W, Arenberger P, Tiplica GS, Stanimirović A, Niewada M, Petrova G, Marinov LT, Péntek M, Brodszky V, Gulácsi L. (2015) Use of biologics for psoriasis in Central and Eastern European countries. *J Eur Acad Dermatol Venereol*, 29: 2222-30.
4. **Rencz F**, Kovács Á, Brodszky V, Gulácsi L, Németh Z, Nagy GJ, Nagy J, Buzogány I, Böszörményi-Nagy G, Majoros A, Nyirády P. (2015) Cost of illness of medically treated benign prostatic hyperplasia in Hungary. *Int Urol Nephrol*, 47: 1241-9.
5. **Rencz F**, Péntek M, Bortlik M, Zagorowicz E, Hlavaty T, Liwczyński A, Diculescu MM, Kupcinkas L, Gece KB, Gulácsi L, Lakatos PL. (2015) Biological therapy in inflammatory bowel diseases: Access in Central and Eastern Europe. *World J Gastroenterol*, 21: 1728-1737.
6. **Rencz F**, Brodszky V, Péntek M, Bereczki D, Gulácsi L. (2015) Health state utilities for migraine based on attack frequency: a time trade-off study. *Neurol Sci*, 36: 197-202.
7. Moradi M\*, **Rencz F\***, Brodszky V, Moradi A, Balogh O, Gulácsi L. (2015) Health Status and Quality of Life in Patients with Psoriasis: An Iranian Cross-Sectional Survey. *Arch Iran Med*, 18: 153-159.

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8. Fábrián M, Tóth V, Somlai B, Hársing J, Kuroli E, **Rencz F**, Szakonyi J, Tóth B, Kuzmanovszki D, Kárpáti S. (2015) Retrospective analysis of clinicopathological characteristics of pregnancy associated melanoma. *Pathol Oncol Res*, 21:1265-71.
9. Baji P, Brodszky V, **Rencz F**, Boncz, I, Gulácsi L, Péntek M. (2015) Health state of the population in Hungary between 2000-2010. *Orv Hetil*, 156: 2043-2052.
10. **Rencz F**, Brodszky V, Varga P, Gajdácsi J, Nyirády P, Gulácsi L. (2014) The economic burden of prostate cancer: a systematic literature overview of registry-based studies. *Orv Hetil*, 155: 509–520.
11. Heredi E\*, **Rencz F\***, Balogh O, Gulacsi L, Herszenyi K, Hollo P, Jokai H, Karpati S, Pentek M, Remenyik E, Szegedi A, Brodszky V. (2014) Exploring the relationship between EQ-5D, DLQI and PASI, and mapping EQ-5D utilities: a cross-sectional study in psoriasis from Hungary. *Eur J Health Econ*, 15: S111-9.  
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12. Gulacsi L, **Rencz F**, Pentek M, Brodszky V, Lopert R, Hever NV, Baji P. (2014) Transferability of results of cost utility analyses for biologicals in inflammatory conditions for Central and Eastern European countries. *Eur J Health Econ* 15: S27-34.
13. Gulacsi L, Rotar AM, Niewada M, Loblova O, **Rencz F**, Petrova G, Boncz I, Klazinga NS. (2014) Health technology assessment in Poland, the Czech Republic, Hungary, Romania and Bulgaria. *Eur J Health Econ*, 15: S13-25.
14. Brodszky V, Péntek M, Baji P, **Rencz F**, Géczi L, Szűcs M, Bercei C, Gulácsi L. (2014) Clinical efficacy and safety of enzalutamide in metastatic castration-resistant prostate cancer: systematic review and meta-analysis *Magy Onkol*, 58: 189-97.