Health-related quality of life and disease burden of psoriasis in Iran

Ph.D. Thesis

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</thead>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BSA</td>
<td>Body surface area</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>COI</td>
<td>Cost-of-illness</td>
</tr>
<tr>
<td>DLQI</td>
<td>Dermatology Life Quality Index</td>
</tr>
<tr>
<td>DQOLS</td>
<td>Dermatology quality of life scales</td>
</tr>
<tr>
<td>HRQOL</td>
<td>Health-related quality of life</td>
</tr>
<tr>
<td>HSEP</td>
<td>Health Sector Evolution Plan</td>
</tr>
<tr>
<td>HTA</td>
<td>Health technology assessment</td>
</tr>
<tr>
<td>MoHME</td>
<td>Ministry of Health and Medical Education</td>
</tr>
<tr>
<td>MTX</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>PASI</td>
<td>Psoriasis Area Severity Index</td>
</tr>
<tr>
<td>PDI</td>
<td>Psoriasis Disability Index</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care</td>
</tr>
<tr>
<td>PGA</td>
<td>Physician’s Global Assessment</td>
</tr>
<tr>
<td>PsA</td>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>PSORIQOL</td>
<td>Psoriasis index of quality of life</td>
</tr>
<tr>
<td>PUVA</td>
<td>Psoralen and UltraViolet A (photochemotherapy)</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality-adjusted life year</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>SF-6D</td>
<td>Short form 6 dimensions</td>
</tr>
<tr>
<td>SF-36</td>
<td>Medical Outcomes Study 36-Item Short Form</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
</tr>
<tr>
<td>WHOQOL</td>
<td>World Health Organization Quality of Life Assessment</td>
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</table>
1 Introduction

The concept of health has dynamically been changing by rise of new needs and diversity in human preferences. Also by improvement of life expectancy from the beginning of 20th century, the concept of health for the person and the society has evolved. Advancements in science and technology has made this possible and has changed human needs. For example, fear of dying has changed to dedication to survival and living healthier for a longer time.

Longer life expectancy leads to larger population of elderly people with higher chance of chronic health problems. Economic evaluation is vital, in order to utilize resources and achieve higher efficiency and effectiveness in decision-making. In order to avoid unfeasible decisions, a careful analysis of all aspects including costs and consequences is needed. Decision-making that are based on preferences for health states, along with the economic analysis focused on the patient's and societal perspective, can improve the distribution of finite resources in the face of a growing and increasingly challenging demand.

New innovative health technologies are developed, often very effective but rather costly. The fourth hurdle ((i.e., requirement of effectiveness and cost-effectiveness data for drug coverage policy decisions) became highly relevant even in economically developed countries (Gulacsi et al., 2004).

Health technology assessment (HTA) is now an established input to health-care decision-making and has been introduced in many countries. HTA involves health economic evaluation that requires input data considering local aspects such as characteristics of the health care system, clinical practice, patients’ characteristics, individual and societal preferences in a given country.

Transferability of international results is often limited due to differences between countries and regions (costs differ, health states might differ, cultural differences might affect people’s preferences), therefore economic evaluation conducted in one setting might not be applicable to another and as a consequence, country-specific evaluations are needed that reflect the needs of the decision-makers in that country.
HTA has been introduced in Iran, however country-specific input data both on health-related quality of life (HRQOL) and disease burden for health economic evaluation are often missing.

The focus of the empirical research of this thesis is on HRQOL, i.e. how individuals or a group perceive physical and mental health and social well-being over time. This subjective perception can be influenced by several factors, including their beliefs, subjective expectations, previous experiences, cultural and religious attitudes, personality-related factors. Moreover, it can vary individually or regionally.

The first study aimed to explore people’s perception on health, which aspects of health are the most relevant for the individuals. It can have implications on HRQOL research and preference measurement.

The second study involved a cross-sectional survey in Iran among patients with a chronic dermatological disease, namely psoriasis. Psoriasis is of high interest due to its prevalence and, from the economic point of view, due to the costly biological drugs. Biological drugs have speeded up HRQOL and cost-of-illness (COI) research in psoriasis in many countries – measure health outcomes considering patients’ preferences (HRQOL measurement), cost-effectiveness, budget impact issues and affordability.

The aims of the study were on the one hand, to assess patients HRQOL and to assess the relationship between disease-specific and generic HRQOL measures in order to provide local data for health economic analyses, to compare the results with other countries and thus provide a basis for transferability analyses. On the other hand, and I find it equally important, this experiment can serve also as useful test how brief cross-sectional surveys developed in a European country (namely in Hungary) can be applied in and adapted to Iran in terms of feasibility and applicability, in order to obtain comparable data in the context of limited research resources and to strengthens international collaboration.
2 Key terms and definitions of the thesis

In this section, I provide a brief introduction to the main terms used in the thesis.

2.1 Health technology assessment

Health technology assessment (HTA) has been defined as “a form of policy research that systematically examines the short- and long-term consequences, in terms of health and resource use, of the application of a health technology, a set of related technologies or a technology related issue” (Henshall et al., 1997).

The focus of HTA is mostly on the medical, organizational, economic and societal consequences of implementing health technologies or interventions within the health system. Thus, HTA is a multidisciplinary activity. It systematically evaluates the effects of a technology on health. It also evaluates the effects of a technology on the availability and distribution of resources and on other aspects of health system performance such as equity and responsiveness (Garrido et al., 2008).

Goodman (2004) states that the goal of HTA is to notify policymaking for technology in health care, where policymaking is used in the broad sense to include decisions made at various levels. For example, the individual or patient level, the level of the health care provider or institution, or the regional, national and international are the mentioned levels (Goodman, 2004).

2.2 Quality of life

Quality of Life according to World Health Organization’s (WHO) definition is 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”(1995). Different factors can play a role in quality of life according to personal preferences. These factors are, for instance, financial security, job satisfaction, family life, health and safety. When quality of life is considered in the context of health and disease, it is commonly referred to as health-related quality of life (HRQOL) to differentiate it from other aspects of quality of life (Lipscomb et al., 2004)
2.3 Health-related quality of life

Strategies and processes for the effective dissemination and diffusion of research findings on health-related quality of life (HRQOL) into practical applications were explored at a workshop held in Montreal in April, 1994 by Wilson and Cleary. Wilson and Cleary published their seminal conceptual model of HRQOL, which provides a causal pathway linking traditional clinical variables to HRQOL (Till et al., 1994, Shiu et al., 2014, Wilson & Cleary, 1995). The Wilson & Cleary model of HRQOL was further revised by Ferrans et al. in 2005 (Ferrans et al., 2005). A conceptual model for dissemination and diffusion of evidence about HRQOL was used to identify five different target groups: HRQOL assessors, policy makers, planners of clinical trials, developers of clinical practice guidelines, and those at the level of patient-practitioner clinical decision making (Till et al., 1994). HRQOL is a multidimensional construct covering physical, psychological with social functioning and well-being that includes both negative and positive aspects.

HRQOL has a focus on the effects of illness and specifically on the impact; treatment may have on Quality of life (QOL). QOL is therefore appears to be a broad and idiosyncratic construct affected only moderately by health (Feldman et al., 2000).

To select measures for evaluating HRQOL, seven issues can be addressed, as follow:

2.3.1 Disease-specific versus global assessment

Measures may concentrate on the symptoms, complaints, disabilities, and distributions in life that are specific to the clinical condition under study. The disease-specific approach has been recommended in the study of arthritis, heart disease, and the evaluation of chemotherapy. Instead, global assessment, evaluate the quality of life resulting from the overall consequences of disease and management on the functional capacities and patients’ perception of well-being (Medicine & Technology, 1989).

2.3.2 Clinical endpoints versus long-term outcomes

Clinical endpoints usually used for evaluating prognoses include evidence of improvement following intervention, remission of disease, and recurrence. Long-term outcomes can be viewed
as crucial to patients as they live with their resulting states of health (Medicine&Technology, 1989).

2.3.3 Patient ratings versus proxy assessments

Analyzer usually would rather that patients measure their own quality of life. When patients are not able to provide information regarding their health status (e.g., children, patients with cognitive problems), proxies (which include close family members or health care professionals) can provide the needed information on behalf of the patient (Punjabi, 2008).

2.3.4 Objective versus subjective measures

Objective measures include indicators of health and living conditions, socio-demographic items and role functioning (Yamauchi et al., 2008). Objective measures can be observed and recorded by various testing procedures and assessors. Whereas, subjective indicators measure life satisfaction in general and within different life domains. Subjective measures provide opportunities for individuals to express their thoughts, knowledge, attitudes, moods, and feelings (Yamauchi et al., 2008, Medicine&Technology, 1989).

2.3.5 Cognitive Functioning

Cognitive functions are detected by studying behavior in defined stimulus–response situations (Daliento et al., 2006).

2.3.6 Ratings and Utilities

As Schuessler and Fisher (1985) indicate, quality of life measures provide ratings or rankings of health and life. Some assessments attempt to move from states of health to judgments of the worth or value of life with a given state of health (Schuessler&Fisher, 1985, Medicine&Technology, 1989).

Analyzers are designing measures of the utilities of health states, with the typical scores ranging from 0 to 1 (“Death” to "Normal Health”). By multiplying the utility values by the number of years individuals live with a given health state, survival time can be demonstrate in Quality-Adjusted Life Years (QALY). Health economists have used this approach to compare technologies in terms
of costs per QALY gained. Utility measures move the measurement of quality of life from rankings to judgments of worth and value (Medicine&Technology, 1989).

### 2.3.7 Timing of the Assessments

Measures like the linear analogue self-assessment scales, the Functional Living Index or the psoriasis disease Questionnaire, are designed for repeated use before, during, and immediately after treatment. The purpose of the repeated measures is to evaluate patients' short-term responses during the course of therapy (Medicine&Technology, 1989).

### 2.4 Quality-adjusted life year

Three different approaches to measuring quality of life are global scales, multi-attribute utility scales and multidimensional scales. Each of these approaches provides different kinds of information about quality of life and each can be used to provide information to healthcare purchasers concerning the relative value-for-money of health interventions. The value-for-money of health interventions, in terms of quality of life, can be demonstrated in 2 ways: a formula-driven approach based on cost-utility analysis, which uses scales generating the unit of a quality-adjusted life year (QALY); and a non-formula-driven approach, which uses scales generating multidimensional profiles of quality of life (Hyland, 1997).

The QALY is a widely used measure, which incorporates both quality and quantity of life. It is applicable to all individuals and diseases (Whitehead&Shehzad, 2010). QALYs are designed to aggregate in a single summary measure the total health improvement for a group of individuals, capturing improvements from impacts on both quantity of life and quality of life – with quality of life broadly defined (Torrance&Feeny, 1989).

QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality of life score (on a 0 to 1 scale) that reflect the preference for the given health state, the so called utility.
Utilities are measured on a cardinal scale of 0–1, where 0 indicates death and 1 indicates full health. Using the ‘anchors’ of 0 and 1, utility measurement is on an interval scale, where the same change means the same irrespective of the part of the scale being considered (e.g. a change in health from 0.2 to 0.3 is equivalent to a change from 0.8 to 0.9). States worse than death can also be accounted for, with such states taking a negative value (Whitehead & Shehzad, 2010).

One form of cost-effectiveness analysis, cost-utility analysis, allows the comparison of different health outcomes (such as prolongation of life, prevention of blindness or relief of suffering) by measuring them all in terms of a single unit — the QALY (Mcgregor, 2003).

### 2.5 Mapping from disease-specific measures to utilities

The main purpose of mapping is to derive utility scores for non-preference-based measures to be used in economic evaluation. Therefore, to perform a mapping two data sets are necessary: first an estimation data set and second a study data set. The estimation data set includes information about both the target (preference-based) measure and the base (non-preference-based) measure from the same population. In contrast, the study data set includes only the base measure. (Chuang & Whitehead, 2012)
Mapping or cross-walking is a methodology used to estimate the relationship between a non-preference-based measure and a generic preference-based measure (Brazier et al., 2010). In randomized controlled trials (RCTs), data on clinical effectiveness are typically collected on disease-specific measures, as these are more sensitive to changes in outcomes as a result of treatments (Wiebe et al., 2003). Meanwhile, preference-based methods are rarely applied in RCTs; therefore, utilities for cost-effectiveness analyses are lacking. Mapping provides an alternative to translate scores of disease-specific measures into utility values (Brazier et al., 2010, Lu et al., 2013).

Mapping process involves the following steps:

1. Regression methods should be used to get a statistical relationship between two measures that we have gathered. Therefore, through regression method we get a formula or algorithm.
2. The algorithm that we got from the regression result, then applied to the base measure in the study data set to obtain the predicted score of the target measure.
3. Then finally, the predicted utility values are now ready for the study data set to conduct the required cost–utility analysis (Chuang & Whitehead, 2012).

### 2.6 Disease burden assessment

Cost-of-illness (COI), also known as burden of disease (BOD), is a definition that encompasses various aspects of the disease impact on the health outcomes in a country, specific regions, communities, and even individuals (Jo, 2014). The aim of a cost-of-illness study is to identify, and measure all the costs of a particular disease, including the direct, indirect, and intangible dimensions. The output, expressed in monetary terms, is an estimate of the total burden of a particular disease to society (Byford et al., 2000, Rice, 1994).

The quantifiable costs associated with human disease and illness are usually categorized into two unique components, including direct (medical and non-medical) and indirect costs (Boccuzzi, 2003).
2.6.1 Direct cost

Direct costs consist of healthcare costs and non-healthcare costs (also called direct medical and non-medical costs). Direct health care costs refer to the healthcare expenditures for diagnosis, treatment, and rehabilitation, etc., while direct non-healthcare costs refer to the costs like transportation, household expenditures, relocating, property losses and informal costs of any kinds (Jo, 2014).

2.6.2 Indirect cost

Indirect cost in cost-of-illness studies refers to productivity losses due to morbidity and mortality, borne by the individual, family, society, or the employer (Sherman et al., 2001, Jo, 2014). (Table 1) Indirect costs cannot be traced to a given cost object without resorting to some arbitrary method of assignment. (Cleverley & Cameron, 2007)

Table 1: Direct and indirect costs of chronic conditions – some examples

<table>
<thead>
<tr>
<th>Direct costs</th>
<th>Indirect costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct healthcare costs</strong></td>
<td><strong>Direct non-healthcare costs</strong></td>
</tr>
<tr>
<td>Doctor’s office visits</td>
<td>Care provided by nonpaid caregivers</td>
</tr>
<tr>
<td>Diagnostic testing</td>
<td>Consumer health education</td>
</tr>
<tr>
<td>Durable and nondurable medical products</td>
<td>Financial assistance to persons with chronic disease</td>
</tr>
<tr>
<td>Hospital, nursing home and home care services</td>
<td>Housekeeping assistance needed because of disease</td>
</tr>
<tr>
<td>Medications, immunizations</td>
<td>Research and construction of healthcare facilities</td>
</tr>
<tr>
<td>Physicians and other professionals</td>
<td>Transportation to and from healthcare visits</td>
</tr>
<tr>
<td>Treatment of general medical conditions attributed to condition</td>
<td></td>
</tr>
</tbody>
</table>

Source: (Cleverley & Cameron, 2007)

2.6.3 Intangible cost

Intangible costs are usually the costs of pain, grief and suffering and loss of quality of life and these kind of costs cannot be quantified directly in monetary terms (Jefferson et al., 2000). Intangible costs are often omitted because of the difficulty in accurately quantifying it in monetary terms. In such a case, the study should note that intangible costs have been omitted (Joel E, 2006, Hodgson & Meiners, 1982, Cooper & Rice, 1976).
2.6.4 Cost-of-illness studies and their use in decision making

Health economic analyses are becoming increasingly important in healthcare systems due to the scarcity of resources in healthcare systems. Disease burden or cost-of-illness (COI) analysis was the first economic evaluation technique used in the field of health economics. The COI study is considered to be an essential evaluation technique in health care. By measuring and comparing the economic burdens of diseases to society, such studies can help health-care decision-makers to set up and prioritize health-care policies and interventions (Jo, 2014).

COI studies serve a different purpose compared to other economic evaluations such as cost-effectiveness analysis (CEA), and cost-benefit analysis (CBA) that mainly compare the costs and outcomes of an intervention. COI always presumes the hypothesis that the emerging cost is the expenditure that return as profit in case of a positive result, so it estimates the amount that could be saved if a disease were to be abolished. Additionally, COI findings offer a good basis for further CEA and CBA studies.

The usefulness of cost-of-illness as a decision-making tool has however been questioned since its inception. The main criticism came from welfare economists who rejected COIs because they were not grounded in welfare economics theory (Tarricone, 2006). Other attacks related to the use of the human capital approach (HCA) to evaluate morbidity and mortality costs since it was said that the HCA had nothing to do with the value people attach to their lives. Finally, objections were made that COI could not be of any help to decision makers and that other forms of economic evaluation (e.g. cost-effectiveness, cost-benefit analysis) would be much more useful to those taking decisions and ranking priorities. Conversely, it is here suggested that COI can be a good economic tool to inform decision makers if it is considered from another perspective. COI is a descriptive study that can provide information to support the political process as well as the management functions at different levels of the healthcare organizations (Tarricone, 2006). To do that, the design of the study must be innovative, capable of measuring the true cost to society; to estimate the main cost components and their incidence over total costs; to envisage the different subjects who bear the costs; to identify the actual clinical management of illness; and to explain cost variability. In order to reach these goals, COI need to be designed as observational bottom-up studies (Tarricone, 2006).
Cost-of-illness studies may be conducted from different perspectives, which determine the types of cost included in the analysis. These perspectives may measure costs to society, the health care systems, participants and their families, and third party payers. (Table 2)

Table 2 Costs included in cost-of-illness (COI) studies using different perspectives

<table>
<thead>
<tr>
<th>Perspective</th>
<th>Medical cost</th>
<th>Productivity (due to morbidity and mortality)</th>
<th>Non-medical cost (time cost, informal care, transportation)</th>
<th>Transfer payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Societal</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>Administration cost and excess burden of taxes</td>
</tr>
<tr>
<td>Health care system</td>
<td>All</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Participants and their families</td>
<td>Out of pocket costs</td>
<td>Lost wages or household production</td>
<td>Out of pocket costs amount received</td>
<td>Amount received</td>
</tr>
<tr>
<td>Third party payer</td>
<td>Covered cost</td>
<td>Covered cost</td>
<td>-</td>
<td>Amount paid by others + administration cost</td>
</tr>
</tbody>
</table>

Source: (Weinstein et al., 1996, Joel E, 2006, Saha&Gerdtham, 2013)

2.6.5 Costing approach

Cost-of-illness studies can be based on three different combinations of costing approaches: incidence or prevalence-based approaches, top-down or bottom-up approaches and prospective or retrospective approaches (Tarricone, 2006).

2.6.5.1 Incidence or prevalence-based approaches

Prevalence-based COI analysis includes the total costs of prevalent cases of an illness or disease within a specified time period, in most cases one year, no matter when the disease first occurred. In other words, prevalence-based estimates are a cross-sectional view of costs associated with the illness. Prevalence-based estimates do not tell us how much can be saved by prevention. They only look at the annual costs of a disease, rather than costs of a disease over the course of a life.

Incidence studies refer to the new number of cases arising in a predefined period of time (Tarricone, 2006) Unlike prevalence-based COI analysis, incidence-based COI analysis calculates the value of lifetime costs for new cases of the disease or illness. Incidence-based analyses are essential for calculating the value of prevention.
2.6.5.2 Top-down versus bottom-up approaches

Two approaches that are commonly used for quantifying the resources are the top-down (population-based) and the bottom-up (person-based) approach.

The top-down approach estimates economic costs by using aggregate data on mortality, morbidity, hospital admissions, general practice consultations, disease-related costs, and other health-related indicators. Various sources and types of data are used to calculate the fractions of resources used that can be attributed to each disease. Generally, this information is collected from national health care statistics, patient registers, insurance databases, etc. The bottom-up approach calculates the resources used and productivity loss in individuals with the health problem in question. The mean per-person costs are then extrapolated to the whole population with relevant epidemiological data. In this case, the patient sample size needs to be unbiased and representative of the national population. The bottom-up approach is more comprehensive and enables detection of the variability related to differences in important demographic characteristics between patients (Tarricone, 2006, Larg&Moss, 2011, Segel, 2006, Akobundu et al., 2006).

Incidence approach requires that the analysis be performed “from the bottom-up”, totaling the lifetime costs of an illness. This, in turn, requires that input data be gathered at a level of detail much greater than that employed in the prevalence approach where, in general, the analysis is performed “from the top-down”, allocating portions of a known total expenditure to each of several broad disease category.

2.6.5.3 Prospective versus retrospective COI studies

In a retrospective approach, all the relevant events have already happened when the study starts, in which we just collect the data that are previously recorded. Conversely, in a prospective approach the relevant events have not already occurred at the beginning of the study, which means that the data collection needs to be done by following-up the patients over time. The prevalence- and incidence-based COI studies can be both performed either in prospective or retrospective way (Jo, 2014, Tarricone, 2006).
3 Health policy and health technology assessment in Iran

3.1 History of medicine in Iran

The history of medicine in Iran is as old as and as rich as its civilization. In the pre-Islamic Iran, the history of medicine dates back to four centuries before Christ and the primary principles of Iranian medicine were mentioned in Avesta (the holy Book of Merian – ancient Iranian religion) (Velayati, 1988).

A great center of learning medicine was founded at Jundishapur (Gundeshapur) University in the 4th century AD, which had a large hospital and an academy, and the first international medical congress was held there (Nikbakht&Kafi, 2008).

Jundishapur University was a breeding ground for the union among great scientists from different civilizations. These centers successfully followed their predecessors' theories and greatly extended their scientific research through history (Pourahmad, 2008). Some experts go so far as to claim that: "to a very large extent, the credit for the whole hospital system must be given to Persia"(Pandit, 2009).

The excellent clinical observations and physical examinations and writings of Iranian scientists such as Rhazes (Al-Razi, 865-925 AD), Haly Abbas (Ali ibn-al Abbas-al Majusi, died 994 AD), Avicenna (Abou Ali Sina, 980-1037) and Jurjan (Osmail ibn al-Husayn al-Jurjani, 110 AD) influenced all fields of medicine.

The new era of medicine in Iran begins with establishment of Dar-ul-funoon in 1851, which was the only center for modern medical education before the establishment of Tehran University. Following the establishment of the Tehran university school of medicine in 1934 and the return of Iranian graduates from the medical schools in Europe, much progress was made in the development and availability of trained manpower and specialized faculties in medicine (Pourahmad, 2008).
3.2 Health System in Iran

Iran as a developing country is an upper middle-income country located in the southwest of Asia – the Middle East. Based on the latest reports of the World Bank, its population is 79.1 million people (2015), its GDP (current US$) is 393.7 billion (2015), its Health expenditure, public (percent of total health expenditure) is 41.2 (2014) and its total expenditure on health is 6.9 percent of GDP (2014) (2015). Article 29 of the Constitution of the Islamic Republic of Iran emphasizes that every Iranian has the right to enjoy the highest attainable level of health. The Ministry of Health and Medical Education is mandated to fulfill this goal through designing and implementing a national-level health policy (1979). According to the law, government has the responsibility to provide services and financial protection for every individual citizen of the country therefore today the largest health care delivery network is owned and run by the Government through Ministry of Health and Medical Education (MOHME) (2008).

Although the Iran health system consists of both public and private sectors, currently all Iranians have access to a government-supported health insurance system. However, due to the lack of sufficient resources in public health sectors and national health insurance schemes, in the past years and up to 2012, out of pocket payments of patients have substantially increased and has topped to over 81.3% of the costs of medical services (Davari et al., 2012).

3.3 Iranian Health Financing System

There are several ways of financing healthcare in Iran and the most important types include general revenue financing, social health care insurance, household out-of-pocket payments and also private actuarial health care insurance.

Private actuarial health care insurance mostly gives secondary coverage to the people who have already social insurance. Private insurance market is small in Iran.

Government pay for general revenue financing health care. General revenue financing of health care mostly give primary health care (PHC) to the people and focus on several secondary care services such as expensive-to-manage diseases. In addition to that, public hospitals’ infrastructure
mostly paid out of government general revenue. Medicine production benefits from significant government subsidies.

Social health care insurance covers around 90% of the population and it focused on non-PHC 'treatment' services, which includes most ambulatory, diagnostic and hospital services. The number of services that they provide varies depending on the service and setting, and to some extent on who is the insurer. However, an important share of health care bill is paid by people as out-of-pocket payments at the time of service utilization.

Total health expenditure has increased very rapidly in the past decade. The per capita health expenditure has increased from $68 in 1995 to $229 in 2000 to $351 in 2014 (Table 3) (2015). World Bank estimated the public health expenditure (% of government expenditure) 12.7 in 2010 and out-of-pocket expenditure is 81.3% in 2014.

The Iranian health care financing system organized through a number of public and non-public insurance schemes. Access to services and choice of provider is determined largely by the type of insurance coverage.

Table 3 Expenditure on healthcare in Iran

<table>
<thead>
<tr>
<th></th>
<th>GDP per capita (current US$)</th>
<th>Total health expenditure per capita (current US$)</th>
<th>Total health expenditure (% of GDP)</th>
<th>Public health expenditure (% of GDP)</th>
<th>Private health expenditure (% of GDP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iran</td>
<td></td>
<td></td>
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<tr>
<td>(1995)</td>
<td>1,664.3</td>
<td>68</td>
<td>3.7</td>
<td>1.7</td>
<td>2.1</td>
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<tr>
<td>(2000)</td>
<td>1,598.5</td>
<td>229</td>
<td>4.5</td>
<td>1.9</td>
<td>2.7</td>
</tr>
<tr>
<td>(2014)</td>
<td>5,442.9</td>
<td>351</td>
<td>6.9</td>
<td>2.8</td>
<td>4.1</td>
</tr>
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3.4 Health Insurance system

The Iranian health system is primarily an insurance based system which represents an important influence on the Iranian healthcare system (Davari et al., 2012). There are two kinds of health packages, which are funded by the health systems and insurance organizations: basic and supplementary packages. First package is basic health services that governments finance the most
part of the costs of this package. The second package includes medical services that are funded by insurance organizations (Barati Marnani et al., 2012).

There are several insurers each with different benefits package co-payments and referral-and counter-referral systems and 90% of the population are under the coverage of at least one kind of health insurance market. Different insurance systems provide different levels of service coverage, so enrollment in different plans makes it easier to shop for services at a lower cost (Mehrdad, 2009).

The main public health insurers are:

1. The Social Security Insurance Organization covers more than 27 million people (36% of the Iranian population) across the country (Davari et al., 2012). Almost all of its customers are workers and employees in the private sector where coverage is compulsory by law (Mehrdad, 2009).
2. Imdad Imdad (Relief) Committee Health Insurance is a charity-based health insurance for the uninsured poor and destitute. About 20% of its revenue comes from charitable donations and the government provides the rest. It covers about 4.5 million disadvantage people (Davari et al., 2012).
3. The Medical Services Insurance Organization (MSIO) covers governmental employees and all individuals of the community with various socioeconomic levels that were not eligible to be covered by other health insurance organizations (Davari et al., 2012). The majority of the health care providers accept patients holding this insurance (Mehrdad, 2009).
4. The Armed Forces Medical Services Insurance Organization (AFMSIO) covers around 4.5 million people in the armed forces and their families (Davari et al., 2012).

Policy with regard to health insurance is developed by the Higher Insurance Council (HIC) and communicated to all health insurance organizations to implement. The council was established in 1994 to undertake policy planning, coordinating and conducting, monitoring and evaluating the quality and quantity of health insurance services (Davari et al., 2012).
Each health insurance company has its own regulation for those who are covering. For example, the regulation provides for those who are covered by the Iranian Social Security Law, medical aids shall be rendered by the Social Security Organization or its affiliated physicians, except in the following cases:

1. The Social Security Organization’s physician considers that the patient’s referral to outside physicians or his treatment outside has been absolutely necessary,
2. The patient has had no access to the Social Security Organization’s medical services, and
3. If the patient notifies the Social Security Organization within 48 hours of his first referral to an outside physicians or hospitalization.

3.5 Health Reform in Iran

Iran’s health system has undergone several reforms in the past three decades with many challenges and successes. The most important reform was the establishment of the National Health Network in 1983, which aimed to reduce inequities and expand coverage and access to health care in deprived areas (Nassemi et al., 1991). The 11th government, elected in June 2013, launched series of reforms in 2014 to respond to some of the known issues in the performance of the health system. The changes, so-called Health Sector Evolution Plan (HSEP) or Health Transformation Plan, were designed by the Ministry of Health and Medical Education (MoHME) based on the fifth 5-year health development national strategies (2011-2016) and the new President’s manifest in order to achieve the universal and comprehensive health services coverage (Moradi-Lakeh & Vosoogh-Moghaddam, 2015).

3.6 Health Sector Evolution Plan

HSEP is a national plan, with two main phases: the first phase relating to improving fair access to healthcare and quality of inpatient and outpatient care in hospitals and the second to the public health care (Moradi-Lakeh & Vosoogh-Moghaddam, 2015, Najafi et al., 2016). The reforms resulted in extensive social reaction and different professional feedback. The official monitoring program shows general public satisfaction. However, there are some concerns for sustainability of the programs and equity of financing (Moradi-Lakeh & Vosoogh-Moghaddam, 2015).
3.7 Health technology assessment in Iran

Iran has one of the first national Health Technology Assessment (HTA) programs in the Eastern Mediterranean Region (2013).

Health Technology Assessment began its activities as a secretariat in the Deputy of Health in 2007 in Iran and it continues as a Health Technology Assessment Office at the Management of Health Technology Assessment, Standardization, and Tariff at the Deputy of curative affairs of Ministry of Health and Medical Education (MOHME) in the beginning of 2010 with structurally enhanced objectives and goals to promote evidence based policy making (Doaee et al., 2012).

The mission of HTA office in Iran is [“systematic and rational assessment of health technologies with the purpose of improving the accessibility and productivity of the health system”] (Doaee et al., 2012).

This assessment is performed by independent experts and evaluates short and long term effects of health technologies until excellence in the quality of health services is achieved. Health technologies include medical equipment, drugs, biological substances, medical procedures, and interventions related to the support, organization, and management systems. HTA measures the effectiveness, efficiency, safety, cost-effectiveness, social effects like justice in access, and ethical and legal outcomes of these technologies as research projects (Doaee et al., 2012).

Olyaeemanesh and Majdzade (2016) stated that [“More than 50 projects were conducted until the end of 2015; however, no evidence is available on the extent to which these projects have been effective.”] (Olyaeemanesh&Majdzadeh, 2016).

Like many developing countries, the process of priority setting and it's criteria in Iran's health care system is not so transparent and explicit (Dehnavieh et al., 2015). Health Technology Assessment has been established in the healthcare system of Iran but what is needed is a clear political will to push forward the objectives of HTA in Iran (Doaee et al., 2012).
4 An empirical investigation into the concept of health

4.1 The Problem of the Investigation on the Level of Theory

Health, illness and hygiene were originally concepts of medical science. These concepts are very important, as without them we cannot understand the functioning of any living systems. Health is both facts and goals of living systems. The first approach is empirical, whereas the second is teleological. Originally the teleological approach was accepted by scholars till the eighteenth century, however later it was rejected by nineteenth century scholars who emphasized working in an empirical manner. After a certain time leading scientists tended to again accept the validity of teleology. Why? Because it became clear that teleology is also a kind of facts established by evolution. (Dawkins, 1991).

We were able to observe that more and more artists, philosophers, scholars and practical, pragmatic actors of intellectual life tended to use the terminology of a goal-oriented way of thinking. This happened not by mere chance. In a number of cases we observe the frequent appearance of goals generating *chains* of acts. These can be called: *functions*. It has also been registered that not all the functions can work smoothly. No wonder that frequently we tend to use the terms health, illness and hygiene often without adequate definitions. Thus, one of the *first* tasks would be to define the above-mentioned notions. The *second* task would be their classification, while the *third* is to model the interaction of the parts in question. Naturally, we will be able to accomplish only a part of this ambitious project.

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1 This chapter draws upon:

### 4.2 The Problem of the Investigation on the Level of Practice

Why are we interested in the above-mentioned set of questions? Well, we humans are not a species that is passive and merely adaptable. We always have some kind or types of values, intentions and goals to arrange both our inner and outer environment. The simple reason for this is the nature of our species. In the case of animals, their planning and regulation of behavior is performed by the genome. But we humans do not have only intact genes. The cause of this is the deterioration of our genes in the course of evolution. Or to give a more general and precise explanation, we are simply saying that *an untrained function disappears like a bird or animal*. Watson and Crick found that around 2% of our genes are ill, while 98% are only so-called “junk” (Marks, 2003). The job of healthy genes is to adapt living organisms to nature, whereas the job of “junk” is to be a basis for changing living creatures, via artificial programs of creativity often called artificial genes, memes or cultures and civilizations. Thus, a preliminary *definition of mankind could be: a creative cultural living system.*

*Health on the level of animals is a trouble-free adaptation. Health on the level of human beings is the free and successful process of problem-solving.* These considerations suggest that there exists one basic, general difference between man and animal and many particular features coming from this basis. Keep in mind that man is mainly determined by culture and subsequently by civilization. People’s survival depends on these programs or cultures. If your program is a pro-life project, then you will be healthy. Alternatively, if your program rests on anti-life axioms, postulates or theses, then your culture will lead you towards illness and death.

It is a matter of course that not only human beings start their existence or being, but so do all animate and inanimate entities. Everything appears, develops, reaches a peak, then declines and ceases to exist. However there is a great difference in this respect between animate and inanimate systems. *Some physicists have maintained that while inanimate systems have only one direction, entropy and disintegration, living systems – on the contrary – can repeatedly reproduce themselves both personally and via children (thus demographically and culturally).* The great miracle of the birth of life from inanimate matter still belongs to the unknown. Philosophers prefer to think paradoxically and put down in their works the principles of dialectics, according to which one extreme produces the opposite one. However, this is not enough for any serious scholarly...
investigator. We need a more exact explanation of life via building mechanisms, models, and experiments illuminating the emergence of life and the ability of self-reproduction. In all likelihood, life itself is an important innovation by which the entities can prolong their existence.

As we – the authors of this paper – are neither philosophers, nor physicists or biologists and so have no competence concerning the miracle of the appearance of the first living systems, it would be more reasonable to limit ourselves to social sciences, psychology, humanities, sociology, history and the like. We know from some writings that man’s biological parts, man himself, the social institutions, organizations, states, cultures and civilization and so on first rise, secondly reach more or less well-balanced states and finally cease to exist. The third section of this path always shows symptoms of illness. Illness is always a process. Recovery and/or curing make life either reversible or self-sustainable. In a word: self-repeatable. One can imagine how many notions, understandings and definitions are needed to cover this large area of study with valid knowledge. The first and self-evident structure where these conceptions and definitions should be arranged is like a cross: we will find both subordinated (Aristotelian) and coordinated (phenomenological) definitions.

4.3 Why Should We Study Such a Difficult Topic? What is the Reason for Our Work?

Humans or mankind itself work according to certain values, norms, intentions and goals. Some happenings are accepted by them, others are rejected. Two options again are possible: pro-life and anti-life. But the simplicity offered by these small classifications is not real. In the old Biblical period, the main value was the growing number of human beings. The most outstanding gift which the God of the Old and New Testaments promised was the multiplication of offspring. In history, culture worked as a huge artificial program, institution, organization and even enterprise, if you wish. It supported large families producing and raising many children. Pro-life culture was extremely successful. Mankind occupied almost all the evolutionary niches.

Alas, today we have to speak of the monster of overpopulation. While in the past health, beauty, identity, morality, intelligence, sociability, traditions and so on were the main issues, in our time illness, ugliness, multiple personality, amorality, ignorance, crime, chaos, social entropy, improvisations and so on are more than fashionable. There is a growing body of literature which
speaks of – and in doing so even urges and promotes – the end of history, of art, of morality, of the multicultural world. Another expression for “end” is the now much more fashionable: “beyond”. *We admit that overpopulation is a major problem. But as far as the means for solving this problem are concerned, we cannot follow the new and dirty course.* We are interested in preserving the pro-life values, and instead of either the multiplication or elimination of offspring, *we again and again propose the regulation of population as the royal road to the sustainable number of/in populations.* So, as a contribution to this end we will take up only a small but important part of this large task, namely the issue of health.

### 4.4 Definitions and Wisdom Concerning Health

#### 4.4.1 A preliminary but long overview

To begin with, we shall repeatedly mention a couple of general principles. Unfortunately, at the end of the 20th century, a strange anti-definitional movement emerged in the fields of sciences. Instead of undertaking the responsibility of defining the topics and concepts, scholars preferred to hide behind the complexity of their subject matter. Many disciplines became a huge market of opinions, where every scholar has the (human) right to create his or her approach, and the field is obliged to accept these opinions as respectable achievements. Far from it! *Science is a realm of findings and has nothing to do with mere opinions.* Why? Because opinion can be – and frequently is – merely subjective, whereas a statement or finding is supported by other findings and/or well established facts. Normal science begins with the simplest starting point and the enrichment of relevant knowledge is a matter of empirical and logical necessity.

Science is by no means a private enterprise with *private* methods and definitions. On the contrary, any specifications should be common in every discipline within the group of experts. Generally speaking, without a precise goal there is no possibility for any reasonable actions. For example, a medical doctor cannot pursue his or her aim of curing people without knowing the essence of health. Otherwise each individual would have to be familiar at the least with his physical and mental conditions and able to cure them, especially if he is seriously ill. It is on the market of material goods that we sell and buy our digital entities. Competition exists everywhere on Earth and consequently also in the realm of science. Nevertheless, cooperation is for the most part the leading and desirable moral principle of investigations.
As far as the method of our modest study is concerned, the specification comes into existence or being by surpassing the limitations of the enormous number of particular definitions. The above-mentioned limitations in our special case can be as follows: positive or negative, well-being or freedom from illness, serious or mild sickness, professional definition of health versus laymen’s opinions, and so on (Blaxter, 2010). Let’s make a preliminary order among these cases!

Figure 2 Possible degrees of health

The figure above shows the possible degrees of health. These concepts can be found in Blaxter’s book, but this two-dimensional “pyramid” and its interpretations are ours (Blaxter, 2010). The closer to the top a notion is, the narrower both its empirical and logical scope. It would also be not only possible but important as well – via serious empirical and theoretical studies – to construct a bipolar scale having a central “zero” point of indifferent state on the margin of health and illness. However, the conditions of living systems usually are not in a clear, clean and transparent state of health or illness. “The suggestion is, therefore, that ‘none of us can be categorized as being either healthy or diseased, (instead) we are all located somewhere along a continuum’ (Sidell, 2010: 27)” (Blaxter, 2010). Perhaps the best subjective psychological indicator of health – although not totally accurate – can be the lack of subjective symptoms, e.g. the absence of pain (Illyés, 1976). The famous Hungarian poet and writer discovered that it is illness which introduces our physiological organs to us.
4.4.2 Our Preliminary Hypotheses

First of all, we immediately have to eliminate a conception widely held in the past and popular among laymen, according to which health is nothing other than a machine-like functioning of living systems. To deal with this mistaken view, we have to define the concept of machine. However, this is now an extremely difficult task. For a long time – thousands of years – a machine was a system of smooth process by an artificial mechanism, which itself could multiply men’s efforts mostly in work and art (e.g. musical instruments). This feature was expressed most clearly by the simple machines (Archimedean lever, pulley, and screw) in a transparent way. “Reuleaux’s definition of a machine has remained a classic: ‘A machine is a combination of resistant bodies so arranged that by their means the mechanical forces of nature can be compelled to do work accompanied by certain determinant motions.’” (Mumford & Winner, 2010) Mumford added to this definition the non-organic nature of classical machine.

However, these sorts of definitions are now outdated. Mumford recognized this: “Instead of simplifying the organic, to make it intelligibly mechanical, as was necessary for the great eotechnic and paleotechnic inventions, we have begun to complicate the mechanical, in order to make it more organic; therefore more effective, more harmonious with our living environment.” (Mumford & Winner, 2010) Informatics – as one of the greatest, newest revolutions of mankind – has gone radically beyond the mechanical, non-organic approach concerning machines. Today’s machines are very anthropological or humanoid and have little to do with the principle of mere mechanics. Now, what is the difference between mechanical and organic? Our preliminary hypothesis is as follows: the mechanical is a system of linear causalities, whereas the organic is a system of circular causalities.

The problem is that while radically new mechanisms were created, the theory of machines failed to enlarge its basic concepts. The new machines can imitate thinking and – soon – also creating. Moreover, the general notion of machine can rather be as follows. For us machines are the imitations of living systems by engineering using inanimate matter in the service of mankind. The part of the definition “in the service of mankind” is the key point of our approach. Before continuing this train of thought, we must emphasize that the nature of the main determination of human beings is not mechanical. People are determined by their problems: they have a problem
structure.

Well. Let us see what health is. It is that kind of self-reproduction by which any living system contributes to the self-reproduction of its meta-systems. The function of the meta system – for the living system – is its preservation. There are basically three cases of health. At first: the health of the emerging living systems (young) is: reproduction of itself by exceeding its original “it”, and thereby extending and improving its meta-system as well. This is what we call development. This is an offensive way or strategy. Secondly: the health of the living system in its mid-ages is: reproduction of itself and thereby of its meta-system on the same level. This is rather a simple repetition, which can be called sustainability. This is the Midfensive case (I coined this terrible – but useful – notion: I.M.B.). Thirdly: the health of the so-called generation X – that is the old – is: reproduction of itself by increasing input under the circumstances of lawfully decreasing output. The strategy of the old is defensive. The price of life becomes higher and higher. Death comes when no effort produces the smallest output. The three phases of life are: Development (up), Plateau (horizontal), Decline (descent). It is better to measure people on the basis of their achievements and not on the basis merely of their biological age. And now let us see the applications of these definitions. Without successful applications no valid science can exist.

4.4.3 Applications

Briefly speaking, the health of physiological organs: a semi-mechanical process. The health of the personality: a constructive private drama. The health of the family: mutual physical and psychological support. By the way, we make a distinction between the family and marriage. The family loves, supports, takes care of and develops its members, while marriage is mostly a formal act, which may or may not be good and bad from the point of view of the above. The health of society: some conflicts and balances between horizontal and vertical power. The health of culture: conflicts and balance between contradictory ideas and identification. The health of ethnic groups: balance between intolerance and tolerance. The health of nations: wealth of nations (Smith, 1776) and European concert (Polanyi, 1944). The health of continents: war and peace. The health of mankind: vertical contra horizontal globalization. Today’s Western globalization has the philosophy of phenomenology as its ideology. This sort of philosophy denies the so-called
“abstraction ladder” and prefers a picture of the world where there are no differences between the concrete and the abstract. That is, phenomenology is a – mutatis mutandis – Renaissance of a pre-Columbian flat world. Western globalization is not above nations, but instead of them. *The above politics and its ideology need considerable improvement in the future.*

4.4.4 Some Other Important Definitions

Do not think that we have presented above the final definitions. Far from it! They are merely hypotheses to be studied and subsequently confirmed or refuted. Our study is in fact a pilot study or work in progress. Thus we must turn to both literature and empirical studies. To begin with, first let us see some examples of definitions of health coined by distinguished authors and organizations who represent the spirit of different historical periods. Neither can all these definitions alone mirror the very essence of health successfully. Nonetheless they are wise, illuminating, clever, useful and usable. This small but valuable collection has been made by Mahshid Moradi

- The World Health Organization (WHO) defined health in its broader sense in 1946 as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”, (Grad, 2002)

- Merriam-Webster dictionary gives three definitions of Health (2014b):
  1- a: the condition of being sound in body, mind, or spirit; especially: freedom from physical disease or pain
     b: the general condition of the body ‘in poor health’ ‘enjoys good health’
  2- a: flourishing condition: well-being ‘defending the health of the beloved oceans — Peter Wilkinson’
     b: general condition or state ‘poor economic health’
  3- a: a toast to someone’s health or prosperity

- The Oxford Dictionary’s definition of health is: the state of being free from illness or injury and a person’s mental or physical condition (2010).
• Medilexicon’s medical dictionary has three definitions for health (2014a):

  1. The state of the organism when it functions optimally without evidence of disease or abnormality.

  2. A state of dynamic balance in which an individual’s or a group’s capacity to cope with all the circumstances of living is at an optimal level.

  3. A state characterized by anatomic, physiologic, and psychological integrity, ability to perform personally valued family, work, and community roles; ability to deal with physical, biologic, psychological, and social stress; a feeling of well-being, and freedom from the risk of disease and untimely death.

• Boon How Chew (2011), family physician and lecturer in family medicine defined health as “Health is defined as the ability to adapt and self manage in the face of social, physical, and emotional challenges.” (Huber et al., 2011)

• Franklin P. Adams defined health as “the thing that makes you feel that now is the best time of year”.

• In 1986, the WHO, in the Ottawa Charter for Health Promotion, said that health is “a resource for everyday life, not the objective of living. Health is a positive concept emphasizing social and personal resources, as well as physical capacities.” (2017c)

• Maloof (1991) argued that a perception of health or mental health is not only defined within the medical context, but it is also defined by the patient within a sociocultural context that includes family and social network as well as a wide selection of potential providers. Such definitions may vary from one culture to another. Research among ethnic groups in the U.S. demonstrates the complexity in a non-clinical definition of health and illness (2017a).

• Earle (2007) mentioned that health has been called “an abstract concept” that people can find difficult to define (Warwick-Booth et al., 2012).

• Johnson (2007) argued that health is one of those things that most people assume they understand. But if we just stop and consider it for a moment and try to focus on it, it starts to float about in our minds (Warwick-Booth et al., 2012).
• Tones and Green (2004) refer to health as dichotomous differences in approaches to defining health. On the one hand there are positive approaches to defining health (health as well-being or as an asset) and on the other hand there are more negative definitions of health – those that are illness- or disease-oriented. When health is viewed in a negative way, then definitions will tend to focus on health as absence of disease. When health is viewed in a positive way definitions tend to be broader and take into account concepts such as ‘well-being’ (Warwick-Booth et al., 2012).

• Aggleton (1990) argues that health is something that can be bought (by investment in private health care) or sold (through disease or injury). (Warwick-Booth et al., 2012)

• Seedhouse (2001) describes health as the ‘foundations for achievement’. Health is a complex and contested concept. Seedhouse views health as the means by which we achieve our potential, both as individuals and as groups. Seedhouse (1986:61) therefore describes a person’s optimum state of health as being ‘equivalent to the set of conditions that enable a person to work to fulfill her realistic chosen and biological potentials’ (Warwick-Booth et al., 2012).

• Dorland's Medical Dictionary defines health as “a state of optimal physical, mental, and social well-being, not merely the absence of disease (Ratson, 2003).

• According to a nurse aged fifty-two from Moscow, “Health is both your inner and your outer state – the state of soul – being more optimistic, not giving in to any kind of difficulties, trying to find some kind of compromise….and also, probably, being needed by society too, however old you are” (Blaxter, 2010).

• “Complete physical, mental, social and spiritual well-being for individuals and populations.” (Edlund, 2012)

• Health is defined as the ability to adapt and self-manage in the face of social, physical, and emotional challenges (Godlee, 2011).

• What is health? For most people, it is a state of “perfection”, thus excluding most of us; but health is a social right, therefore it should be a possibility for all. This makes us wonder what health really is, and in this aim centering our attention on people with disabilities as
a paradigm is really useful (Bellieni, 2014).

4.4.4.1 A Short Quasi-Classification of the Definitions Above

Investigating the short but valuable set of health definitions, we regard it as important to classify them merely on a level of plausibility. This method of classification is an age-old means of reasoning, created by Aristotle. Without it not only the means of definitions is impossible, but the whole rationality, moreover rationalism as well (rationality being an instance of the preconscious, while rationalism being an instance of the conscious). It is true that today’s scientific life and the whole intellectual climate prefer such terms and directions as metaphor, phenomenology and postmodern; we will remain old-fashioned, conservative thinkers. **Constructive conservatism is not a kind of backwardness. It is rather the preservation of successfully tested results.** For us science and intellect are not the tools of omniscience. We accept Kant’s view that reason has its limitations. However, what is beyond our **actual** reason cannot be understood by us at all. In our “philosophy” the only way of understanding reality is the enlargement of reason and not cowardly flight from it (Gross et al., 1996). **The brick of the building of classification is definition, and the building of classification is made of the bricks of definitions.** Without classification rational models and constructs cannot be built, or they collapse. However, it is also true that to give here and now a correct and final classification is impossible. **So we tried to arrange the cited classification on appropriate levels of the ladder of abstraction.** This would be a door to the second step – after the first one of collecting– towards further – but also preliminary – classifications. This venture will be performed by us only in a rudimentary way.

4.4.4.2 On the Ladder of Abstractions

Working on the above definitions, we identified a number of aspects. Namely: capacities, resources, assets, well-being, absence of disease, physical, psychological, mental, social, state of perfection, social right, ability to adapt, cope with challenges, emotional, self-manage, relative, spiritual, subjective, longevity, optimism, fitness, compromise, achievement, realism, biological, balance, integrity, identity, coping with stress, freedom,
stress, risk. The number of aspects shows the complexity of the notion of health. However, we were also able to reduce this complexity. Counting the number of occurrences of these aspects in these definitions, we found the winner. This was “well-being”, a psychological, economic, subjective and so on term. “Well-being” in general got 7 points. Physical well-being has 8 points, mental well-being – 5 points, social well-being – 3 points, spiritual well-being – 2 points. That is, special cases of well-being have altogether 18 points. If we add the general and special points, which is not an entirely correct method, the result will be 25 points. In second place we find “asset”, “absence of disease” and finally “ability to adapt”. These aspects scored only 4 points each. All the other aspects lagged far behind the winner.

What can we add to this overall picture? There are wide gaps between the complexity of the phenomenon of health and the simplicity of theoretical considerations in this domain. No wonder that not only laymen but also medical doctors, politicians, sociologists, psychologists, managers, artists, philosophers and scholars are ignorant concerning the issue of health. Just a further remark: health and sickness can be detected in both vertical and horizontal dimensions. As far as the horizontal dimension is concerned, we can speak of the health or illness of every profession, whereas on the vertical dimension it is possible to study the issue of health and illness on the levels of individuals, family, groups, social layers, cultures and so on. Moreover, the aspects of health and illness on the transcendental level are also absent. Thus, we are far from solving all the problems in this area. Well-being itself was more general in practice and not theoretically. We did not find even the shadow of either a horizontal or a vertical approach to the matter to be studied. Well-being seems to be only one of the stereotypes and remnants of the wealthy society that has already collapsed.

4.4.5 Wise Sayings

Below our readers will find a number of wise sayings, “coined” again by great minds from different historical eras and from different countries and cultures. I hope that the readers of this work will make successful use of them. Let’s read them:
Publilius Syrus: “There are some remedies worse than the disease.”

Hippocrates: “We must turn to nature itself, to the observations of the body in health and in disease to learn the truth.”

- **Johann Wolfgang von Goethe**: “Take care of your body with steadfast fidelity. The soul must see through these eyes alone, and if they are dim, the whole world is clouded.”
- **Sydney Smith**: “I am convinced digestion is the great secret to life.”
- **H.G. Bohn**: “Nature, time and patience are three great physicians.”
- **Henry Miller**: “Our own physical body possesses a wisdom which we who inhabit the body lack. We give it orders which make no sense.”
- **Benjamin Disraeli**: “Time is the great physician.”
- **Spanish Proverb**: “A man too busy to take care of his health is like a mechanic too busy to take care of his tools.”
- **Alexander the Great**: “I am dying with the help of too many physicians.”
- **Benjamin Franklin**: “God heals, and the doctor takes the fee.”
- **Mark Twain**: “The only way to keep your health is to eat what you don’t want, drink what you don’t like, and do what you’d rather not.”
- **Francois Voltaire**: “The art of medicine consists of amusing the patient while nature cures the disease.”
- **Napoleon**: “Water, air, and cleanliness are the chief articles in my pharmacopoeia.”
- **Mahatma Gandhi**: “It is health that is real wealth and not pieces of gold and silver.”
- **Hippocrates**: “A wise man should consider that health is the greatest of human blessings, and learn how by his own thought to derive benefit from his illnesses.”
- **Plato**: “Attention to health is life’s greatest hindrance.”
- **Bill Gates**: “As you improve health in a society, population growth goes down. You know, I thought it was... before I learned about it, I thought it was paradoxical.”
- **Buddha**: “The secret of health for both mind and body is not to mourn for the past, worry about the future, or anticipate troubles but to live in the present moment wisely and earnestly.”
• **Albert Einstein:** “The devil has put a penalty on all things we enjoy in life. Either we suffer in health or we suffer in soul or we get fat.”

### 4.5 Research Design

We decided to take a survey of *laymen’s opinions concerning the everyday notions of health* (originally we planned to have expert’s definitions as well, but none of the famous Hungarian universities responded to our request to participate in this important survey, which would use the well-known strategy of a typical expert method). The non-professional participants were – as a rule – asked to indicate their sex, age, level of education, profession, and ethnic group. We gathered thirty-four factors (Table 4) – usually associated with the domain of health – and asked the participants to rate the importance of each factor in respect of health in general and also asked them to add factors which they think are important in these respects. In our questionnaire, the degree of possible importance was from 0 to 6 as follows: most irrelevant, irrelevant, not at all relevant, neutral, less relevant, relevant, and most relevant.

*Table 4 List of factors the authors could choose to ask the participants to find the most relevant to the most irrelevant factor which contribute to health in general*

<p>| | | | | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
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<td>Attractiveness</td>
<td>25</td>
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<tr>
<td>2</td>
<td>Reproduction of Society</td>
<td>14</td>
<td>Fitness</td>
<td>26</td>
<td>Engagement</td>
</tr>
<tr>
<td>3</td>
<td>Sociability</td>
<td>15</td>
<td>Workability</td>
<td>27</td>
<td>Inner Freedom</td>
</tr>
<tr>
<td>4</td>
<td>Well-balanced</td>
<td>16</td>
<td>Ability to Relax</td>
<td>28</td>
<td>Productivity</td>
</tr>
<tr>
<td>5</td>
<td>Machine-like</td>
<td>17</td>
<td>Sport</td>
<td>29</td>
<td>Innovativeness</td>
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<tr>
<td>6</td>
<td>Flow</td>
<td>18</td>
<td>Goals, Harmony</td>
<td>30</td>
<td>Positive Emotional Feeling</td>
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<tr>
<td>7</td>
<td>Constructive Programs of Personality</td>
<td>19</td>
<td>Religiousness and Belief</td>
<td>31</td>
<td>Constructive Hobby</td>
</tr>
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<td>Normal Genes</td>
<td>20</td>
<td>Optimism</td>
<td>32</td>
<td>Morality</td>
</tr>
<tr>
<td>9</td>
<td>Identity or Rooted in one’s Culture</td>
<td>21</td>
<td>Realism</td>
<td>33</td>
<td>Love</td>
</tr>
<tr>
<td>10</td>
<td>Creativity</td>
<td>22</td>
<td>Maturity</td>
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<td>Responsibility</td>
</tr>
<tr>
<td>11</td>
<td>Longevity</td>
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<td>Playfulness</td>
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</tr>
<tr>
<td>12</td>
<td>Beauty</td>
<td>24</td>
<td>Discipline</td>
<td></td>
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</tr>
</tbody>
</table>
4.5.1 Instructions for scoring each factor

We calculated how many participants answered to each degree for each factor. The maximum total score can be 735 and the minimum 7 for each factor. The higher the score, the more important the factor is to the overall health of a person.

4.5.2 Scoring

The scoring of each factor is as follows:

- 0. Most Irrelevant scored 1
- 1. Irrelevant scored 2
- 2. Not at all Relevant scored 3
- 3. Neutral scored 4
- 4. Less Relevant scored 5
- 5. Relevant scored 6
- 6. Most Relevant scored 7

Scoring of each factor is calculated by counting how many times participants answered most irrelevant, irrelevant, not at all relevant, neutral, less relevant, relevant and most relevant to each factor, then the total number of each factor was multiplied by the score we gave to each degree and finally we add up all the numbers. The formula is: \((\text{Numbers choosing most irrelevant} \times 1) + (\text{numbers choosing irrelevant} \times 2) + (\text{numbers choosing not at all relevant} \times 3) + (\text{numbers choosing neutral} \times 4) + (\text{numbers choosing less relevant} \times 5) + (\text{numbers choosing relevant} \times 6) + (\text{numbers choosing most relevant} \times 7)\). For example, 105 participants answered the factor of Ability to relax, the numbers of participants who chose most irrelevant, irrelevant, not at all relevant, neutral, less relevant, relevant, and most relevant, for the factor of ability to relax were 0, 0, 1, 8, 14, 29, 53, respectively. One participant did not answer for this factor. The total value for the factor of ability to relax calculated in this way:

\[(0 \times 1) + (0 \times 2) + (1 \times 3) + (8 \times 4) + (14 \times 5) + (29 \times 6) + (53 \times 7) = 530\]
Table 5 Calculation of factors based on the participants’ answers 1-9.

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<td>F*S V</td>
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<td>1</td>
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<td>0</td>
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<td>22</td>
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<td>0</td>
<td>0*2</td>
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<td>30</td>
<td>8*3</td>
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<td>12</td>
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<td>3</td>
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<td>30*5</td>
<td>150</td>
<td>27*5</td>
<td>13</td>
<td>5</td>
<td>15*5</td>
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<td>8</td>
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<td>14</td>
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<td>14</td>
<td>0</td>
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</table>

* Frequency * score of each degree (Most Irrelevant: scored 1, irrelevant: scored 2, not at all relevant: scored 3, neutral: scored 4, less relevant: scored 5, relevant: scored 6, most relevant: scored 7)

**Value
Table 6 Calculation of factors based on the participants’ answers 10-18.

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<td>-</td>
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<td>6*2</td>
<td>12</td>
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<td>7*2</td>
<td>14</td>
<td>0*2</td>
</tr>
<tr>
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<td>4*3</td>
<td>12</td>
<td>6*3</td>
<td>18</td>
<td>13*3</td>
<td>39</td>
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<td>100</td>
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<td>96</td>
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<tr>
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<td>32*5</td>
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<td>34*5</td>
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Table 7 Calculation of factors based on the participants’ answers 19-27.

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<td>0 Most Relevant</td>
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<td>0</td>
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<td>4*1</td>
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<td>0</td>
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<td>1 Irrelevant</td>
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<td>6</td>
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<td>2 Not at all</td>
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<td>3 Neutral</td>
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<td>17*4</td>
<td>68</td>
<td>18*4</td>
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<td>602</td>
<td>481</td>
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I do not know means the participant did not answer.
Most Relevant means the participant answered the most.
Most Relevant

I do not know
Table 8 Calculation of factors based on the participants’ answers 28-34.

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<td>2 -</td>
<td>2 -</td>
<td>1 -</td>
<td>1 -</td>
</tr>
<tr>
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<td>1*1 1</td>
<td>2*1 2</td>
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</tr>
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<td>2 Not at all</td>
<td>6*3 18</td>
<td>9*3 27</td>
<td>1*3 3</td>
<td>7*3 21</td>
<td>12*3 36</td>
<td>5*3 15</td>
<td>7*3 21</td>
</tr>
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<td>3 Neutral</td>
<td>12*4 48</td>
<td>18*4 72</td>
<td>3*4 12</td>
<td>13*4 52</td>
<td>21*4 84</td>
<td>7*4 28</td>
<td>15*4 60</td>
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<tr>
<td>4 Less Relevant</td>
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<td>28*5 140</td>
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<td>23*6 138</td>
<td>33*6 198</td>
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<td>14*7 98</td>
<td>55*7 385</td>
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<td>659</td>
<td>553</td>
<td>503</td>
<td>627</td>
<td>560</td>
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</table>
Finally, factors were sorted in descending order in the basis of the sums explained above. We present it in more visible form:

1. Positive emotional feeling 659
2. Optimism 633
3. Fitness or Goal, Harmony 630
4. Love 627
5. Well-balanced 614
6. Inner freedom 608
7. Lack of illness 602
8. Sport 588
9. Productivity or sociability 572
10. Workability or creativity 570
11. Responsibility 560
12. Constructive hobby 553
13. Realism 542
14. Discipline 539
15. Ability to relax 530
16. Innovativeness 527
17. Maturity 522
18. Constructive program of personality 517
19. Morality 503
20. Normal genes 499
21. Longevity 488
22. Engagement 481
23. Self-reproduction 474
24. Identity rooted in one's Culture or Attractiveness 473
25. Playfulness 456
26. Beauty 440
27. Reproduction of society 415
28. Flow 382
29. Religiousness and belief 380
30. Machine-like 327
4.5.3 Results

Survey questionnaires distributed to 105 participants aged 19 to 63 years. The mean age was 31 (SD 9.1), 66.7 % (n=70) of the participants were female and 33.3 % (n=35) male. 2 % had completed secondary school, 45.7 % had a Bachelor’s degree, 35.2% a Master’s degree, 13.3% a PhD and 3.8% others.

Table 5,6,7,8 show the factors from the point of view of evaluation expressed in numbers given by the members of the population studied. The first five most relevant factors are Positive emotional feeling, Optimism, Fitness, Goal and harmony, and Love, respectively, and the five most irrelevant factors are Machine-like, Religiousness and beliefs, Flow, Reproduction of society, and beauty. Some of the most important aspects of health, such as – Discipline, Ability to relax, Innovativeness and Maturity – were placed by participants in the mid part of our rank order. Not to speak of Creativity. It occupies the 10th place in the rank order of aspects of health. Participants were asked to add factors which they thought were important and they were as follows: no stress, patience, security, proper partner relations, education, healthy diet, social responsibility, motivation, loving animals, spiritual well-being, internal and external balance, faithful and reliable friends.

4.6 Discussion

We cannot be especially happy about these results. The “Positive emotional feeling” is a dubious criterion, especially if we do not know why a person experiences “positive emotional feeling”. If, for example, somebody is a sadist, they will have a positive emotional feeling when they torture the victim. A dictator enjoys acting without any moral and/or practical limitation. An idle person is happy even avoiding work that is necessary for him or her. As far as the aspect of “Optimism” is concerned, this is a very important but by no means an omnipotent feature of health. An optimist can also be a heavy drinker who harms himself and the life of his or her family. The same can be said about the drinker’s style of life and social relationships. “Fitness or Goal and Harmony” are again, beyond doubt, very important factors of soundness. However, they have to be understood correctly. Fitness in its classical conceptions spoke of a person’s good adaptation to the conditions of niches of his bio-cultural environment, and not simply to be smart and strong. Similar statements
can be made for goal and harmony. Without goals we live in psycho-physical entropy, whereas harmony is essential for all animate and inanimate matter. “Love” is again a notion applicable on both the transcendental and worldly levels. The famous Greek philosopher Empedocles applied it to the solar system, while Jesus Christ applied it to human relationships. It was Newton who first coined from it a secular term. What is in fact the concept of “Well-balanced”? This qualification is appropriate for the large systems which can be characterized by three properties, namely: being complex, contradictory and random. These properties are obligatory because both beyond and beneath the human being and including also the latter, we have not found a unique feature of living systems.

Likewise the items in the middle of the scale present very important aspects from the point of view of health. They are as follows: “Discipline”, “Ability to relax”, “Innovativeness”, “Maturity”. These features are even more important than the first five winners of this unusual race. All of them contribute much more and better to private and public health than the first five. There are a lot of average people and medical practitioners who have many things to do with public health questions. Now, let’s see the most “inferior” aspects of our scale! They are: “Machine-like”, “Religiousness and beliefs”, “Flow”, “Reproduction of society” and “Beauty”. To our great surprise these aspects have the most importance as regards human soundness. “Machine-like” – if it is identified with strict and strong determination – is unacceptable. But if the term machine includes new techniques like the Internet, the matter seems different: strict determination immediately evaporates and the notion of human-like becomes acceptable, important and appropriate. Now, “Religiousness and belief” are the most important values in history. Without them no enlightenment and progress are possible. Mutatis mutandis, the same can be said of humanity and health. “Flow” – the term coined by Csíkszentmihályi – is one of the best characteristics of healthy functioning of man and mankind.

This proto-psychological type of psychological concept expresses the lack of obstacles in living systems’ functioning, without which health is impossible. Finally: “Reproduction of society” and “Beauty” mean, on the one hand, sustainability and on the other hand signal a biological, psychological and mental excellence.
4.7 Summary

Concluding our work, let me be very brief at the end of the paper. Our first remark is: that the laymen’s concepts of health are usually upside down notions. What is health and soundness for a layman is the opposite of logic and good sense. Can we illuminate the background of these approaches? We all know that our historical age is the age of liberalism. But what is liberalism? Is it a possibility or is it a necessity? For us liberalism is first all a necessity. Why? Because we, in the Euro-Atlantic culture, have developed our culture to such an extent that it is impossible for the average man to keep up with the changes. The balance between the general and particular values vanishes to the benefit of particularities. As a result poor man confronts a huge amount of problems in his mental helplessness. Under these circumstances freedom is not a gift, it is a compulsion. Busy with solving their particular problems, people’s minds are occupied by particular opinions. The only and useful issue in liberalism is that its practice is similar to the diversity in psychological studies. It can considerably contribute to the growing number of ideas and conceptions and subsequently to selecting and finding the best solution for the time and place. It is no wonder that we found such a distorted picture not only in the health question but in almost all domains of thinking and acting. The only way out of liberalism – a historical phase between the past and the future – lies in the substantial elaboration of a new set of integrative principles which make the culture again simpler, more collective, transparent and helpful. We have to enter a new period of history as soon as possible.
5 Description of the discussed health problem – psoriasis

5.1 Epidemiology and definition

Psoriasis is a chronic inflammatory disease affecting approximately 2% of the population globally (Michalek et al., 2017). In Europe, the prevalence of psoriasis varies largely across countries, it ranges between 0.73% in the United Kingdom to 2.90% in Italy. In Iran, the prevalence of psoriasis is estimated to be around 1% (Baghestani et al., 2005, Noorbala&Kafaie.P., 2010). In the US, the estimated prevalence of diagnosed psoriasis is 3.15%. However, it is reported to be less prevalent in Asia than in Europe (Chandran&Raychaudhuri, 2010). A quarter of patients develop the disease before the age of 20 years. A further peak in incidence is recorded in the fifth and sixth decades (Leman&Burden, 2008).

The literature suggest that four-fifth of patients present with mild disease, whereas 20% have moderate to severe disease (Menter et al., 2011). According to the European consensus, the severity of psoriasis is defined based on the extent of body surface area (BSA) affected, Psoriasis Area and Severity Index (PSA) and Dermatology Life Quality Index (DLQI) (Mrowietz et al., 2011). Mild disease is defined as (BSA $\leq 10$ or PASI $\leq 10$) and DLQI $\leq 10$, while moderate to severe psoriasis is defined as (BSA > 10 or PASI > 10) and DLQI > 10 (Finlay, 2005).

5.2 Diagnosis of psoriasis

Psoriasis is a chronic dermatological condition with multiple phenotypical variations and degrees of severity.

Diagnosis is primarily based on the clinical symptoms. The most common clinical subtype is chronic plaque psoriasis, which is also called psoriasis vulgaris, and it is characterised by well-demarcated bright red plaques covered by adherent silvery white scales (Boehncke&Schon, 2015). These may appear in any localisation, most often symmetrically, especially the scalp and extensor surfaces of extremities. The differential diagnosis includes other dermatological conditions, such as eczema, lichen planus and systemic lupus erythematosus (Boehncke&Schon, 2015). Another clinical subtype, guttate psoriasis is characterized by the rapid development of multiple small papules over wide areas of the body. Generalised pustular psoriasis is a rather rare form, presenting...
as multiple non-follicular pustules within plaques of psoriasis. If occurs acutely, it is often associated with fever. There are many genetic and environmental factors described to determine the induction and/or exacerbation of psoriasis (Zeng et al., 2017), for example, stress is a well-known trigger factor playing a role in acute exacerbation of psoriasis (Ferreira et al., 2016). Psychological stress or an abnormal response to stressors were reported to modify the evolution of skin disorders (Basavaraj et al., 2011).

5.3 Characteristics of the disease

Psoriasis has a variety of different presentations. The classic presentation is of well-defined red plaques with silver scale. The characteristic scale makes the disorder highly visible and intrusive on the patient's lifestyle. The visible nature of the disease ensures that psoriasis has both physical and psychosocial effects. In normal skin, epidermal cell reproduction and proliferation takes 28 days. In psoriasis this process is considerably accelerated to approximately 4 days, resulting in the deposit of immature cells on the skin (Ryan, 2008).

Up to 50% of patients with psoriasis have concurrent nail psoriasis, with a lifetime incidence of 80% to 90% in psoriasis patients (Reich, 2009). Clinical manifestations of nail psoriasis are pitting, discolouration, onycholysis and subungual hyperkeratosis as well as nail plate crumbling and splinter haemorrhages. Nail psoriasis is associated with discomfort in many patients and leads to significant functional impairment and psychological stress. The often distressing appearance of affected nails impacts the patient tremendously in both work and social activities. Importantly, 80% of patients with psoriatic arthritis have nail psoriasis (Baran, 2010).

The physical symptoms of psoriasis include itching, irritation, burning/stinging, sensitivity, and pain. Patients also suffer psychological distress, especially as a result of stigmatization, self-consciousness, and embarrassment, which can in turn affect employment and social activities (Van Voorhees & Fried, 2009). Disease management will be dependent on disease severity, psychosocial effects and the patient's lifestyle (Ryan, 2008).

Psoriasis is often associated with a number of comorbid conditions (Takeshita et al., 2017a, Takeshita et al., 2017b). Psoriatic arthritis (PsA) is the inflammation of the joints, which is present in 20–40% of individuals with psoriasis and has an estimated prevalence of 0.1–1.0% in the
general population (Gladman et al., 2005, Mease & Armstrong, 2014). Obesity, type 2 diabetes, metabolic syndrome (Takeshita et al., 2017a), depression and suicide, smoking, and alcohol consumption are also more common in patients with psoriasis (Menter et al., 2011, Gupta et al., 1987, Ginsburg & Link, 1989). Patients with psoriasis demonstrate a higher prevalence of cardiovascular risk factors and may have an increased risk for coronary heart disease, cerebrovascular disease or peripheral arterial disease (Patel et al., 2011). Epidemiology studies found that psoriasis and Crohn’s disease (CD) share common genetic background, with a 3.8 to 7.5 fold incidence of Crohn’s disease among psoriasis patients compared with the general population (Najarian & Gottlieb, 2003, Menter et al., 2011).

5.4 Health-related quality of life

Psoriasis may interfere significantly with patients’ health related quality of life (HRQOL) (Bhosle et al., 2006, De Korte et al., 2004, Gonzalez et al., 2016). Despite being a non-life-threatening disease, it poses a great deal of social and financial burden to the patients and the societies (Raho et al., 2012).

The literature suggest that even if the disease involves small BSA, it can have a substantial psychological impact on one’s personal well-being, especially when it affects face, décolletage, handnails or the genital area (Menter et al., 2011). For example, psoriatic lesions on the face or scalp may be associated with considerable embarrassment and may considerably impair quality of life (De Korte et al., 2004). Involvement of the genital skin occurs in 29–40% of patients with psoriasis, which may interfere with psychosocial well-being of patients (Meeuwis et al., 2011).

It has been estimated that patients with moderate to severe psoriasis suffer from a significant (15–20%) decrease in working ability (Mustonen et al., 2015, Chan et al., 2009, Pearce et al., 2006, Meyer et al., 2010). In recent years, introduction of biological agents opened up new horizons in the treatment of the patients. Compared to standard treatment, they proved clinical efficacy, but at a higher cost (Iskandar et al., 2017).

Measurement of HRQOL in psoriasis has a growing literature. A large number of generic as well as disease-specific questionnaires have been used in psoriasis patients so far (e.g. EQ-5D, Medical Outcomes Study 36-Item Short Form (SF-36), Dermatology Life Quality Index (DLQI), Skindex-
29, Skindex-17, Skindex-16, The Psoriasis Index of Quality of Life (PSORIQOL), Dermatology Quality of Life Scales (DQOLS))(Ali&Cueva, 2017). Using valid HRQOL questionnaires both routine practice and clinical research is crucial (Bronsard et al., 2010).

In randomized controlled trials (RCTs) of psoriasis treatments, DLQI is the most commonly used HRQOL instrument (83%), followed by the SF-36 (31%), EQ-5D) (15%), and Psoriasis Disability Index (14%) and Skindex (5%)(Ali&Cueva, 2017). The EQ-5D is the most commonly applied HRQOL measure in cost-effectiveness analyses of psoriasis interventions (Gutknecht et al., 2016).

The DLQI plays a particularly important role in the management of psoriasis patients, it is not only recommended to use the DLQI to assess the burden of plaque-type psoriasis on the HRQOL in adult patients before the initiation of a systemic treatment and during follow-up to evaluate the therapeutic effect, but it is among eligibility criteria to receive biological therapy in many countries (Wakkee et al., 2008, Rencz et al., 2015).

5.5 Treatments of psoriasis

The goals of psoriasis treatment are to gain initial and rapid control of the disease process, decrease the percentage of body surface area involved, decrease plaque lesions, achieve and maintain long-term remission, minimize adverse events, and improve patient HRQOL (Lebwohl, 2005).

Treatment modalities are chosen on the basis of disease severity, relevant comorbidities, patient preference (including cost and convenience), efficacy, and evaluation of individual patient response (Menter&Griffiths, 2007). Therapy varies depending on disease severity and spread and will shift from control of acute flares to long-term maintenance. For patients with less than 20% body surface involvement, topical therapy is the most appropriate choice for initial treatment (Tristani-Firouzi&Krueger, 1998). Primary treatment options for localized psoriasis include tar preparations, corticosteroids, calcipotriene, tazarotene and anthralin. Tar has reported to show limited effectiveness and may be used at night with more appealing topical corticosteroid preparations during the day. Topical calcipotriene may be the safest treatment for long-term control of face or genital disease because there is no risk of atrophy. Topical tazarotene is more effective with less irritation when used in combination with topical corticosteroids. (Feldman,
For lesions that are difficult to control with initial therapy, anthralin or tazarotene may be tried (Pardasani et al., 2000).

The use of the various forms of phototherapy remains an essential treatment option for moderate to severe forms of psoriasis vulgaris and represents a safe and very effective treatment (Zanolli, 2003).

Systemic therapy is suggested primarily for patients with moderate to severe psoriasis who cannot be sufficiently treated with topical therapy and/or phototherapy. Treatment of moderate to severe psoriasis includes systemic therapies, such as methotrexate, acitretin, cyclosporine, and biologic agents(Sukarovska et al., 2007, Lebwohl, 2005). Methotrexate (MTX) is used most frequently for the treatment of moderate to severe plaque-type psoriasis, especially in cases with joint involvement or in pustular or erythrodermic forms (Smith, 2000, Haider et al., 2014). Ciclosporin is indicated in patients with the most resistant forms of psoriasis, especially with plaque-type disease. Ciclosporin is used as a short-term therapy for 2 to 4 months; courses of treatment can be repeated at intervals (Pathirana et al., 2009). Ciclosporin can be considered for long-term therapy only in individual cases, with frequent monitoring, particularly for kidney toxicity.

For decades, topical and oral retinoids have been used as antipsoriatic treatments. Etretinate, acitretin, and isotretinoin have been used in the treatment of psoriasis. Approved indications for acitretin are severe psoriasis that cannot be managed by topical treatments or phototherapy, as well as erythrodermic or pustular psoriasis. The acitretin treatment of women of reproductive age is discouraged due to the teratogenic potential of the drug (Pathirana et al., 2009).

Over the past two decades, the treatment of psoriasis has undergone a revolution with the advent of biologic therapies including infliximab, etanercept, adalimumab, efalizumab, and ustekinumab and they are designed to target specific components of the immune system and are a major technological advancement over traditional immunosuppressive medications (Sivamani et al., 2013). In Iran, only adalimumab and infliximab are available (2017b). Also, there are three new biologic drugs – brodalumab, secukinumab, and ixekizumab targeting the interleukin-17 signaling pathway, which are very promising for the treatment of psoriasis (Lønnberg et al., 2014). However, suicidal ideation and completed suicides had been observed in patients with brodalumab (Danesh&Kimball, 2016).
It is also important to mention that an increasing number of biosimilar drugs are available to treat psoriasis (e.g. biosimilar infliximab, etanercept and adalimumab). Biosimilars are biotechnologically processed protein substances whose amino acid sequence is identical to the reference product (Radtke&Augustin, 2014, Nast et al., 2015).

5.6 Assessment of treatment response in psoriasis

The measures recommended to be used for the assessment of response to treatment by the European Medicines Agency (EMA) (2004) are summarized in Table 9.

Table 9 Outcome measures suggested to be used in psoriasis by the EMA

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual assessment of index lesions</td>
<td>Measurements of at least 2 index lesions representative of the disease (one from refractory area - elbow or knee, and one from trunk) for separate variables including erythema, scale and elevation on a 3-point scales. Among skin signs, elevation is considered the most critical, scale the least.</td>
</tr>
<tr>
<td>Body Surface Area (BSA)</td>
<td>Estimation of BSA affected by psoriasis may be done by using hand area, which represents approximately 1% of total body surface.</td>
</tr>
<tr>
<td>Clinical signs score - Total severity sign score (TSS)</td>
<td>Sum of signs (redness/erythema, scale/crusting, thickening/elevation) and symptoms (pruritus) using 3-point scales (e.g. 0=none, some=1, extensive=2). Score varies from 0 to 12. Each level of severity (clear, mild, moderate) is defined in a standardised fashion.</td>
</tr>
<tr>
<td>Physician’s global assessment of improvement (PGA)</td>
<td>Global assessment of the patient’s overall severity of the disease on 6 or 7-point scale, scored from « severe » to « clear »</td>
</tr>
<tr>
<td>Lattice System Physicians Global Assessment (LS-PGA)</td>
<td>LS-PGA incorporates ranges of the percent of BSA involved and the overall plaque morphology.</td>
</tr>
</tbody>
</table>

Health-related quality of life (HRQOL) may be a secondary or tertiary endpoint in pivotal clinical trials. Only validated HRQOL measures are recommended to measure the impact of a treatment, such as the dermatology-specific DLQI or Dermatology Quality Life Scales (DQOLS) or Skindex, or the psoriasis-specific Psoriasis Disability Index (PDI) and Psoriasis Life Stress Inventory (PLSI). However, these HRQOL measures have the drawback that they are not able to generate health utility values for economic evaluations.

5.7 Costs of psoriasis

In this chapter a brief summary is provided on the costs of psoriasis in various countries from data published after 2010.

5.7.1 Economic burden in European countries

5.7.1.1 Europe

In Denmark and Norway, Larsen et al. conducted a prospective, non-interventional study in a private dermatologist care setting, before and after the initiation of biological therapy (Larsen et al., 2013). Overall, 163 psoriasis patients were enrolled to the study, who all received biological therapy. Total annual costs before and after the biological therapy were DKK 78,000 and DKK 286,000, respectively (year of costs 2010).

In France, a retrospective COI study based on health insurance database was performed by Le Moigne et al. from the third-party payer perspective (Le Moigne et al., 2014). The mean annual total direct medical costs with and without biological therapy were €16,214 and €3,356 per patient, respectively (year of costs 2011). Cost of hospitalizations and biological drugs were responsible for the majority of between-group differences.

In Finland, Mustonen et al. assessed the direct and indirect costs of psoriasis a societal perspective(Mustonen et al., 2013). According to data of 232 patients, total annual medication costs were €1,083 per patient. Costs of physician visits amounted to €673 and €359 in mild and severe psoriasis patients respectively. Biological therapy was associated with very high costs.

Three studies evaluated costs of psoriasis in Germany. In a multicentre, cross-sectional, retrospective study, Berger et al. measured the direct and indirect costs from patient’s, third-party
payer and societal perspectives in German departments and hospitals (year of costs 2002) (Berger et al., 2005). Altogether 192 patients were included. From a third-party payer perspective, per patient costs of psoriasis were €864 annually. Main cost drivers were prescribed medications (60%) and inpatient stays (22%). Complementary and alternative medications cost €596 to the patients per annum. Annual average cost of patients treated by systemic and photo therapy were €4,985 and €1,173, respectively. Indirect costs were as much as €1,440 per year.

Schöffski et. al. conducted a retrospective analysis, based on data of 184 patients from dermatological practices and hospital outpatient departments (Schöffski et al., 2007). Total costs of psoriasis per patient was €6,709 on average (year of costs 2004). Higher costs were associated with more severe disease, higher hospitalization rate and larger number of sick leaves.

Steinke et al. compared costs of inpatient and outpatient care in psoriasis, and according to different treatment modalities from a societal perspective in a retrospective study with 120 patients between 2005 and 2006 (Steinke et al., 2013). They found that mean total annual costs per patient added up to €7,092 in Germany. Annual per patient costs of in- and outpatients were €13,042 and €2,984, respectively. Costs of patients treated by systemic biological therapy were €30,200 (inpatient) and €11,601 (outpatient).

In Hungary, Balogh et al. conducted a non-interventional, cross-sectional questionnaire survey involving 200 moderate-to-severe psoriasis patients from two academic dermatology departments (Balogh et al., 2014). Cost calculation was performed from a societal perspective. The majority of the patients (52%) were treated by biologics at the time of the survey. The mean annual total cost per patient was €9,254 (SD €8,502), with direct costs accounting for 86% (year of costs 2012). The mean total cost of patients treated by biologics was €15,790.

In Italy, Colombo et al. evaluated the COI associated with moderate to severe psoriasis based on data from 150 patients in multicenter, prospective study (Colombo et al., 2008). The total costs, including direct and indirect items were measured from the patient’s, societal and third-party payer’s perspectives. Mean annual total costs of psoriasis amounted to €8,371 per patient (year of costs 2004). Moderate disease was associated with half the costs of the severe disease (€5,226 vs. €11,434). Hospitalization was identified as the main driver of costs.
In the Netherlands, Driessen et al. collected health care resource utilization data 12 months before and after starting biologic therapy including 67 patients (Driessen et al., 2010). Direct costs before and after biological therapy were €10,146 and €17,712 per patient per year, respectively.

In Spain, Carrascosa et al. performed a 12-month, multicentre, prospective longitudinal and observational study enrolling 797 psoriasis patients from a third party payer as well as a societal perspective (Carrascosa et al., 2006). The mean total cost per patient was €1,079/year including direct and indirect costs. Prescription drugs accounted for the majority of costs (46.6%).

In Sweden, a prevalence-based prospective study was carried out by Ghatnekar et al. including 164 psoriasis patients (Ghatnekar et al., 2012). The mean total cost was €994 per patient per month, which results in a mean annual cost of €11,928/patient (year of costs 2009). Outpatient visits and phototherapy (49%), biological drugs (20%) and productivity loss (22%) were accounted for the majority of costs.

Navarini et al. analysed resource utilisation data of 383 psoriasis patients in Switzerland. The analysis adopted a societal perspective (Navarini et al., 2010). Annual total costs per patient were CHF1,800, 3,600 and 17,000-20,000 in mild, moderate and severe psoriasis, respectively (year of costs 2005).

In the UK, Fonia et al. conducted a retrospective observational study with 76 patients. Only direct medical costs were included from a third party payer perspective (Fonia et al., 2010). Total cost of psoriasis care prior to biological treatment were £4,207 per patient annually, while after the initiation of biological treatment total costs increased significantly to £11,981 per patient (year of costs 2004).

5.7.1.2 Outside of Europe

In the US, Yu et al. conducted a COI study enrolling 56,528 psoriatic patients from societal perspective (Yu et al., 2009). Compared with controls, psoriatic patients had significantly greater total healthcare costs ($US5,529 vs $US3,509) (year of costs 2010). In the line with the literature, patients with more severe psoriasis had greater total healthcare costs than patients with mild psoriasis ($US10,593 vs $US5,011), including higher drug costs ($US4,738 vs $US1,283).
Another study in the US by Beyer and Wolverton assessed the current total cost of systemic therapy for psoriasis (Beyer&Wolverton, 2010). Authors examined the annual trends in psoriasis drug spendings between 2000 to 2008 from a third party payer perspective. Overall, costs for systemic treatment of psoriasis ranged from $US1,197 for methotrexate to $US27,577 for alefacept.

In a large study, based on the IMPACT database Kimball et al. estimated the incremental economic burden associated with psoriasis (Kimball et al., 2011). The sample consisted of 114,512 psoriasis patients with and without comorbidities. The mean costs were $1,980 and $4,992 per patient per 6 months in patients with and without comorbidities, respectively (year of costs 2011).

In Canada, a COI study conducted by Levy et al. analysed 90 psoriasis patients’ resource utilisation in three Canadian dermatology clinics from societal perspective (Levy et al., 2012). The estimated mean annual cost of psoriasis was $7,999 per patient (year of costs 2008). Direct costs accounted for more than half of the total costs (57%) The mean lost productivity costs were $3442 per patient.

In Malaysia, Tang and his colleagues conducted a retrospective study including 250 psoriasis patients from eight dermatology clinics (Tang et al., 2013). The total annual per patient cost of psoriasis was RM 1,307 (year of costs 2008).

5.7.1.3 Comparison of studies

Cost-of-illness analysis is a well-recognized tool to demonstrate the financial burden of a disease. A better understanding of the psoriasis economic literature can help inform health policy decision-makers regarding the burden of the disease. The literature suggests that psoriasis poses a considerable economic burden on societies. Main costs generated by biological drugs. The selected studies cover the period between 2002 and 2014. The studies outlined above cannot be directly compared because of the different countries, currencies, patient populations, health systems and unit costs. It seems that the annual health care spending on psoriasis patients has increased a lot by the introduction of biological drugs. While before the era of biologics, hospitalisation was the main driver of costs, now biologicals are (Raho et al., 2012). In studies by Larsen, Driessen and Fonia 100% of the patients received biological therapy, while Balogh examined a sample where 52% of the patients received biological drugs (Larsen et al., 2013, Driessen et al., 2010, Fonia et al., 2010, Balogh et al., 2014). All these studies revealed significant increase in costs following
the initiation of biologic therapy. Fonia found approximately £9,500 rise in drug costs, Driessen €7,566 PPPY in the direct costs mainly due to biological drugs, while Larsen observed DKK 208,000 mainly due to the cost of etanercept treatment (Fonia et al., 2010, Driessen et al., 2010, Larsen et al., 2013). Besides, they found that inpatient admissions were significantly less frequent in patients treated with biologicals. Driessen reported that the number of day-care and hospital admission days per year was reduced by 94% and 64%, respectively, after the introduction of biologics (Driessen et al., 2010).

Other significant cost drivers are productivity loss and physician visits. The presence of comorbidities may also increase the costs, for example, in the study by Kimball et al., where incremental costs of comorbidities associated with psoriasis were investigated (Kimball et al., 2011), the presence of cardiovascular diseases increased mostly the costs related to psoriasis.

Disease severity was observed as an important predictor of costs in psoriasis. In the study by Yu et. al. patients with moderate to severe psoriasis had greater total health care costs compared with patients with mild psoriasis ($10,593 vs. $5,011) (Yu et al., 2009). Navarini et al. made a comparison regarding out-of-pocket payments in different disease severity, they found a considerable increase in total average out-of-pocket expenses depending on the severity of disease from CHF 630 per patient per year in mild psoriasis to CHF 2,400 in severe psoriasis (Navarini et al., 2010).
<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Year of costs</th>
<th>Perspective of the analysis</th>
<th>N</th>
<th>Time horizon of the analysis</th>
<th>Rate of biological therapy</th>
<th>Cost drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy (Levy et al., 2012)</td>
<td>Canada</td>
<td>2008</td>
<td>Societal</td>
<td>90</td>
<td>1 year</td>
<td>13%</td>
<td>43% - productivity loss</td>
</tr>
<tr>
<td>Larsen (Larsen et al., 2013)</td>
<td>Denmark and Norway</td>
<td>2010</td>
<td>Societal/hospital point of view</td>
<td>163</td>
<td>4 years</td>
<td>100%</td>
<td>89% - medication costs</td>
</tr>
<tr>
<td>Mustonen (Mustonen et al., 2015)</td>
<td>Finland</td>
<td>2010</td>
<td>Societal</td>
<td>236</td>
<td>1 year</td>
<td>5%</td>
<td>18% - medication and phototherapy</td>
</tr>
<tr>
<td>Le Moigne (Le Moigne et al., 2014)</td>
<td>France</td>
<td>2012</td>
<td>Third party payer</td>
<td>1924</td>
<td>9 years</td>
<td>0.30%</td>
<td>Biological therapy</td>
</tr>
<tr>
<td>Berger (Berger et al., 2005)</td>
<td>Germany</td>
<td>2002</td>
<td>Third-party payer, societal, patient</td>
<td>192</td>
<td>1 year</td>
<td>0%</td>
<td>46% - early retirement; 18% - medication</td>
</tr>
<tr>
<td>Schöffski (Schöffski et al., 2007)</td>
<td>Germany</td>
<td>2004</td>
<td>Third-party payer, societal</td>
<td>184</td>
<td>1 year</td>
<td>0%</td>
<td>46% - medication, 30% indirect costs</td>
</tr>
<tr>
<td>Steinke (Steinke et al., 2013)</td>
<td>Germany</td>
<td>2006</td>
<td>Societal</td>
<td>120</td>
<td>1 year</td>
<td>6%</td>
<td>32% - inpatient treatment; 28% - outpatient medication</td>
</tr>
<tr>
<td>Balogh (Balogh et al., 2014)</td>
<td>Hungary</td>
<td>2012</td>
<td>Societal</td>
<td>200</td>
<td>1 year</td>
<td>52%</td>
<td>79% - biological therapy</td>
</tr>
<tr>
<td>Colombo (Colombo et al., 2008)</td>
<td>Italy</td>
<td>2004</td>
<td>Third-party payer, societal, patient</td>
<td>150</td>
<td>1 year</td>
<td>0%</td>
<td>32% - productivity loss; 30% - hospitalization</td>
</tr>
<tr>
<td>Tang (Tang et al., 2013)</td>
<td>Malaysia</td>
<td>2008</td>
<td>Societal</td>
<td>250</td>
<td>1 year</td>
<td>0%</td>
<td>73% - outpatient management</td>
</tr>
<tr>
<td>Study (Authors, Year)</td>
<td>Country</td>
<td>Year</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Duration</td>
<td>Coverage</td>
<td>Cost Components</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------</td>
<td>------</td>
<td>--------------</td>
<td>-------------</td>
<td>----------</td>
<td>----------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Driessen et al., 2010</td>
<td>The Netherlands</td>
<td>2009</td>
<td>Societal</td>
<td>67</td>
<td>1 year</td>
<td>100%</td>
<td>Biological therapy</td>
</tr>
<tr>
<td>Carrascosa et al., 2006</td>
<td>Spain</td>
<td>2003</td>
<td>Third-party payer, societal</td>
<td>797</td>
<td>1 year</td>
<td>N/A</td>
<td>47% - treatment costs; 19% - hospitalization</td>
</tr>
<tr>
<td>Ghatnekar et al., 2012</td>
<td>Sweden</td>
<td>2009</td>
<td>Societal</td>
<td>164</td>
<td>1 month</td>
<td>16%</td>
<td>49% - outpatient visits and light therapy; 20% - biological drugs</td>
</tr>
<tr>
<td>Navarini et al., 2010</td>
<td>Switzerland</td>
<td>2005</td>
<td>Societal</td>
<td>3,596</td>
<td>1 year</td>
<td>N/A</td>
<td>Ambulatory costs</td>
</tr>
<tr>
<td>Fonia et al., 2010</td>
<td>UK</td>
<td>2008</td>
<td>Societal</td>
<td>76</td>
<td>1 year</td>
<td>100%</td>
<td>Intensive care</td>
</tr>
<tr>
<td>Yu et al., 2009</td>
<td>US</td>
<td>2003</td>
<td>Societal</td>
<td>56,528</td>
<td>1 year</td>
<td>0%</td>
<td>29% - drug costs</td>
</tr>
<tr>
<td>Beyer &amp; Wolverton, 2010</td>
<td>US</td>
<td>2008</td>
<td>Third-party payer</td>
<td>N/A</td>
<td>9 years</td>
<td>N/A</td>
<td>Alefacept treatment</td>
</tr>
<tr>
<td>Kimball et al., 2011</td>
<td>US</td>
<td>2011</td>
<td>Third party payer</td>
<td>114,512</td>
<td>6 months</td>
<td>N/A</td>
<td>Treatment of cardiovascular comorbidities</td>
</tr>
</tbody>
</table>
6 Health-related quality of life and disease burden of psoriasis patients in Iran

Psoriasis represents a social and financial burden for patients and the healthcare system (see chapter 2). Patients often suffer from disfigurement and from social stigmatization. Because the disease is usually persistent, patients with a diagnosis of psoriasis usually need lifelong care, which also means a lifetime of expenses. Raho et al. performed a systematic literature search to review the evidence available concerning the social burden and costs of psoriasis (the search included 'quality of life', 'burden' or 'stigmatization', 'psychological factors' in PubMed up to January 2010) (Raho et al., 2012). Results suggest that quality of life was affected by psoriasis to a degree comparable with diabetes or cancer.

6.1 Research questions and hypotheses

Several questionnaires have been used to measure health-related quality of life (HRQOL) in patients with psoriasis in Iran, including generic (e.g., SF-36) and disease-specific questionnaires (e.g., Psoriasis Disability Index - PDI, Dermatology Life Quality Index - DLQI, Psoriasis Area and Severity Index - PASI) but to our knowledge there cannot be found any studies in the literature that assessed HRQOL of psoriasis patients with EQ-5D in Iran. (Ghajarzadeh et al., 2012, Ansar et al., 2013, Aghaei et al., 2009, Zandi et al., 2011)

Over the past decade, the literature on mapping the generic preference-based measure, EQ-5D in different diseases has rapidly grown. Heredi et al. mentioned that “According to the University of Oxford HERC online database of mapping studies (Dakin, 2013) only two papers and a conference abstract have been published about mapping EQ-5D in psoriasis, so far” (Blome et al., 2013, 2013).

---

2 This chapter draws upon the following journal article:

Currie&Conway, Norlin et al., 2012, Heredi et al., 2014). Therefore, four papers have been published about mapping EQ-5D in psoriasis.

All these researches investigated the relationship between the dermatology-specific DLQI questionnaire and the EQ-5D index or EQ VAS. These models could explain only 27.0–48.8% of the variance of EQ-5D.

To our knowledge, no research has been published about disease burden in psoriasis from Iran until now.

The objectives of this cross-sectional study were:

1. To measure HRQOL of psoriasis patients in Iran with the general measure of EQ-5D and several disease-specific instruments, and analyze the relationship between these outcome measures. Additionally, we compare HRQOL differences between subgroups of patients regarding treatment, clinical subtypes and localization of psoriatic lesions.
2. Mapping EQ-5D index scores and EQ VAS scores from DLQI to provide utility values for economic evaluations.

### 6.2 Methods

#### 6.2.1 Study design

A cross-sectional questionnaire survey of 62 psoriasis patients from May to August 2013 was conducted at Moradi Skin Laser Clinic in Shiraz, Iran. We used a questionnaire that incorporated self-designed items and validated HRQOL and disease severity measures (Balogh et al., 2014, Heredi et al., 2014). The questionnaire consisted of two parts; the first was filled out by the patients and the second by their dermatologist. Patients were asked about demographic data (age, sex, marital status, weight, and height) and medical history (disease duration, family history, affected body sites). HRQOL was assessed by EQ-5D, EQ VAS, DLQI, and self-assessed disease severity visual analogue scale. All the patients were managed by a single dermatologist who provided data on clinical type of psoriasis, psoriasis treatment in the last 12 months, and moreover, he completed PASI, and physician’s global assessment of disease activity visual analogue scale (PGA VAS) regarding each patient.
In the Hungarian questionnaire, patient could choose among these areas: face, neck, hands and palms, forearm, fingers and finger nails, legs and thigh in order to state in which part of their body they have the problem. In the Iranian Questionnaire some other parts were added into the questionnaire as follows: knee, ankle, chin, groin, elbow, armpit, finger and toenails according to the talk we had with two dermatologists in Iran. In Iran, usually patients with psoriasis do not use a travel coupon and ambulance mostly used for emergency reasons. So, this part was deleted from the Iranian version of questionnaire compared to that by Balogh et al.

Patients were asked to respond questions about their socio-economic background and demographics. In the Iranian questionnaire, salary categories were as follows: none to 2,500,000 Rials, 2,500,000 to 5,500,000 Rials, 5,500,000 to 7,500,000 Rials, 15,000,000 to 25,000,000 Rials and 25,000,000 to 35,000,000 Rials and more than 35,000,000 Rials. (1 Euro= 40400 Rial (17 March 2017))

6.2.2 EQ-5D

In many countries, utility measures are required for allocation decisions. The EQ-5D is a standardised instrument for use as a measure of health outcome which was introduced in 1990. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status (Shaw et al., 2005, Wu et al., 2007).

The EQ-5D is one of the generic QoL instruments which has been extensively validated and been shown to be sensitive, internally consistent, and reliable in the general population and other patient groups including psoriasis (Hurst et al., 1994, Dorman et al., 1997, Schrag et al., 2000). The conceptual basis of the EQ-5D is the holistic view of health, which includes the medical definition, as well as the fundamental importance of independent physical, emotional and social functioning. The concept of health in EQ-5D also encompasses both positive aspects (well-being) and negative aspects (illness) (Gusi et al., 2010). Yaling and his colleagues indicated (2014) that the validity and responsiveness of the EQ-5D was found to be good in people with skin diseases, especially plaque psoriasis or psoriatic arthritis (Yang et al., 2015).

The EQ-5D consists of 2 pages - the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression (Euroqolgroup, 1990). Each of these
dimensions can be rated as 1 (no problem), 2 (some problem) or 3 (major problem) – this is the so-called EQ-5D-3L version of the EQ-5D questionnaire (Schrag et al., 2000). A new version has been launched recently with 5 levels, named as EQ-5D-5L. An EQ-5D health state may be converted to a single summary index by applying a formula that essentially attaches weights to each of the levels in each dimension (Golicki et al., 2014, Herdman et al., 2011). This formula is based on the valuation of EQ-5D health states from general population samples thus EQ-5D index reflects the utility of a health status from the societal point of view.

While the general health status measure SF-36 has been used in previous studies comparing psoriasis treatments, there have been few applications of the EQ-5D in clinical trials of patients with moderate to severe plaque psoriasis. In a recent study, Blome et al. aimed to develop and test an algorithm for the transformation of DLQI scores into utilities. Both EQ-5D global score and EQ VAS were used as utility measures. Correlations were computed to identify predictors of EQ-5D utilities. Linear stepwise regressions were conducted using DLQI and further possible predictors to find the optimal mapping algorithm. According to the findings, mapping of DLQI on EQ-5D in psoriasis patients currently has severe limitations in validity and clinical relevance (Blome et al., 2013).

In our study, the validated Farsi version of the EQ-5D was administered in this study. Due to absence of local value set in Iran, the UK weights were applied to calculate EQ-5D scores (i.e. utilities) that can range from -0.594 to +1, with higher scores referring to better quality of life (Dolan, 1997). EQ-5D is accompanied by a visual analogue scale (EQ VAS) on which patients are asked to provide a self-assessment of their own health in a range from 0 (worst imaginable health state) to 100 (best imaginable health state).

### 6.2.3 Dermatology Life Quality Index (DLQI)

Dermatology Life Quality Index (DLQI) is the most commonly used dermatology-specific HRQOL questionnaire (Finlay&Khan, 1994, Lewis&Finlay, 2004b). It consists of 10 questions covering symptoms, feelings, daily activities, leisure, work and school, personal relationships and treatment side effects that assess patients’ perception of the impact of skin condition of their HRQOL last week. Each question is scored on a 4-point Likert scale (0, not at all/not relevant; 1, a little; 2, a lot; 3, very much). DLQI score is calculated by summing up the score of each question
and therefore, total scores range between 0 (least impact on HRQOL) and 30 (maximum impact on HRQOL).

The Dermatology Life Quality Index (DLQI), developed in 1994, was the first dermatology-specific Quality of Life instrument. It is a simple 10-question validated questionnaire which has been used in over 30 different skin conditions in over 33 countries and is available in 85 languages (Basra et al., 2008). Its use has been described in over 800 publications including many multinational studies. The DLQI is the most frequently used instrument in studies of randomised controlled trials in dermatology (Ali&Cueva, 2017).

The DLQI questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self-explanatory and can be simply handed to the patient who is asked to fill it in without the need for detailed explanation. It is usually completed in one to two minutes. Each question is answered by a tick box: “not at all”, “a little”, “a lot” or “very much”(Lewis&Finlay, 2004a). Each question refers to the impact of the skin disease on the patient’s life over the previous week. The scoring of each question is described in Table 12.

The Dermatology Life Quality Index consists of 10 questions concerning symptoms and feelings, daily activities, leisure, work, and school, personal relationships and treatment (Table 13).

**Table 11 Scoring of DLQI questions**

<table>
<thead>
<tr>
<th>Answer</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very much</td>
<td>3</td>
</tr>
<tr>
<td>A lot</td>
<td>2</td>
</tr>
<tr>
<td>A little</td>
<td>1</td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>Not relevant</td>
<td>0</td>
</tr>
<tr>
<td>Question unanswered</td>
<td>0</td>
</tr>
<tr>
<td>Question 7: &quot;prevented work or studying&quot;</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: (Finlay&Khan, 1994)

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more QOL is impaired. The DLQI can also be expressed as a percentage of the maximum possible score of 30 (Power et al., 2009). The possible score range is from 0 (meaning no impact of skin disease on quality of life) to 30 (meaning maximum impact
on quality of life) (table 13). Score 0 or 1 means that psoriasis has no effect on patient’s life. Score 2 to 5 mean that psoriasis has a small effect on patient’s life, score 6 to 10 means that psoriasis has a moderate effect on patient’s life, score 11 to 20 means psoriasis has a very large effect on patient’s life and score 21 to 30 means psoriasis has an extremely large effect on patient’s life.

Table 12: Meaning of DLQI scores

<table>
<thead>
<tr>
<th>Score</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>no effect at all on patient's life</td>
</tr>
<tr>
<td>2-5</td>
<td>small effect on patient's life</td>
</tr>
<tr>
<td>6-10</td>
<td>moderate effect on patient's life</td>
</tr>
<tr>
<td>11-20</td>
<td>very large effect on patient's life</td>
</tr>
<tr>
<td>21-30</td>
<td>extremely large effect on patient's life</td>
</tr>
</tbody>
</table>

Source: (Hongbo et al., 2005)

Table 13 The six dimensions of the DLQI

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Number of question</th>
<th>Maximum total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and feelings</td>
<td>Questions 1 and 2</td>
<td>6</td>
</tr>
<tr>
<td>Daily activities</td>
<td>Questions 3 and 4</td>
<td>6</td>
</tr>
<tr>
<td>Leisure</td>
<td>Questions 5 and 6</td>
<td>6</td>
</tr>
<tr>
<td>Work and School</td>
<td>Question 7</td>
<td>3</td>
</tr>
<tr>
<td>Personal relationships</td>
<td>Questions 8 and 9</td>
<td>6</td>
</tr>
<tr>
<td>Treatment</td>
<td>Question 10</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: (Finlay&Khan, 1994, Hongbo et al., 2005)

6.2.4 Psoriasis Area and Severity Index (PASI)

A wide variety of scoring system has been proposed to assess severity of psoriasis. More than 44 different scoring systems were used in 171 randomized clinical trials of psoriasis therapies reviewed by Naldi et al. between 1997 and 2000 (Puzenat et al., 2010).
According to the literature, the Psoriasis Area and Severity Index (PASI) seems to be the most valid and reproducible clinical severity score in the management of adult patients with plaque-type psoriasis. Other scores (Lattice System Physician’s Global Assessment - LS-PGA, Self-Administered Psoriasis Area Severity Index - SAPASI and Salford Psoriasis Index SPI), however, appear to be interesting and require better evaluation (Puzenat et al., 2010).

The PASI can be used in everyday clinical practice in the management of adult patients with plaque-type psoriasis, in particular, if a systemic treatment is considered. To assess the severity of plaque-type psoriasis in adult patients, it is recommended to assess during the examination the following symptoms: pruritus, cutaneous pain, burning sensations, bleeding, desquamation, sexual-life impairment and functional disability secondary to specific localisations of skin lesions (face, hands, nails, genital areas) (Paul et al., 2010).

PASI is a gold standard to measure the severity of psoriasis (Puzenat et al., 2010, Fredriksson&Pettersson, 1978). PASI-72 (hereinafter PASI) combines the assessment of severity of lesions and the area affected into a single score in a range of 0 and 72 where highest score refers to worse disease severity. To make up the score, the three features of erythema, induration and desquamation are each assigned a number from 0 to 4 with 4 being the worst; and the extent of involvement of each body region is scored from 0 to 6.

A patient’s PASI is a measure of overall psoriasis severity and coverage. PASI consists of two major steps, for each body section (head, arms, trunk and legs) specify:

1. **BSA (Body Surface Area):** The body is divided into four regions comprising the head (h), upper extremities (u), trunk (t), and lower extremities (l). In each of these areas, the fraction of total surface area affected is graded on a 0-6 scale (0 for no involvement; up to 6 for greater than 90% involvement). The various body regions are weighted to reflect their respective proportion of body surface area (BSA). (Louden et al., 2004)

2. **Severity of lesions**

   When using the PASI, psoriatic plaques are graded based on three criteria: redness (R), thickness (T), and scaliness (S). Severity is rated for each index on a 0-4 scale (0 for no involvement up to 4 for severe involvement).
The composite PASI score can then be calculated by multiplying the sum of the individual-severity scores for each region by the weighted area-of-involvement score for that respective region, and then summing the four resulting quantities; mathematically this evaluation is as follows:

\[
PASI = 0.1(R_h + T_h + S_h)A_h + 0.2(R_u + T_u + S_u)A_u + 0.3(R_t + T_t + S_t)A_t + 0.4(R_l + T_l + S_l)A_l
\]

Where \( R_h, R_u, R_t, R_l = \) redness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4); \( T_h, T_u, T_t, T_l = \) thickness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4); \( S_h, S_u, S_t, S_l = \) scaliness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4); and \( A_h, A_u, A_t, A_l = \) area of psoriatic involvement score for the head, upper extremities, trunk, and lower extremities, respectively (0-6). (Louden et al., 2004)

All calculations are combined into a single score (PASI score) in the range of 0 (no psoriasis on the body) and up to 72 (the most severe case of psoriasis).

Typically, the PASI would be calculated before, during and after a treatment period in order to determine how well psoriasis responds to the treatment.

### 6.2.5 Physician’s global assessment visual analogue scale

Physician’s global assessment visual analogue scale (PGA VAS) is a 100-mm-long visual instrument that allows dermatologists to evaluate easily the current disease activity of the patient. Self-assessed disease severity visual analogue scale is basically similar to PGA VAS but it is scored by the patients themselves.

### 6.2.6 Data analysis

Data analysis was performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). At first, descriptive statistics were implemented. Data were not normally distributed and therefore, the nonparametric Mann-Whitney U-test or Kruskal-Wallis test were used to test for differences in EQ-5D, EQ VAS, DLQI and PASI within subgroups of patients. Spearman’s correlation was applied to evaluate the relationship between the outcome measures. Also, bivariate linear
regression was formulated to analyze the relationship between the general HRQOL measures EQ-5D and EQ VAS, and the disease specific instrument DLQI (mapping).

6.3 Results

6.3.1 Patient characteristics

Altogether 62 patients and their dermatologist completed the questionnaire. Mean age was 40.40 (SD 17.53, range 16-86), with 75.8 % males (Table 14). The mean disease duration was 13.60 (SD 11.37) years. Twenty-four (38.7%) participants were normoweight, 25 (40.3%) were overweight, 5 (8.1%) were indicated obese based on their Body Mass Index (BMI) score. Regarding the number of affected body sites, 27 (43.5%), 20 (32.3%) and 14 (22.6%) patients reported involvement of 1-2, 3-4 and 5-7 regions, respectively. Most common localizations were ankles (38.7%), elbows (38.7%), knees (33.9%), forearms (33.9%), feet/legs (32.3%), face (27.4%), hands/palms (24.2 %), and neck/décolletage (22.6 %).

In total, 66.1% of the patients were diagnosed with chronic plaque psoriasis followed by scalp psoriasis 35.5%, palmoplantar involvement 27.4%, inverse psoriasis 25.8%, guttate psoriasis 19.4%, and nail psoriasis 19.4 %. Overall, 30 (48.4%) patients used only topical therapy in the last 12 months and 24 (38.7%) patients received systemic non-biological therapy, of whom 16 also applied topicals (Table 14).
### Table 14 Characteristics of the psoriasis patient population (n=62)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N, % or mean, SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males (n, %)</strong></td>
<td>47 (75.8%)</td>
</tr>
<tr>
<td><strong>Age, years (mean, SD)</strong></td>
<td>40.40 (17.53)</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Psoriasis duration, years (mean, SD)</strong></td>
<td>13.60 (11.37)</td>
</tr>
<tr>
<td><strong>Body mass index - BMI, kg/m2 (mean, SD)</strong></td>
<td>25.66 (3.29)</td>
</tr>
<tr>
<td><strong>Localization of psoriatic lesions (n, %)</strong></td>
<td></td>
</tr>
<tr>
<td>Ankles</td>
<td>24 (38.7%)</td>
</tr>
<tr>
<td>Armpits</td>
<td>11 (17.7%)</td>
</tr>
<tr>
<td>Elbows</td>
<td>24 (38.7%)</td>
</tr>
<tr>
<td>Face/forehead</td>
<td>17 (27.4%)</td>
</tr>
<tr>
<td>Forearms</td>
<td>21 (33.9%)</td>
</tr>
<tr>
<td>Feet/legs</td>
<td>20 (32.3%)</td>
</tr>
<tr>
<td>Groin</td>
<td>11 (17.7%)</td>
</tr>
<tr>
<td>Hand/palm</td>
<td>15 (24.2%)</td>
</tr>
<tr>
<td>Infraammary fold</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>Knees</td>
<td>21 (33.9%)</td>
</tr>
<tr>
<td>Neck/décolletage</td>
<td>17 (22.6%)</td>
</tr>
<tr>
<td><strong>Number of body sites affected (n, %)</strong></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>27 (43.5%)</td>
</tr>
<tr>
<td>3-4</td>
<td>20 (32.3%)</td>
</tr>
<tr>
<td>5-7</td>
<td>14 (22.6%)</td>
</tr>
<tr>
<td><strong>Clinical types (n, %)</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic plaque psoriasis</td>
<td>41 (66.1%)</td>
</tr>
<tr>
<td>Erythrodermic psoriasis</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>Inverse psoriasis</td>
<td>16 (25.8%)</td>
</tr>
<tr>
<td>Guttate psoriasis</td>
<td>12 (19.4%)</td>
</tr>
<tr>
<td>Nail psoriasis</td>
<td>12 (19.4%)</td>
</tr>
<tr>
<td>Palmoplantar psoriasis</td>
<td>17 (27.4%)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>Pustular psoriasis</td>
<td>2 (3.2%)</td>
</tr>
<tr>
<td>Scalp psoriasis</td>
<td>22 (35.5%)</td>
</tr>
<tr>
<td><strong>Treatment in the last 12 months (n, %)</strong></td>
<td></td>
</tr>
<tr>
<td>Systemic non-biological*</td>
<td>24 (38.7%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>21 (33.9%)</td>
</tr>
<tr>
<td>Retinoid</td>
<td>4 (6.5%)</td>
</tr>
<tr>
<td>Only topical*</td>
<td>30 (48.4%)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>30 (48.4%)</td>
</tr>
<tr>
<td>Calcipotriol</td>
<td>8 (12.9%)</td>
</tr>
<tr>
<td>Salicylic acid</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>None</td>
<td>6 (9.7%)</td>
</tr>
</tbody>
</table>
6.3.2 Health-related quality of life and disease severity

Mean EQ-5D, EQ VAS, DLQI and PASI scores were 0.62 (SD 0.37), 60.18 (27.26), 10.19 (SD 6.46) and 12.94 (SD 8.28), respectively (Table 15). Average PGA VAS was found significantly lower than self-assessed disease severity VAS (34.66 vs 53.60, p<0.001). In terms of the five underlying dimensions of EQ-5D, 17.7%, 25.8%, 27.5%, 62.9%, and 62.9% marked having some or severe problem in mobility, self-care, usual activities, pain/discomfort and anxiety/depression, respectively (Figure 3).

Table 15 Quality of life and disease severity of the Iranian psoriasis patients

<table>
<thead>
<tr>
<th></th>
<th>N, % or mean, SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D score (-0.59 to 1)</td>
<td>0.62 (0.37)</td>
</tr>
<tr>
<td>EQ VAS (0-100)</td>
<td>60.18 (27.26)</td>
</tr>
<tr>
<td>DLQI (0-30)</td>
<td>10.19 (6.46)</td>
</tr>
<tr>
<td>PASI (0-72)</td>
<td>12.94 (8.28)</td>
</tr>
<tr>
<td>PGA VAS (0 –100 mm)</td>
<td>34.66 (22.63)</td>
</tr>
<tr>
<td>Self-assessed disease severity VAS (0–100 mm)</td>
<td>53.60 (26.72)</td>
</tr>
</tbody>
</table>
HRQOL and disease severity results of subgroups are presented in Table 17. No significant HRQOL difference was noted between males and females. Amongst clinical types, chronic plaque psoriasis patients showed the best or the second best general health state measured with any instrument; however this difference was not statistically significant. Nail psoriasis was associated with the highest HRQOL impairment in EQ-5D, EQ VAS and DLQI scores, neither this was significant. Besides, scalp psoriasis patients indicated significantly higher disease severity compared to the other clinical types (PASI=16.27, p<0.05). HRQOL was found significantly worse in those who had more body sites affected assessed by any outcome measure. To focus on localization of psoriatic lesions, patients with neck/décolletage involvement showed significantly

Figure 3 Proportion of the patients reporting problem in EQ-5D domains
higher HRQOL reduction in either instruments. Also psoriasis on feet/legs was related to fairly low EQ-5D and high PASI scores (0.46 and 16.54).

Comparing patients based on their treatment applied in the last 12 months, those who received only topical therapy reported better HRQOL, although this difference was proven significance only regarding PASI scores (Table 16).

Table 16 Subgroup analysis of EQ-5D, EQ VAS, DLQI and PASI scores

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EQ-5D</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.71(0.22)</td>
</tr>
<tr>
<td>Male</td>
<td>0.60(0.40)</td>
</tr>
<tr>
<td><strong>Clinical types</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic plaque psoriasis</td>
<td>0.66(0.36)</td>
</tr>
<tr>
<td>Inverse psoriasis</td>
<td>0.55(0.33)</td>
</tr>
<tr>
<td>Guttate psoriasis</td>
<td>0.59(0.37)</td>
</tr>
<tr>
<td>Nail psoriasis</td>
<td>0.47(0.38)</td>
</tr>
<tr>
<td>Palmoplantar psoriasis</td>
<td>0.52(0.43)</td>
</tr>
<tr>
<td>Scalp psoriasis</td>
<td>0.57(0.36)</td>
</tr>
<tr>
<td><strong>Number of body sites affected</strong></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>0.77(0.24)*</td>
</tr>
<tr>
<td>3-4</td>
<td>0.60(0.41)*</td>
</tr>
<tr>
<td>5-7</td>
<td>0.38(0.40)*</td>
</tr>
<tr>
<td><strong>Localization of the lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Ankles</td>
<td>0.61(0.40)</td>
</tr>
<tr>
<td>Armpits</td>
<td>0.54(0.43)</td>
</tr>
<tr>
<td>Elbows</td>
<td>0.64(0.33)</td>
</tr>
<tr>
<td>Face/forehead</td>
<td>0.53(0.42)</td>
</tr>
<tr>
<td>Feet/legs</td>
<td>0.46(0.44)*</td>
</tr>
<tr>
<td>Forearms</td>
<td>0.57(0.42)</td>
</tr>
<tr>
<td>Groat</td>
<td>0.75(0.25)</td>
</tr>
<tr>
<td>Hands/palms</td>
<td>0.54(0.52)</td>
</tr>
<tr>
<td>Knees</td>
<td>0.52(0.39)</td>
</tr>
<tr>
<td>Neck/décolletage</td>
<td>0.36 (0.49)*</td>
</tr>
<tr>
<td><strong>Treatment in the last 12 months</strong></td>
<td></td>
</tr>
<tr>
<td>Topical</td>
<td>0.73 (0.23)</td>
</tr>
<tr>
<td>Systemic non-biological</td>
<td>0.46 (0.47)</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test or Kruskal-Wallis test p <0.05. For DLQI and PASI ‘0’ and for all other measures, the highest value is the best possible outcome.
Correlations between EQ-VAS, DLQI, PASI, PGA VAS and self-assessed disease severity VAS are described in Table 18. Both EQ-5D and EQ VAS showed a moderate negative correlation with DLQI ($r_s = -0.44$ for both, $p < 0.001$), and PGA VAS as well as self-assessed disease severity VAS ($r_s = -0.35$ for both, $p < 0.01$). Only EQ VAS was significantly associated with PASI ($r_s = -0.31$, $p < 0.01$), however no significant association was reported with EQ-5D. Moderate positive correlations were found between DLQI, PASI, PGA VAS, and self-assessed disease severity VAS, This relationship was shown to be stronger compared to those with either EQ-5D or EQ VAS.

**Table 17** Spearman’s correlations between the outcome measures

<table>
<thead>
<tr>
<th></th>
<th>EQ-5D score (0-0.59-1)</th>
<th>EQ VAS (0-100)</th>
<th>DLQI</th>
<th>PASI</th>
<th>PGA VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ VAS (0-100)</td>
<td>0.41*</td>
<td>-</td>
<td>-0.44*</td>
<td>-0.31*</td>
<td>-0.51*</td>
</tr>
<tr>
<td>DLQI (0-30)</td>
<td>-0.44*</td>
<td>-0.44*</td>
<td>-</td>
<td>0.58*</td>
<td>0.61*</td>
</tr>
<tr>
<td>PASI (0-72)</td>
<td>-0.12</td>
<td>-0.31*</td>
<td>0.58*</td>
<td>-</td>
<td>0.58*</td>
</tr>
<tr>
<td>PGA VAS (0–100 mm)</td>
<td>-0.35*</td>
<td>-0.51*</td>
<td>0.55*</td>
<td>0.58*</td>
<td>-</td>
</tr>
<tr>
<td>Self-assessed disease severity VAS (0–100 mm)</td>
<td>-0.35*</td>
<td>-0.54*</td>
<td>0.48*</td>
<td>0.48*</td>
<td>0.55*</td>
</tr>
</tbody>
</table>

* Spearman’s rho significant $p< 0.05$. For EQ-5D and EQ-VAS the lowest value, whereas for all other measures the highest value is the worst possible outcome.

### 6.3.3 Mapping EQ-5D utilities

A simple linear regression with EQ-5D as a function of the total DLQI score was performed (Fig. 4). Figure 4 shows a scatter plot of EQ-5D as a function of DLQI.

The black diagonal line in Figure 4 is the regression line and consists of the predicted score on EQ-5D for each possible value of DLQI. The distance between the points and the regression line represents the errors of prediction. As it shows there are many points that are near the regression line; that shows the error of prediction for those points are small. Linear relationship of DLQI onto both EQ-5D and EQ-VAS was estimated: EQ-5D= 0.88 – 0.02*DLQI (adjusted $r^2$=0.213, ANOVA $p< 0.001$), EQ-VAS= 80.14 – 1.98 * DLQI (adjusted $r^2$=0.206, ANOVA $p< 0.001$). Thus, 1 point increase in the DLQI results in 0.02 point decrease in the EQ-5D and 1.98 points decrease in EQ VAS. The DLQI score explained 22.6% of variance of EQ-5D and 22 % of the variance of EQ-VAS (Figures 4 and 5).
Figure 4 Scatterplot and a linear relationship between EQ-5D and DLQI

Figure 5 Scatterplot and a linear relationship between EQ-VAS and DLQI
6.4 Discussion
6.4.1 Principal findings and comparison with previous studies on HRQOL from Iran

Present study was undertaken to assess HRQOL of adult psoriasis patients from Iran applying general and disease-specific HRQOL instruments. To our knowledge, this is the first study from Iran that measured HRQOL with EQ-5D and EQ VAS. Considerable general HRQOL impairment experienced by psoriasis patients was observed expressed either in EQ-5D (0.62) or in EQ VAS (60.18). Previous studies from Iran have mainly used non-preference-based outcome measures; nevertheless, these instruments except for SF-36 are not feasible to calculate utilities that can be used in economic evaluations. In a survey by Ghajarzadeh et al. involving 100 psoriasis patients with mean age of 36.2 years reported SF-36 and DLQI scores of 59.8 (SD 19.8) and 12.8 (SD 6.1), respectively (Ghajarzadeh et al., 2012). Ansar et al. reported mean SF-36 score 65.05 (SD 15.51) of 100 psoriasis patients with mean age of 40.45 years (Ansar et al., 2013). (However, none of these two studies calculated utilities from SF-36 scores. Aghaei et al. described HRQOL of mean 28 (SD 10.66), 10.3 (SD 5.2), and 11.35 (SD 6.00) scores on PDI\(^3\), DLQI, and PASI, respectively in 125 chronic plaque psoriasis patients (Aghaei et al., 2009). In a study of Zandi et al. 97 psoriasis patients with mean age of 35.3 years were characterized by mean HRQOL of 14.1 on DLQI and 18.6 scores on PASI, respectively (Zandi et al., 2011).

Amongst the 5 dimensions beyond the EQ-5D score, 62.9% patients reported having some or severe problems in anxiety/depression and pain/discomfort (Figure 3). This seems consistent with earlier evidences that suggested prevalence of clinical depression about 69.4% amongst Iranian psoriasis patients (Layegh et al., 2010). This is also supported by findings of Ghajarzadeh et al. where average Beck Depression Scale (BDI)\(^4\) score of psoriasis patients was observed 17.1 (SD 12.3) which approximates the upper borderline between mild and moderate depression (Ghajarzadeh et al., 2012).

Interestingly, psoriasis on the face and/or forehead was not accompanied by significantly worse HRQOL compared to other body sites measured with any instrument including PASI. This finding contradicts to results of a recent Iranian research where authors argued that facial psoriasis patients

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\(^3\) ranges from 0 to 45, where higher score refer to worse HRQOL

\(^4\) ranges from 0 to 63, where higher score refers to worse depression state
had significantly higher PASI scores compared to those without facial involvement (Keshavarz et al., 2013). In an earlier Iranian study conducted by Zandi et al. erythrodermic and pustular types of psoriasis were predictors of the greatest HRQOL impairment measured by DLQI (22.3 and 20.8 scores); nonetheless the comparison of our results with these evidences is hampered by the very small patient number in these subgroups of our study (Zandi et al., 2011).

Females of our survey showed better HRQOL measured with EQ-5D, DLQI or PASI but not significantly. In contrast, a recently published study from Iran pointed out that female patients reported significantly lower scores in SF-36 than males (Ansar et al., 2013).

Analyzing the correlations between the outcome measures revealed moderate correlation between the general measure of EQ-5D and EQ VAS and disease-specific DLQI and PASI. Not unexpectedly, disease-specific tools (DLQI, PASI, PGA VAS, self-assessed disease severity VAS) correlated with each other stronger than with EQ-5D or EQ VAS. The relationship of DLQI and PASI in psoriasis was discussed in a prior study from Iran and found lower DLQI related higher PASI scores (p<0.001) but authors did not report correlation coefficient between these two measures (Zandi et al., 2011).

It is notable that average PGA VAS was found significantly lower than self-assessed disease severity VAS (34.66 vs 53.60, p<0.001) and suggests an immense discrepancy in disease perception between patients and their physician. Thus, more attention should be paid on assessment of patients’ HRQOL that might also support finding the optimal treatment choices.
6.4.2 Comparison between the findings of Iranian and the Hungarian study

A very similar questionnaire to this survey was used to assess HRQOL of Hungarian moderate-to-severe psoriasis patients by Herédi et al. (Heredi et al., 2014); therefore we can compare some main findings of these two studies. A comparison between the findings of Iranian and Hungarian studies are summarized in Table 18, Table 19 and Table 20. (Heredi et al., 2014, Moradi et al., 2015)

Mostly the same cross-sectional questionnaire survey was carried out in two countries, Iran and Hungary. Details of the questionnaire and little difference between the questionnaires explained in study design part (6.2.1). Altogether 200 adult psoriasis patients enrolled from two Hungarian university clinics and 62 from an Iranian clinic. Besides HRQOL assessment, data on demographics, applied treatments, affected body sites and clinical types were collected. Mean age of the Hungarian and Iranian patients were 51.2 ±12.9 years with 69% males, and 40.4±17.5 years with 76% males, respectively (Table 18).

<table>
<thead>
<tr>
<th></th>
<th>Hungary</th>
<th>Iran</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>200</td>
<td>62</td>
</tr>
<tr>
<td>Age (mean, SD)</td>
<td>51.2 (12.9)</td>
<td>40.4(17.5)</td>
</tr>
<tr>
<td>Males %</td>
<td>69%</td>
<td>76%</td>
</tr>
<tr>
<td>BMI (mean, SD)</td>
<td>29.89 (5.44)</td>
<td>25.66 (3.29)</td>
</tr>
<tr>
<td>Disease duration (mean, SD)</td>
<td>21.96 (11.67)</td>
<td>13.60 (11.37)</td>
</tr>
</tbody>
</table>

This chapter draws upon the following conference abstract:

Moradi M, Rencz F. A comparative cross-sectional study on health-related quality of life in psoriasis from Hungary and Iran. Value in Health, Volume 17, Issue 7, Page A612
First of all, it should be highlighted, that more than half of the Hungarian patients used systemic biological therapy in the last 12 months but none in the Iranian study. Amongst the Hungarian patients 18% used none or only topical therapy in the last 12 months, 31% systemic non-biological treatment and 52% biologicals, whereas in Iran 48% of the patients applied only topicals and 39% treated with non-biological systematic therapy.

Mean EQ-5D, DLQI and PASI of the Hungarian and the Iranian sample were 0.69±0.3, 6.29±7.3, 8.01±10, and 0.62±0.37, 10±6.5, 13±8.3, respectively (Table 19). In both researches, psoriatic lesions on the neck/décolletage were associated with the highest HRQOL impairment (p<0.05). In this current study a very likely explanation for this is that out of the 17 patients with neck/décolletage involvement, 10 reported skin lesions on 5-7 body sites. Regarding clinical types, in Hungary the palmoplantar involvement while in Iran nail psoriasis patients reported the worst general HRQOL (mean EQ-5D scores: 0.36±0.3 and 0.47±0.4). In Iran patients received only topical therapy in the last 12 months reported better HRQOL, compared to those on systemic non-biological treatment while in Hungary, patients on biologicals reported the best HRQOL (Heredi et al., 2014).

Table 19 Health-related quality of life and disease severity of Hungarian and Iranian patients

<table>
<thead>
<tr>
<th>Health-related quality of life and disease severity (mean, SD)</th>
<th>Hungary</th>
<th>Iran</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D</td>
<td>0.69 (0.3)</td>
<td>0.62 (0.37)</td>
</tr>
<tr>
<td>DLQI</td>
<td>6.29 (7.3)</td>
<td>10 (6.5)</td>
</tr>
<tr>
<td>PASI</td>
<td>8.1 (10)</td>
<td>13 (8.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment (during the last 12 months)</th>
<th>Hungary</th>
<th>Iran</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or topical therapy</td>
<td>18%</td>
<td>48%</td>
</tr>
<tr>
<td>Systematic non-biological</td>
<td>31%</td>
<td>39%</td>
</tr>
<tr>
<td>Biological</td>
<td>51%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Correlation between EQ-5D and DLQI was found very similar across the two countries ($r_s$=-0.43- and -0.44, p<0.001), but EQ-5D showed significant correlation with PASI ($r_s$=-0.43, p<0.001) only in Hungary (Table 20). Strong positive correlation was identified between DLQI and PASI in both countries but only in those patients who received systemic therapy: Iran ($r_s$=0.72, p<0.001) and
Hungary (systemic non-biological: $r_s=0.65$, $p<0.001$, biological: $r_s=0.76$, $p<0.001$). Correlation between EQ-5D and DLQI was found very similar across the two countries ($r_s=-0.43$- and -0.44, $p<0.001$), but EQ-5D showed significant correlation with PASI ($r_s=-0.43$, $p<0.001$) only in Hungary. (Table 20)

A strong positive correlation was identified between DLQI and PASI in both countries but only in those patients who received systemic therapy: Iran ($r_s=0.72$, $p<0.001$) and Hungary (systemic non-biological: $r_s=0.65$, $p<0.001$, biological: $r_s=0.76$, $p<0.001$). (Table 21)

Table 20 Spearman’s correlations between the outcome measures in Iran and Hungary

<table>
<thead>
<tr>
<th></th>
<th>IRAN</th>
<th>HUNGARY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EQ-5D score</strong></td>
<td><strong>DLQI</strong></td>
<td><strong>PASI</strong></td>
</tr>
<tr>
<td><strong>EQ VAS (0-100)</strong></td>
<td>0.41*</td>
<td>-0.44*</td>
</tr>
<tr>
<td><strong>DLQI (0-30)</strong></td>
<td>-0.44*</td>
<td>-</td>
</tr>
<tr>
<td><strong>PASI (0-72)</strong></td>
<td>-0.12</td>
<td>0.58*</td>
</tr>
</tbody>
</table>

Significant $p<0.05$. For DLQI and PASI ‘0’ and for all other measures the highest value is the best possible outcome.

Results of the comparison suggest that disease severity, treatments, and culture or country-specific differences might lead to variations in the relationship between the outcomes measures used in psoriasis.

6.4.3 International comparison of results

We compared our findings to results of earlier cross-sectional studies regarding the relationships between the investigated HRQOL measures (Table 21). We noticed weak correlation between EQ-5D and PASI similarly to a paper of Norlin et al. from Sweden and of Blome et al. from Germany (Norlin et al., 2012, Blome et al., 2013). EQ VAS correlated stronger with PASI likewise according to Blome et al. (Blome et al., 2013). In the line with all of the previous studies, we identified similar moderate correlation between DLQI and both EQ-5D and EQ VAS. DLQI and PASI were
moderately correlated with the value of $r_s=0.58$ and also, Norlin et al. found similar result in Sweden (Norlin et al., 2012).

In a study from Iran, mean age of the patients was 40.4, however in the other studies the mean age of the patients were more than 50.

EQ-5D has a greatest value in Hjortsberg et al. from Sweden and Finland (0.75) and in Moradi et al. from Iran has the lowest value (0.62). DLQI has the greatest value in Moradi et al. (10.19) and then in Blome et al. (8.6 and 7.5), Hjortsberg et al. (6.8) and the lowest value in from Herédi et al. (6.29). Therefore, psoriasis has more effect on Iranian patients and also Iranian patients have the lowest quality of life compare to the other studied countries.

**Table 21 Comparison of the relationship between EQ-5D, DLQI and PASI with previous studies**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country</th>
<th>N (mean age)</th>
<th>HRQOL and disease severity (mean)</th>
<th>Correlations</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study, 2014</td>
<td>Iran</td>
<td>62 (40.4 years)</td>
<td>EQ-5D= 0.62, EQ VAS=60.18, DLQI=10.19, PASI=12.94</td>
<td>$-0.12$</td>
</tr>
<tr>
<td>Herédi et al. 2014**</td>
<td>Hungary</td>
<td>200 (51.2 years)</td>
<td>EQ-5D=0.69, EQ VAS=64.4, DLQI=6.29, PASI=8.01</td>
<td>$-0.43^*$</td>
</tr>
<tr>
<td>Blome et al. 2012</td>
<td>Germany</td>
<td>Development database: 1,511 (50.5 years)</td>
<td>EQ-5D=77.1, EQ VAS=64.4, DLQI=8.6, PASI=11.4</td>
<td>$-0.17^*$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cross-validation database: 2,009 (51.5 years)</td>
<td>EQ-5D=n.a., EQ VAS=64.5, DLQI=7.5, PASI=10.1</td>
<td>-</td>
</tr>
<tr>
<td>Norlin et al. 2011</td>
<td>Sweden</td>
<td>2,450 (54 years§)</td>
<td>EQ-5D=0.77, DLQI=4§, PASI=4.7§</td>
<td>$-0.25^*$</td>
</tr>
<tr>
<td>Hjortsberg et al. 2011**</td>
<td>Sweden</td>
<td>163 (51 years)</td>
<td>EQ-5D=0.75, DLQI=6.8</td>
<td>-</td>
</tr>
</tbody>
</table>
6.4.4 Comparison with other EQ-5D studies in Iran

A research conducted on 28 March 2017 on US National Library of Medicine, National Institutes of Health (Pubmed database, https://www.ncbi.nlm.nih.gov/pubmed/) to identify previous studies using the EQ-5D in Iran. The research detail was “eq-5d[All Fields] AND ("iran"[MeSH Terms] OR "Iran"[All Fields])”.

Sixteen studies were found. Five numbers of studies were not related to Iran and Iranian, so as a result only 11 of them remained (Table 22). The earliest study published in year 2012, 2 studies in 2013, one study in 2014, 2 studies in 2015 and 5 studies in 2016. Our psoriasis study was among the 11 studies that were found (Moradi et al., 2015).

One study used EQ-5D and demographic questionnaire in their study on haemodialysis patients (Saffari et al., 2013). The other 10 studies used EQ-5D along with other kinds of methods or questionnaires, such as a socio-demographic questionnaires, SF-36, TTO, VAS, DLQI, PASI, Type 2 Diabetes and Health Promotion Scale (T2DHPS) (Seyedifar et al., 2016, Karyani&Rashidian, 2016, Yousefi et al., 2016, Goudarzi et al., 2016, Assadi&Afshari, 2016, Javanbakht et al., 2015, Moradi et al., 2015, Saffari et al., 2015, Hosseini Nejhad et al., 2013, Javanbakht et al., 2012).

A cross-sectional analytical study was conducted by Karyani et al. to measure HRQOL in B-thalassemia patients using ED-5D along with information about participants' demographic, socioeconomic, and health status was gathered (Karyani&Rashidian, 2016). Another study also used ED-5D with information about participants' demographic in order to conduct their survey on patients with type 2 diabetes (Saffari et al., 2015).

Six studies used Visual Analogue Scale (VAS) along with ED-5D includes the paper we published (Seyedifar et al., 2016, Goudarzi et al., 2016, Hosseini Nejad et al., 2013, Javanbakht et al., 2012, Moradi et al., 2015, Assadi&Afshari, 2016).
Table 22 EQ-5D studies in Iran

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Method used</th>
<th>Population studied</th>
<th>Sample size</th>
<th>Mean EQ-5D score</th>
<th>Mean EQ VAS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seyedifar, 2016 (Seyedifar et al., 2016)</td>
<td>EQ-5D-3L</td>
<td>Beta Thalassemia</td>
<td>528</td>
<td>0.85 (SD 0.01)</td>
<td>72.5 (SD 0.81)</td>
</tr>
<tr>
<td>Karyani, 2016 (Karyani&amp;Rashidian, 2016)</td>
<td>EQ-5D-3L</td>
<td>General population</td>
<td>600</td>
<td>0.74 (SD 0.16)</td>
<td>N/A</td>
</tr>
<tr>
<td>Yousefi, 2016 (Yousefi et al., 2016)</td>
<td>EQ-5D-5L, SF-6D</td>
<td>Breast cancer</td>
<td>163</td>
<td>0.685 (0.216)</td>
<td>N/A</td>
</tr>
<tr>
<td>Goudarzi, 2016 (Goudarzi et al., 2016)</td>
<td>EQ-5D-3L, VAS</td>
<td>General population</td>
<td>869</td>
<td>N/A</td>
<td>79.58 (SE = 0.54)</td>
</tr>
<tr>
<td>Assadi, 2016 (Assadi&amp;Afshari, 2016)</td>
<td>TTO, VAS, EQ-5D-3L, EQ VAS</td>
<td>Acute poisoning</td>
<td>82</td>
<td>N/A</td>
<td>45-81</td>
</tr>
<tr>
<td>Javanbakht, 2015 (Javanbakht et al., 2015)</td>
<td>EQ-5D-3L, EQ VAS, SF-36</td>
<td>Beta Thalassemia</td>
<td>196</td>
<td>0.86 (95% CI: 0.83-0.89)</td>
<td>71.85 (95% CI: 69.13-74.58)</td>
</tr>
<tr>
<td>Moradi, 2015 (Moradi et al., 2015)</td>
<td>EQ-5D-3L, EQ VAS, DLQI, PASI</td>
<td>Psoriasis</td>
<td>62</td>
<td>0.62 (0.37)</td>
<td>60.18 (27.26)</td>
</tr>
<tr>
<td>Saffari, 2015 (Saffari et al., 2015)</td>
<td>Type 2 Diabetes and Health Promotion Scale (T2DHPS), EQ-5D-3L</td>
<td>Type 2 diabetes</td>
<td>368</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hosseini Nejhad, 2013 (Hosseini Nejhad et al., 2013)</td>
<td>EQ-5D-3L, VAS</td>
<td>Type 2 diabetes</td>
<td>3472</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Saffari, 2013 (Saffari et al., 2013)</td>
<td>EQ-5D-3L</td>
<td>Haemodialysis</td>
<td>362</td>
<td>Males: 0.71 (SD 0.33), Females: 0.59 (SD 0.45)</td>
<td>Males: 64.01 (SD 16.61), Females: 0.479 Female 65.47 (SD 21.72)</td>
</tr>
<tr>
<td>Javanbakht, 2012 (Javanbakht et al., 2012)</td>
<td>EQ-5D-3L, VAS</td>
<td>Type 2 diabetes</td>
<td>3472</td>
<td>0.70 (95% CI 0.69-0.71)</td>
<td>56.8 (95% CI 56.15-57.5)</td>
</tr>
</tbody>
</table>

N/A: not available - scores were not reported in the study, only psychometric properties, e.g. correlations with other HRQOL instruments.
The SF-36 measures general health in clinical studies and SF-6D is a classification for describing health derived from a section of SF-36. Yousefi and et al. compared the performance of the EQ-5D and the SF-6D in different state of breast cancer (Yousefi et al., 2016). Another cross-sectional study, gathered data by using a socio-demographic questionnaire, EQ-5D, and SF-36 instruments on patients with β-thalassemia (Javanbakht et al., 2015).

The study that we conducted on patients with psoriasis was the only study that have been done in Iran with using 4 different kinds of instruments EQ-5D index, EQ VAS, DLQI, PASI to identify health status and HRQOL in patients with psoriasis (Moradi et al., 2015).

6.4.5 Limitations and conclusions

Some limitations of this study should be noted. At first, sample size was quite small, only a few patients involved with rare clinical types, e.g., pustular and erythrodermic psoriasis; and all the patients treated by a single physician at a clinic in Shiraz, Iran. Secondly, there were no inclusion criteria specified to this survey and hence, every patient regardless of disease severity was allowed to participate. And finally, none of the patients of this study received biological therapies; however, infliximab, etanercept, and adalimumab have legal license for distribution in Iran. Further researches might measure HRQOL with EQ-5D in a larger sample and explore more variables that influence HRQOL of Iranian psoriasis patients.

In conclusion, this is the first study from Iran that assesses HRQOL of psoriasis patients with EQ-5D and EQ VAS. HRQOL impairment measured with either EQ-5D or EQ VAS is considerable; some or severe problems were most frequently emerged in anxiety/depression and pain/discomfort dimensions. Moreover, EQ-5D scores evaluated in this study provide country-specific data for cost-utility analyses.
7 Summary

Specific points related to the topics of this thesis were discussed in details at the end of each Chapter. Therefore, here I provide a brief summary of the main findings and highlight some points that are specifically relevant to Iran and point out some health economic and policy implications of the studies.

Technological innovation has brought a remarkable development to the health care sector over the past decades. In recent years, breakthroughs in various clinical fields have contributed greatly to the quality improvements in health care and the patient's condition. However, due to the high costs of the new technologies, it became increasingly important to assess the health economic aspects of their introduction.

The process of priority setting and its criteria in Iran's health care system is not so transparent and explicit like in many developing countries. Health Technology Assessment (HTA) has been established in the healthcare system of Iran but what is needed is a clear political will to push HTA objectives forward. Health system in Iran has gone through several reforms in the past thirty years with many challenges and successes. Generally, health-sector reforms should include sustainable and purposeful changes to improve efficiency, equity, and effectiveness, otherwise change could be harmful rather than useful.

This thesis focus on health-related quality of life (HRQOL), a key outcome in both clinical care and health economic analyses. HRQOL assessments rely on patients’ reports, how they perceive their life affected by a disease. In health economic evaluations, however, societal perspective is used to evaluate different health states, therefore, it is important to understand how lay people value different aspects of health. In our first study, therefore, we investigated the notion of health among the general population. Results suggest that people attach high importance both to emotional and physical factors (e.g., positive emotional feeling, optimism, fitness) and social aspects (e.g. goal and harmony, love). The study revealed some further aspects that are outside the narrow definition of health, i.e. people reported (among other factors) security, education, social responsibility, motivation, loving animals as relevant factors for health. This experimental study highlights how broad the concept of health can be across individuals and points out the importance of involving patients in medical decision-making by exploring their thoughts, perspective and
needs regarding their health and treatment. More importantly, these findings open a nice avenue for further research by raising the question whether the health state evaluations (e.g. the EQ-5D questionnaire) used for health economic analyses sufficiently represent and cover all the important aspects that the society considers highly relevant for health.

Concept of health and the importance people attach to different attributes of it, how people perceive health, is highly influenced by cultural factors. These factors also can affect peoples’ health related lifestyle, their decisions on participation in health care and acceptance of treatments. Therefore, subjective reports on health, the HRQOL results found in one jurisdiction are not necessarily applicable in other countries. Hence, the second empirical study of this thesis aimed to adapt a Hungarian disease burden survey to Iran, in order to assess the HRQOL of Iranian patients with psoriasis and compare with the Hungarian results. Psoriasis is a lifelong dermatological chronic disease. Biological drugs have been developed in the past decades for the treatment of psoriasis and revolutionized psoriasis care being more effective than traditional treatments. However, biological drugs have put economic pressure on the societies due to their high costs. Availability and financing of these agents highly varies between countries, thus the benefits also bring challenges and concerns about the value for money. Nevertheless, there is very little information on the HRQOL and economic impact of the disease in the international literature, and practically none in Iran. Little is known on how people in Iran perceive psoriasis, how it affects their health, including their beauty/attractiveness perception, whether the disease has stigma effects and/or deterioration in sociability – aspects that can vary substantially between cultures and societies and thus cannot be directly transferred from one country to another. Moreover, there is a lack of HRQOL and cost data that hampers cost-effectiveness analyses based on country-specific inputs.

Our findings revealed that the negative impact on patients’ HRQOL was higher for men than women. In addition, the impact on HRQOL increased with the number of body areas involved by the disease. The highest negative impact on HRQOL was observed when the skin of the neck/décolletage region or hands were involved, and the lowest when the groin was affected. Comparison between the findings of Iranian and Hungarian study revealed that, disease severity, treatments, and culture or country-specific differences might lead to variations in the relationship between the outcome measures used in psoriasis.
This research has various economic and health policy implications for Iran. Although biological drugs brought the potential to dramatically change the management of patients with psoriasis, in Iran, access to biological drug treatment is limited. Due to the high cost of biological drugs, most of the patients cannot have access to the biologic therapies. Lack of insurance coverage of the biological drugs can lead to economic problems for the patient in obtaining them. Private companies (not related to the state) import these kinds of medicines and due to the frequent change of the currency value, the price of imported drugs are unstable. I believe that our findings can contribute to the improvement of psoriasis care by highlighting that this chronic skin disease imposes high burden on the individuals and has significant economic impact to the society. Moreover, our study provides reliable input data for cost-effectiveness analyses of biological drugs that can support sustainable financing decisions and long term health planning. Our experiences with adapting a disease burden survey from another country to Iran can serve as a useful experience for other clinical fields with lack of HRQOL and disease burden data.
8 Publications related to the thesis

Published paper


Poster presentations

Moradi M. Pricing and reimbursement of pharmaceuticals in Iran. Value in Health, Volume 16, Issue 7, November 2013, Pages A474-A475
Presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 16th Annual European Congress, 2-6 November 2013, Dublin, Ireland

Presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 16th Annual European Congress, 2-6 November 2013, Dublin, Ireland

Presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 17th Annual European Congress, 8-12 November 2014, Amsterdam, The Netherlands

Conference papers

Moradi M. Health system in Iran. PhD student conference at Corvinus University of Budapest, 30 May 2013

Moradi M. Evaluation of the quality of life in patients with psoriasis; cross sectional study from Iran. Corvinus Health Policy and Health Economics Conference Series 2014/2, at Corvinus University of Budapest, 31 March 2014
9 References


### 10 Appendix
### 10.1 Appendix 1- Questionnaire

In your opinion what factors contribute the most to the health of a person in general?

Degree of Importance in respect of health in general:

0: Most Irrelevant, 1: Irrelevant, 2: Not at all Relevant, 3: Neutral, 4: Less Relevant, 5: Relevant,
6: Most Relevant

Please do not answer if you do not understand the term.

<table>
<thead>
<tr>
<th>Aspects</th>
<th>Degree of Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>02</td>
<td>Self-reproduction</td>
</tr>
<tr>
<td>03</td>
<td>Reproduction of society</td>
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<tr>
<td>04</td>
<td>Sociability</td>
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<td>05</td>
<td>Well-balanced</td>
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<td>06</td>
<td>Machine-like</td>
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<td>07</td>
<td>Flow</td>
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<td>08</td>
<td>Constructive Programs of Personality</td>
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<tr>
<td>09</td>
<td>Normal Genes</td>
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<tr>
<td>10</td>
<td>Identity or Rooted in one’s Culture</td>
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<tr>
<td>11</td>
<td>Creativity</td>
</tr>
<tr>
<td>12</td>
<td>Longevity</td>
</tr>
<tr>
<td>13</td>
<td>Beauty</td>
</tr>
<tr>
<td>14</td>
<td>Attractiveness</td>
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<tr>
<td>15</td>
<td>Fitness</td>
</tr>
<tr>
<td>16</td>
<td>Workability</td>
</tr>
<tr>
<td>17</td>
<td>Ability to Relax</td>
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<tr>
<td>18</td>
<td>Goals, Harmony</td>
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<tr>
<td>19</td>
<td>Religiousness and Belief</td>
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<tr>
<td>20</td>
<td>Optimism</td>
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<tr>
<td>21</td>
<td>Realism</td>
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<tr>
<td></td>
<td>Factor</td>
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<tr>
<td>---</td>
<td>------------------------------</td>
</tr>
<tr>
<td>22</td>
<td>Maturity</td>
</tr>
<tr>
<td>23</td>
<td>Playfulness</td>
</tr>
<tr>
<td>24</td>
<td>Discipline</td>
</tr>
<tr>
<td>25</td>
<td>Lack of Illness</td>
</tr>
<tr>
<td>26</td>
<td>Engagement</td>
</tr>
<tr>
<td>27</td>
<td>Inner Freedom</td>
</tr>
<tr>
<td>28</td>
<td>Productivity</td>
</tr>
<tr>
<td>29</td>
<td>Innovativeness</td>
</tr>
<tr>
<td>30</td>
<td>Positive Emotional Feeling</td>
</tr>
<tr>
<td>31</td>
<td>Constructive Hobby</td>
</tr>
<tr>
<td>32</td>
<td>Morality</td>
</tr>
<tr>
<td>33</td>
<td>Love</td>
</tr>
<tr>
<td>34</td>
<td>Responsibility</td>
</tr>
</tbody>
</table>

Please write the names of any factor(s), which you think is/are important in the overall well-being of a person.

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10.2 Appendix 2 – Dermatology life quality index

DERMATOLOGY LIFE QUALITY INDEX (DLQI)

Hospital No: ........................................ Date: ........................................
Name: .................................................. Score: ........................................
Address: .................................................. Diagnosis: ...................................

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick (√) one box for each question.

1. Over the last week, how itchy, sore, painful or stinging has your skin been?
   - Very much
   - A lot
   - A little
   - Not at all

2. Over the last week, how embarrassed or self conscious have you been because of your skin?
   - Very much
   - A lot
   - A little
   - Not at all

3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

4. Over the last week, how much has your skin influenced the clothes you wear?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

5. Over the last week, how much has your skin affected any social or leisure activities?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

6. Over the last week, how much has your skin made it difficult for you to do any sport?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

7. Over the last week, has your skin prevented you from working or studying?
   - Yes
   - No
   - Not relevant

   If "No", over the last week how much has your skin been a problem at work or studying?
   - A lot
   - A little
   - Not at all

8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

9. Over the last week, how much has your skin caused any sexual difficulties?
   - Very much
   - A lot
   - A little
   - Not at all
   - Not relevant

10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?
    - Very much
    - A lot
    - A little
    - Not at all
    - Not relevant

Please check you have answered EVERY question. Thank you.

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10.3 Appendix 3 – EQ-5D-3L

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

**Mobility**
- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

**Self-Care**
- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

**Usual Activities** *(e.g. work, study, housework, family or leisure activities)*
- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

**Pain/Discomfort**
- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

**Anxiety/Depression**
- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.