Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients: A Study Protocol

Master Thesis in Public Health, 20 Points

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May 2007
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FOREWORD

After receiving my Board Certificate in Dermatology in 2002, I joined the Center for Research and Training in Skin Diseases and Leprosy (CRTSDL), Tehran University of Medical Sciences and Health Services (recently, renamed to Medical Sciences/University of Tehran), Tehran, Iran, where I am working now as a full time Assistant Professor of Dermatology. I try to briefly explain how joining the CRTSDL resulted in writing this thesis.

Presence of Dr. Yahya Dowlati, Director, and Dr. Alireza Firooz, Deputy-Director of Research of the Center, as professional and personal role models enlightened my way through both my academic career and my life. Their love for learning to help patients and their willingness for sharing their knowledge with other colleagues led me to follow their discipline and enhanced my passion for life-long learning.

Shortly after joining the Center, I involved in a research project which was a randomized double-blind, controlled clinical trial for comparison of efficacies of two different drugs in the treatment of acute Old World cutaneous leishmaniasis (CL). This occasion introduced me to two important subjects: medical research and CL which is a major health problem not only in Iran but also in several other countries. Since that time, my main job has been research and CL is the main topic of my research projects.

As a researcher, I felt a need for obtaining more knowledge and skill in medical research. In addition, I noticed the necessity of a population-based view in the field of dermatology. For these reasons I decided to study a course related to epidemiology and public health. I hope that through obtaining this dermato-epidemiology knowledge I can contribute more to disease prevention and health promotion with regard to skin diseases.

This thesis is a point that my three important wishes meet each other, it has been written as my Master Degree Thesis, which I study for my learning objectives, it is about the quality of life of patients with CL, a disease that can adversely affect patients’ life, and it is a research protocol which hopefully will provide me another opportunity for learning more and doing further research to achieve my main goal “promotion of people’s health”.

Alireza Khatami

May 2007-Umeå, Sweden
ACKNOWLEDGEMENTS

First and foremost, I should say my sincere gratitude to God for everything I have.

I deeply appreciate kindness of the Swedish government for issuing my student residence permit which let me to come here, study and meet the best people that someone can imagine—Swedes. I will never forget Swedes incredible kindness and hospitality.

I warmly thank my supervisors Dr. Berndt Stenberg, Dr. Berit Edvardsson and Dr. Alireza Firooz for guiding me to obtain the required knowledge for writing this thesis and reviewing my work critically.

Without receiving personal and professional supports from Dr. Yahya Dowlati, Director of the Center for Research and Training in Skin Diseases and Leprosy (CRTSDL), Tehran University of Medical Sciences and Health Services, and President of the Iranian Society of Dermatology and Dr. Alireza Firooz, Associate Professor of Dermatology and Deputy-Director of Research of the CRTSDL, it was impossible for me to come to Sweden and study a Master Degree. I acknowledge their kindness from the bottom of my heart.

In addition, I wish to thank other faculty members at the CRTSDL in particular Dr. Ali Khamesipour for his continuous encouragement and support in many ways as well as all administrative staff of the Center in particular Mrs. Alizadeh and Mrs. Taherzadeh who helped me to handle the bureaucratic process for obtaining my leave permission.

Special thanks to Ms. Karin Johansson and Ms. Birgitta Åström for their support and kindness, which began before commencement, continue during and presumably will continue after the end of my studies in Umeå!

I am really grateful to all other staff at the Umeå International School of Public Health, Division of Epidemiology and Public Health Sciences, as well as the international group of MPH students for creating a warm, encouraging and friendly study environment.

Last but not least, I wish to thank my dear parents, Aliakbar Khatami and Parvin Mortazavi Nejad, who have devoted their lives to support me in all ways always.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACL</td>
<td>Anthroponotic cutaneous leishmaniasis</td>
</tr>
<tr>
<td>AOWCL</td>
<td>Acute Old World cutaneous leishmaniasis</td>
</tr>
<tr>
<td>CL</td>
<td>Cutaneous leishmaniasis</td>
</tr>
<tr>
<td>CRF</td>
<td>Case Report Form</td>
</tr>
<tr>
<td>CRTSDL</td>
<td>Center for Research and Training in Skin Diseases and Leprosy</td>
</tr>
<tr>
<td>DCL</td>
<td>Diffuse cutaneous leishmaniasis</td>
</tr>
<tr>
<td>DLQI</td>
<td>Dermatology Life Quality Index</td>
</tr>
<tr>
<td>DSQL</td>
<td>Dermatology Specific Quality of Life</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>EuroQoL 5</td>
</tr>
<tr>
<td>HRQoL</td>
<td>Health Related Quality of Life</td>
</tr>
<tr>
<td>LCL</td>
<td>Localized cutaneous leishmaniasis</td>
</tr>
<tr>
<td>MCL</td>
<td>Mucocutaneous leishmaniasis</td>
</tr>
<tr>
<td>MOS</td>
<td>Medical Outcome Study</td>
</tr>
<tr>
<td>MoH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>PI</td>
<td>Principal Investigator</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>QoLIAD</td>
<td>Quality of Life Index for Atopic Dermatitis</td>
</tr>
<tr>
<td>SF-36</td>
<td>36-item Short Form</td>
</tr>
<tr>
<td>SIP</td>
<td>Sickness Impact Profile</td>
</tr>
<tr>
<td>STAI</td>
<td>State Trait Anxiety Inventory</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
</tr>
<tr>
<td>VL</td>
<td>Visceral leishmaniasis</td>
</tr>
<tr>
<td>ZCL</td>
<td>Zoonotic cutaneous leishmaniasis</td>
</tr>
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1. SUMMARY

**Background:** Cutaneous leishmaniasis is prevalent in 88 countries including 77 developing ones. Globally, at least tens of millions of people are at risk of acquiring this disease and it is estimated that each year 1-1.5 million new cases occur. Patients’ perspective about their disease is of paramount importance in both medicine and public health and assessment of their quality of life is one way to gain knowledge about their point of view. It has been shown that acute Old World cutaneous leishmaniasis (AOWCL) can adversely affect quality of life of patients in several ways.

**Rational:** Due to some characteristics of this disease, generic or dermatology-specific QoL instruments might fall short to assess quality of life in AOWCL patients appropriately. To measure quality of life of these patients, development of a disease-specific QoL instrument is rational.

**Aim:** The aim of this thesis is to write a protocol for developing a disease specific instrument to evaluate the quality of life in adult Iranian patients with AOWCL.

**Methods:** According to this protocol a qualitative research will be conducted to understand patients’ perspective about the impact of AOWCL on their quality of life. Adult patients from four endemic areas for cutaneous leishmaniasis due to *Leishmania tropica* and *L. major* and one referral center in Tehran will be recruited. A purposive sampling method with maximum variation will be used. In-depth interviews and focus group discussions with volunteer patients will be conducted and collected data will be interpreted using the Grounded Theory. After expert checking for content validity of the developed instrument and completion of a pilot study it will be further assessed for psychometric properties through a survey.

**Expected results:** After implementation of this protocol into the research, a needs-based disease-specific questionnaire for evaluation of quality of life in adult Iranian patients with AOWCL will be developed. Hopefully this instrument will be validated and used later in other communities suffering from this disease.

**Conclusion:** Development of an instrument for evaluation of QoL in AOWCL patients has many advantages from provision of patients’ perspective about their disease which can promote the health care delivery to these patients to the possibility of using the developed instrument in research such as an outcome measure in clinical trials.

**Keywords:** cutaneous leishmaniasis, quality of life, dermatology
2. BACKGROUND

2.1. Leishmaniasis: Overview and Classification

Leishmaniasis is a group of diseases caused by several species of the genus *Leishmania*, a protozoa transmitted by the bite of a tiny insect vector, the sandfly. Infections in wild animals usually are not pathogenic, with the exception of dogs, which may be severely affected [1].

The major clinical patterns of the disease in the human host are: cutaneous leishmaniasis (CL), which itself can be sub-classified as either localized CL (LCL) or diffuse cutaneous leishmaniasis (DCL); mucocutaneous leishmaniasis (MCL), and visceral leishmaniasis (VL) [1]. Traditionally, CL has been divided into New World and Old World. Nosology of different types of leishmaniasis in human is demonstrated in figure 1.

![Figure 1](image_url)

**Figure 1.** Nosology of different types of leishmaniasis in human.
2.2. Epidemiology

2.2.1. Global Aspect

CL occurs in Asia, southeast Europe and Latin America [2]. With the exception of Australia and Antarctica, the parasites have been identified throughout the world [3].

The prevalence of leishmaniasis is in excess of 12 million cases and 350 million people in 88 countries, including 77 developing ones, are at risk. The annual incidence of leishmaniasis is about 1.5-2 million cases and of CL is 1-1.5 million cases, respectively, which is accounted for about 75% of all new cases of leishmaniasis. Ninety percent of all CL cases occurs in only 7 countries; Afghanistan, Algeria, Brazil, Iran, Peru, Saudia Arabia and Syria. It is considered as a major health problem in 14 countries [4]. Figure 2 shows the global distribution of CL [5].

![Endemic areas for CL in world. Source: WHO, 2003](image-url)
In their recently published review, Bailey and Lockwood noted that above mentioned figures would be expected to rise as a result of changes in human environment including global warming [2]. In addition, they mentioned that epidemics might occur when large numbers of non-immune humans become exposed to infection for the first time. This may occur because of human migration or that of the reservoir hosts. Also, travels from non-endemic areas to endemic areas during activities like wars, military exercises, civilian works, and tourism may result in outbreak of the disease in certain populations [2].

2.2.2. Epidemiology of CL in Iran

Iran is endemic for CL. Almost all CL cases are caused by either *L. tropica* or *L. major*. CL has been reported from all provinces and is endemic in many of them of. In some villages surrounding Kashan, cumulative incidence of CL was estimated to be around 13.1 % in 1996 [6]. After a major earthquake in December 2003, cumulative incidence of CL in Bam increased form about 0.2 % in 2003 to more than 2 % in 2005 (A. Khamesipour, personal communication). Khuzestan and Khorasan Razavi provinces are known to be endemic for *L. major* and *L. tropica* and *L. major*, respectively [6]. Distribution of CL in Iran is demonstrated in figure 3.

![Distribution of CL in Iran](image_url)

**Figure 3.** Distribution of CL in Iran. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission)
2.3. Etiology

The causative agents of CL in the Old World are *L. major*, *L. tropica*, *L. aethiopica*, and rarely *L. infantum*. For most species of *Leishmania*, an animal reservoir is required for endemic conditions to persist. Common hosts in Old World are domestic and feral dogs, rodents, foxes, jackals, wolves, raccoon-dogs and hyraxes. Most commonly observed Old World vectors are sandflies belonging to the genus *Phlebotomus* and include: *Ph. sergenti* and *Ph. papatasi* for transmission of *L. tropica* and *L. major*, respectively. Humans are generally considered as accidental hosts [2, 7].

2.4. Clinical Manifestations

Old World and New World CL are quite different in their epidemiology, causative parasites, vectors, reservoirs as well as the clinical presentation, treatment indications, and prognosis, so it looks reasonable to consider them as different diseases [4]. Since clinical presentations of other types of leishmaniasis are irrelevant to this study and CL due to *L. aethiopica*, and *L. infantum* are extremely rare in Iran [8], herein clinical manifestations of Old World CL due to *L. major* and *L. tropica* are discussed.

Clinically, acute Old World CL (AOWCL) is seen in two forms: anthroponotic cutaneous leishmaniasis (ACL) and zoonotic cutaneous leishmaniasis (ZCL). ACL is also known as dry, urban or late ulcerative form and is generally attributed to *L. tropica*. Other names for the ZCL form which is caused by *L. major* are wet, rural, or early ulcerative form. In human, the initial sign of infection is the appearance of an erythematous papule or nodule at the feeding site of the female sandfly. It appears within 1 week to 3 months after sandfly bite. In a typical ZCL infection, the primary lesion usually develops into an ulcer with a violaceous border which heals spontaneously in several weeks to months, resulting in a scar. Ulceration is not a characteristic feature of ACL lesions. Due to presence of a thick adherent scale on the lesion, hyperkeratosis is the dominant feature of ACL lesions [1, 7, 8].
Figure 4. AOWCL lesion due to *L. major* on the face of an Iranian boy. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission)

Figure 5. AOWCL lesion due to *L. major* on the hand of an Iranian young man. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission)
Figure 6. AOWCL lesion due to *L. major* on the dorsal foot. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission)

Figure 7. Extensive scar formation after infection with *L. major*. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission).
Figure 8. AOWCL caused by *L. tropica* on the nose of an Iranian girl. (Courtesy of Dr. Ali Khamisipour, with permission)

Figure 9. Development of leishmaniasis recidivans following infection with *L. tropica*. (Courtesy of the Center for Research and Training in Skin Diseases and Leprosy, with permission)
Major differences in clinical course and prognosis of ACL and ZCL are compared in table I.

**Table I. Major clinical differences between ACL and ZCL.**

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>AOWCL Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACL</td>
</tr>
<tr>
<td><strong>Clinical course</strong></td>
<td>Slow</td>
</tr>
<tr>
<td><strong>Incubation period</strong></td>
<td>Long: 2-8 months</td>
</tr>
<tr>
<td><strong>Typical lesions</strong></td>
<td>Dry, hyperkeratotic</td>
</tr>
<tr>
<td><strong>Number of lesions</strong></td>
<td>1 or 2, usually &lt; 5</td>
</tr>
<tr>
<td><strong>Size of the lesion</strong></td>
<td>Usually smaller in comparison with ZCL</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Self-healing at 12 months</strong></td>
<td>68 %</td>
</tr>
<tr>
<td><strong>Duration of self healing</strong></td>
<td>Long: up to 2 years</td>
</tr>
<tr>
<td><strong>Potential Progression to LCR</strong></td>
<td>Yes</td>
</tr>
</tbody>
</table>

2.5. Treatment and Prevention

Treatment is indicated in many cases of AOWCL due to *L. major* as well as AOWCL due to *L. tropica* which have to be treated because of the prolonged course of disease, possibility of progression to LCR and the fact that the cases are the reservoirs [2, 9]. Many treatment modalities have been used in the treatment of CL, but, pentavalent antimonies are considered as the first line drugs for treatment of CL so far. They have to be administered only as intramuscular, intravenous or intralesional injections and could be associated with severe side effects and significant discomfort [10]. There is no vaccine available for prevention of CL for general human use [11].
2.6. Quality of Life: Overview

The questions of what is the quality of life and how life gains its quality are not new. Throughout the history, many philosophers have tried to find answers for these questions and their different points of views have been resulted in considerable controversies. So it is not surprising that nowadays at the beginning of the 21st century, the quality of life is still a matter of debate and is no specific definition for quality of life (QoL) [12, 13].

Halioua et al. have defined QoL as a broad concept that encompasses physical health, psychologic status, level of independence, social relations, beliefs, and so on [14]. As is mentioned in upcoming pages different approaches to QoL exist and each of them has focused on one or more aspects of QoL.

2.7. Applications of QoL measurement in Clinical Medicine

Fayers and Machin have discussed different uses of QoL measurement in medicine from their use in either curative or palliative clinical trials, to provide better communication with patients and understanding their preferences [13]. They have described three broad categories of application of QoL measurement in clinical medicine:

1. As a discriminative measure: which reflects changes of disease burden over time.

2. As an evaluative tool: which is used to measure health status or the impact of a certain disease at a point in time

3. As a predictive measure: which is the use of the instrument for predicting future outcomes for patients.

2.8. Evolution of Quality of Life Measurement Instruments

As have previously mentioned, it is still under debate that how life gets its quality. On one hand, as according to the definition by World Health Organization (WHO) health is “a state of complete physical, mental and social well being and not merely the absence of disease or infirmity”, the nature of health is multidimensional. [15]. On the other hand, the relation between health status and QoL is not completely clear. These controversies
have resulted in different approaches to the QoL. Two major relevant approaches to QoL in AOWCL patients are health-related quality of life (HRQoL) and needs-based QoL [16].

In HRQoL approach, health is central to QoL and its focus is on the individual’s role in society which explains why it is known as a functionalistic approach. The majority of generic QoL such as Sickness Impact Profile (SIP) and Medical Outcome Study (MOS) 36-item Short Form (SF-36) are based on this approach [13].

Needs-based model for QoL was first suggested by Hunt and McKenna in 1992 and has derived from theories of human motivation. Since then, at least 20 disease-specific QoL measurement instruments have been developed. Items in each of these instruments reflect the concerns of the patients rather than those of investigators because the content of each of them was developed directly from interviews with relevant patients [16].

General characteristics of HRQoL and needs-based QoL instruments are compared and contrasted under the section 7.3.

2.9. Types of Quality of Life Instruments

2.9.1. Generic Instruments

These instruments are intended for assessing general issues with regard to health irrespective of the disease or condition of the patient. Some of them were initially used to define health and are better called “measures of health status” rather than QoL measurement instruments [13]. The properties of SF-36, SIP and EuroQoL (EQ-5D) are demonstrated in table II [13, 17].
Table II. Properties of SF-36, SIP and EuroQoL (EQ-5D).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SF-36</td>
</tr>
<tr>
<td>Developed by</td>
<td>Sherbourne CD and Ware JE</td>
</tr>
<tr>
<td>Objective</td>
<td>The SF-36 was developed during the Medical Outcomes Study (MOS) to measure generic health concepts relevant across age, disease, and treatment groups</td>
</tr>
<tr>
<td>Number of items</td>
<td>36</td>
</tr>
<tr>
<td>Population</td>
<td>Adult/adolescent</td>
</tr>
<tr>
<td>Mode of administration</td>
<td>Computer-administered</td>
</tr>
<tr>
<td></td>
<td>Interviewer-administered, self-administered, telephone-administered†</td>
</tr>
<tr>
<td>Time recall</td>
<td>Last month</td>
</tr>
</tbody>
</table>

*Visual analogue scale. †Note: Interviewer-administered by a trained interviewer in person or by telephone
‡ Observer, proxy and telephone versions are available on request

2.9.2. Specialty (Dermatology)-Specific QoL Instruments

The vast majority of dermatology practice is out-patient and most of the dermatology patients suffer diseases that are chronic with almost no survival impairment. Consequently, traditional health outcomes like mortality, hospital stay and so on are not relevant to many dermatological diseases [18]. To make more appropriate patient-concerned outcomes dermatology-specific QoL Instruments have been developed. These instruments are also known as dermatology-generic QoL instruments. Three well-known dermatology-specific QoLs are:

a. Dermatology Life Quality Index (DLQI) [19]
b. Dermatology Specific Quality of Life (DSQL) [20]

c. Skindex [18, 21]

Characteristics of DLQI, DSQL and Skindex are demonstrated in table III [18-21].

**Table III. Characteristics of DLQI, DSQL and Skindex.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DLQI</th>
<th>DSQL</th>
<th>Skindex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed by</td>
<td>Finlay AY</td>
<td>Anderson RT and Rajagopalan R</td>
<td>Chren MM et al</td>
</tr>
<tr>
<td>Year of Development</td>
<td>1994</td>
<td>1997</td>
<td>1996</td>
</tr>
<tr>
<td>Objective</td>
<td>To measure the impact of skin disease on patients' quality of life</td>
<td>To quantify the effects of a skin disease on physical discomfort and symptoms, psychologic well-being, social functioning, self-care activities, performance at work or school, and self-perceptions in patients with a certain dermatosis</td>
<td>To distinguish the burden of skin disease in different population at one point in time as well as a outcome measure to show how patient’s QoL changes as their skin disease changes over time</td>
</tr>
<tr>
<td>Number of items</td>
<td>10</td>
<td>34</td>
<td>61</td>
</tr>
<tr>
<td>Population</td>
<td>Adult (&gt; 15 years)</td>
<td>Adult</td>
<td>Adult</td>
</tr>
<tr>
<td>Mode of Administration</td>
<td>Self-administered</td>
<td>Self-administered</td>
<td>Self-administered</td>
</tr>
<tr>
<td>Time recall</td>
<td>Last week</td>
<td>Last month</td>
<td>Last month</td>
</tr>
</tbody>
</table>

2.9.3. Disease (Condition)-Specific QoL Instruments

Due to the wide spectrum of skin diseases in terms of clinical manifestations and diagnostic entities, dermatology-specific QoL tools like DLQI and Skindex can not be universally used to assess QoL in patients with skin diseases. This has resulted in development of so called disease (condition)-specific QoL instruments in the field of dermatology which out-number the dermatology-generic QoL tools [17]. Just to provide a handful of examples Scalpdex a disease-specific instrument for evaluation of QoL in
patients with scalp dermatitis in particular seborrheic dermatitis and psoriasis; DSQL-A and DSQL-CD which are QoL instruments based on DSQL with one and two extra items to evaluate QoL in patients with acne and contact dermatitis, respectively; and a modified DLQI instrument for measurement of QoL in patients with lymphatic filariasis can be listed [18-23].

2.10. Quality of Life in Dermatology

A review of dermatology-specific QoL instruments and disease-specific QoL instruments in dermatology reveals that they usually assess 3 to 8 constructs in order to evaluate patients QoL [17, 20-22]. Chren et al., considered 4 main constructs, physical, emotional, social and cognitive in Skindex. They subdivided physical construct to 2 sub-constructs: limitation and discomfort, and emotional construct to 4 sub-constructs: depression, fear, embarrassment and anger. Taking into account all the sub-constructs Skindex has 8 constructs [18]. Anderson and Rajagopalan reported 5 constructs: physical, social, activities of daily life, work and self-perception in DSQL [20]. During development of disease-specific QoL instrument, Chen et al. detected 3 constructs: physical, emotional and social in Scalpdex [22].

3. JUSTIFICATION AND RATIONAL

3.1. Magnitude of Problem

As has previously mentioned, globally, hundreds of millions of people are at risk of being affected by CL and more than one million new CL cases are reported each year. In many developing countries CL is prevalent and in several of them it is considered as a major health problem [4]. It is important to assess the impact of CL on the life of this considerable population which as is described below can adversely affect the QoL of the patient.

3.2. AOWCL Impact on QoL

Although CL is generally considered as a self-healing disease, ZCL and ACL both can adversely affect life of the patients. At its ulcerative stage, ZCL can result in discomfort
and even disability, which can result in significant loss of working hours and wages. In addition, when ZCL lesions remained to be self-healed, they can result in disfiguring scars, life-long stigmas usually on the exposed sites of skin. Generally, ACL lesions are more chronic and at the worst scenario, they can develop into a long-lasting, destructive and disfiguring form, known as recidivans leishmaniasis, which is very difficult to treat [4].

Yanik et al. assessed the psychological impact on CL patients in an endemic area Turkey [24]. They reported significantly higher anxiety and depression scores, a lower body satisfaction score as well as reduced quality of life in patient with active CL in comparison with health controls (p < 0.05). To assess their patients, they used Turkish validated Hospital Anxiety Depression (HAD) and Body Image Satisfaction (BID) scales as well as a Dermatology Quality of Life (DQL) Scale which had been developed in Turkish population. They concluded that CL could affect all three dimensions of health mentioned in definition of health by the WHO [24].

In 2005, Reithinger et al. published the finding of their study of social impact of CL in Kabul, Afghanistan [25]. They reported that affected people were excluded from communal life which might range from minor restrictions such as avoidance of sharing of cups, plates and so on to more severe isolation. In addition, they reported an associated trauma from the disease in children with CL because of disfigurement, pain and discomfort associated with treatment and exclusion from playing with other children [25]. Also, some respondents noted that women with active CL or remaining scars had difficulty in finding husbands [25].

Different ways that AOWCL through which can adversely affects QoL of patients are summarized in table IV.
Table IV. Summary of different ways through which AOWCL can adversely affect patients’ quality of life.

<table>
<thead>
<tr>
<th>Clinical Concerns</th>
<th>Subjective Concerns</th>
<th>Main Affected Construct(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presence of lesion(s)</strong></td>
<td>Resulted anxiety ± depression for getting disease</td>
<td>Emotional</td>
</tr>
<tr>
<td></td>
<td>Anxiety ± depression about transmission the disease to others</td>
<td>Emotional</td>
</tr>
<tr>
<td></td>
<td>Anxiety ± depression about the future of disease</td>
<td>Emotional</td>
</tr>
<tr>
<td></td>
<td>Anxiety ± depression ± embarrassment for disfigurement</td>
<td>Emotional, social</td>
</tr>
<tr>
<td></td>
<td>Stigmatization</td>
<td>Emotional, social</td>
</tr>
<tr>
<td></td>
<td>Isolation</td>
<td>Social, emotional</td>
</tr>
<tr>
<td></td>
<td>Physical limitation and discomfort</td>
<td>Physical, emotional, social, economic</td>
</tr>
<tr>
<td></td>
<td>Daily activities†</td>
<td>Physical, emotional, social</td>
</tr>
<tr>
<td></td>
<td>Loss of occupation</td>
<td>Economic, emotional, social</td>
</tr>
<tr>
<td><strong>Treatment‡</strong></td>
<td>Expense(s)</td>
<td>Economic</td>
</tr>
<tr>
<td></td>
<td>Availability</td>
<td>Emotional, economic</td>
</tr>
<tr>
<td></td>
<td>Associated anxiety/pain</td>
<td>Emotional</td>
</tr>
<tr>
<td></td>
<td>Adverse effects</td>
<td>Physical, emotional, economic</td>
</tr>
</tbody>
</table>

*Described subjective concerns and affected constructed have been described for simple uncomplicated AOWCL lesion(s). † include: hygiene like washing hands, bathing, and so on, housework such as cleaning and cooking, religious duties, prayers. ‡Described subjective concerns and affected constructed have been described for the treatment of uncomplicated AOWCL lesion(s).
4. THESIS AIM

The aim of this thesis is to write a study protocol for developing a disease-specific instrument for evaluation of quality of life in adult Iranian patients who suffer from acute Old World CL.

5. PROTOCOL OF PLANNED STUDY

To write the protocol of the planned study the general formats suggested by Persson and Wall and writing a research proposal provided by the WHO have been followed [26, 27]. Few minor modifications have been made.

5.1. Title

Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients

5.2. Background

Background information has been provided under section 2.

5.3. Aim

The overall aim of this study is to develop an instrument to evaluate the QoL of Iranian adult patients who suffer AOWCL.

5.4. Objectives

1. To understand how patients with AOWCL feel about their disease.
2. To identify the main aspects of life affected by the AOWCL from patients’ perspective.
3. To determine the AOWCL patients beliefs about their disease and its burden on their quality of life.
4. To test face, content, construct and discriminant validity of the developed instrument.
5. To test *internal consistency, interrater, test retest reproducibility* of the developed instrument.

6. To evaluate the *responsiveness* of the developed instrument.

**5.5. Methods**

**5.5.1 Study Type**

A qualitative study is designed to understand how the AOWCL patients feel and believe about their disease and its impacts on their QoL. The Grounded Theory will be used for data interpretation. Psychometric properties of the instrument will be evaluated through a survey.

**5.5.2 Study Area**

The study will be conducted in a referral center for CL in Tehran and four different endemic areas for CL in Iran.

1. The Center for Research and Training in Skin Diseases and Leprosy (CRTSDL) in Tehran capital and largest city of Iran. Tehran is a metropolis with a calculated population of 7,185,831 in 2007 [28]. Tehran is located at 35.67° N and 51.43° E. Certain regions of Tehran were considered as endemic areas for CL, but at present the disease is limited to its certain suburbs. However, many cases of different kinds of CL are admitted to dermatology clinics at both academic institutions and private offices. CRTSDL is one of the referral centers for CL cases in Tehran.

2. Suburbs of Mashhad, where ACL is endemic. After Tehran, Mashhad is the second largest city of Iran. It is the capital of Khorasan Razavi province with a calculated population of 2,463,393 in 2007 [28]. It is located at 36.27° N and 59.57° E. It is about 775 km north-east of Tehran.

3. City of Bam, where ACL is endemic. City of Bam has a calculated population of 108,024 in 2007 [28]. The city is located at 29.08° N 58. 35° E and is about 1000 km far from Tehran.

4. Suburbs of Kashan, Central Iran, where ZCL is endemic. Kashan is located 170 km south-east of Tehran and has a calculated population of 320,774 in 2007 [28]. It is located at 33.98° N and 51.58° E.
5. Suburbs of Ahvaz, where is ZCL endemic. Ahvaz which sometimes is transcribed as Ahwaz is the capital of Khuzestan province in Iran. The city is located at 31.28° N, 48.72° E in 881 km south-west of Tehran. Its population in 2007 is calculated to be 832,969 [28].

Figure 3 demonstrates the locations of selected endemic areas for the planned study as well as the common AOWCL types in these regions.

5.5.3. Study Population

The study population is adult Iranian AOWCL patients who live in any of the four aforementioned endemic regions as well as those AOWCL cases who refer to CRTSDL during the time of study.

5.5.4. Sampling Method

Purposive sampling with maximum variation sampling will be used. AOWCL patients with any kind of clinical lesions of both sexes from different socio-economic classes who meet the following inclusion criteria will be recruited. Before conducting any part of the research a local coordinator will inform the AOWCL cases to come to the local health facility on a certain date. The research team member who is responsible for conducting the research in that area will meet the invited patients on the determined date, examine their lesions and will recruit them to either in-depth individual interviews or focus groups after giving a brief explanation about the overall aim of research project and obtaining their preliminary willingness to participate. The schedule for interviews and focus group discussions will be set. Sample size for each data collection methods is as follows:

1. In-depth individual interviews: Review of development of some other disease-specific QoL instruments shows that in-depth interviews has been performed with 8 patients during development of Scalpdex and with 65 interviewees in Whalley et al. study to develop Quality of Life Index for Atopic Dermatitis (QoLIAD) [22, 29]. It should be mentioned that 65 is the total number of interviewees in three different countries, the UK, Italy and the Netherlands, where Whalley et al. conducted their study. Assuming an empirical classification of clinical presentation of AOWCL to mild, moderate, severe besides a presumption of differential influence of gender on patients QoL, a preliminary sample size of
three men and women each with a certain severity of disease and from each of 5 study areas, totally 30 individuals, looks reasonable. Definitely, this number is a subject to change based on getting redundancy. The estimated time of each interview will be 60-90 minutes.

2. Focus group discussion: In each area two focus group discussion sessions one for men and one for women will be conducted. This will result in a total of 10 group discussion sessions. Each group will consist of 5 participants, so totally 50 informants will be recruited. The number of groups is a subject to change according to the preliminary results from the informants [30, 31]. The estimated time of each focus group discussion will be about 120 minutes. A moderator assistant will be present in the sessions to change the tapes and taking notes.

3. Free listing: each informant will be asked to list as many impacts of AOWCL on his/her life as possible. The number of informants is related to the required sample sizes for interviewees and participants in focus group discussion.

5.5.5. Inclusion, Exclusion and Withdrawal Criteria

1. Inclusion criteria:
   a. Patients with clinical manifestations of AOWCL in whom the disease has been parasitologically confirmed. Parasitological confirmation refers to existence of a positive laboratory result for presence of Leishman parasites in samples taken from relevant skin lesions in either direct smear or Nicolle-Novy-Mac Neal (NNN) culture medium.
   b. Age equals to or more than 18 years
   c. Willingness to participate

2. Exclusion criteria:
   a. Duration of disease more than 6 months
   b. Significant mental disorder according to medical records
   c. Significant chronic physical illness or disability that can have an influence on the possible AOWCL-related QoL or to communicate
3. Withdrawal criteria:
   a. Withdrawal of consent

5.5.6. Methods for Data Collection

In order to increase credibility of the study and get triangulation a combination of three different data collection methods is used:

1. In-depth individual interview: Semi-structured thematic interviews with open-ended questions will be performed.
2. Focus group discussion: Predetermined topics will be provided in a questioning rout format.
3. Free listing: Patients will be asked to list the different ways their disease influence their life.

All interviews and discussions will be conducted in Persian and in case of necessity a predetermined member of the local research team will interpret the interview/discussions. General themes for individual in-depth interviews and focus group discussions are physical, emotional, social and economic impacts of AOWCL on patients’ lives as well as any other feature of the disease that they find relevant and want to talk about.

In addition, data on age, sex, occupation, place of residence, marital status, socio-economic status, symptoms related to and clinical characteristics of the AOWCL lesion(s) will be obtained by filling a Case Report Form (CRF) for each participant. All participants will be examined and clinical characteristics of their lesions will be recorded on the same CRF. A sample CRF is available as Appendix I.

An overview of the planned study is demonstrated in figure 10.
* Includes reporting of preliminary results. † Includes expert checking and a pilot study

**Figure 10.** Flowchart of the general process of the study.
5.5.7. Documentation

1. Field notes: will be taken systematically throughout the whole process. During in-depth interviews notes will be taken by the researcher. In focus group discussion sessions a note-taker will take the notes while the researcher conducts the discussions.

2. Tape-recording: will be done after obtaining written permission from individuals with regard to in-depth individuals and all group members in case of focus group discussions.

3. Transcription: full transcription of tape-recordings of interviews and focus group discussion sessions will be done immediately after the end of each interview or group session.

5.5.8. Quality Control and Data Management

As described under section 5.5.6., three different data collection methods will be used to increase the credibility of the obtained data. Training of research team members and local supporters is planned. Monthly meeting with research team members at CRTSDL will be scheduled and problems will be discussed. One member of the research team will be responsible for conduction of research in each of the five fields. It is his/her responsibility to check the collected data including cross-checking of the transcriptions with the tapes for possible errors, made corrections and hand in them to the principal investigator (PI) after completion of each part of the study as well as to keep the confidentiality of the documents at the local level. The PI at CRTSDL will recheck the collected data and return the erroneous data to the responsible member of research team for correction. At the next step, all text data will be typed in Persian using Microsoft Office Word 2003® Software (Microsoft Corporation) and then translated to the US English. The English text will be typed with the same software and saved for open coding. Microsoft Office Access 2003® (Microsoft Corporation) will be used to develop a relational database for the whole project. In order to provide data security and confidentiality, the database will be secured on one personal computer in the PI’s office at CRTSDL and the PI will be the only one who will have full access to the database. According to the regulations of CRTSDL, one
expert in field of study out of the research team of the current project will be assigned by the CRTSDL Research Council to monitor the process of research.

5.5.9. Data Interpretation and Analysis

The Grounded Theory will be used to abstract interpretation of the collected data. As suggested by Dahlgren et al., data analysis will be done simultaneously with data collection. Modifications in the content of data collection methods will be considered, if data interpretation indicates its necessity [30]. Programme OpenCode which has been developed by the Division of Epidemiology and Public Health Sciences and Programming Staff from Computer Centre at Umeå University, Umeå, Sweden, will be used for coding the data. Collected data will be transformed to more abstract form according to the six-step technique described by Dahlgren et al. [30]. At the first stage PI and responsible members for each field will take part in meetings to discuss emerging issues and problems while interviews/focus group discussions are in progress in the fields. After the end of the fieldwork discussions, the transcripts will be reread and discussed to identify the most important constructs. Further analysis will be done by the PI to understand specific constructs. Each construct will be consisted of several items and each item will be scaled with using a five score Likert scale and will be scored from 0 to 4. Final wording and total number of the items will be decided after completion of the pilot study of psychometric evaluation and making necessary revisions.

5.6. Organization of Fieldwork

As mention under section 5.5.2., fieldwork will be done at CRTSDL as well as in four endemic areas for CL. In each study area out of Tehran a local coordinator from the Undersecretary of Health of relevant University of Medical Sciences will be assigned to facilitate the logistics and communication between the research team and local health care providers. One local health care provider will be chosen for further communication with research team, inviting participants and if necessary doing interpretations. The place for meetings for free listing, in-depth interviews and focus group discussions will be decided after consultation with local coordinator. Free listing, in-depth interviews and focus group discussions will be done by one of the research team members who will be determined for data collection in that field. Moderator assistants will be selected from
either CRTSDL research assistants or local health care providers. The PI will organize the research conduction at CRTSDL in collaboration with the CRTSDL staff.

5.7. Ethical Considerations

The proposal and its consent form (Appendix II) will be reviewed by the Medical Ethics Committee of the Center for Research and Training in Skin Diseases and Leprosy, Medical Sciences/University of Tehran. Issues of autonomy, confidentiality, beneficence and avoiding malfeasance will be discussed.

1. Beneficence of the study:

   a. Direct:

      i. This study will help a better understanding of ideas, beliefs, feelings and perceptions of AOWCL patients about their disease, which can potentially help the physicians and health care providers to provide a more patient-concerned care through a better rapport and knowing what patients need.

      ii. Feedbacks of this study will be sent to relevant organizations including officials in the areas of field work and MoH. This will help the local decision makers and national health policy makers to obtain a better understanding of the impact of AOWCL on QoL of patients, which by itself can be resulted in improvement of policy/decision making with regard to this disease.

      iii. With regard to AOWCL, Iran, Afghanistan, Saudi Arabia, Syria and Iraq are similar in several aspects: the most common AOWCL causative parasite is either \textit{L. major} or \textit{L. tropica}, all of those countries are located in the Middle East, which results in some shared features in terms of geographical and racial characteristics and the majority of these populations are Muslims, which results in a roughly similar socio-cultural background. Algeria is also quite similar to those countries in terms of having same causative parasite as well as geographical and population characteristics. For these reasons, the instrument, of course after being evaluated for its psychometric properties in each country, can be used in 5 out of 7 countries from which 90 % of the
world CL cases are reported. In addition, it can facilitate making another instrument for QoL measurement in New World CL patients.

**iv. Development of such instruments is invaluable in terms of provision of a common outcome measure through which findings of different studies like clinical trials can be compared. This can assist clinical researchers to look for the most appropriate treatments which include patient-need in their efficacy.**

**b. Indirect:**

i. Participants in the study who need treatment for their disease will be treated freely.

ii. Capacity building for performing future research projects through training of staff at different levels.

2. Harm avoidance: The fieldwork will be scheduled to result in minimal interruption in routine health care service delivery. Participants in focus group discussions will be informed about the importance of not sharing the information or problems of other participant with any one outside the group.

3. Autonomy: Patients will be requested to give their voluntary written informed consent if they wish to participate in the study. This will be done after provision of a verbal or written description of the aim and a brief explanation of the study, to illiterate or literate participants, respectively, by an authorized member of the research team.

4. Confidentiality: will be kept in reports by using initials of participants. To keep the confidentiality of participants, prevention of data spreading in the focus group discussion sessions will be discussed with the participants.

**5.8. Limitations and Suggestions for Reducing Them**

1. Lack of knowledge and experience of qualitative methodology among some members of the research team: The research team members are planned to take part in short term workshops of qualitative research methodology with focus on the methods that will be used in this study. At the beginning, a researcher with
previous training and experience in qualitative methods will be present in each study area. Later on, the researcher can decide if it is possible to delegate parts of or the whole process of one or more of data collection methods and analyses in an area to a co-researcher, at first under meticulous supervision.

2. Language barrier: Persian is the official language in Iran and most people can understand and communicate through this language. If there was any participants who could not communicate in Persian one of the local supporters will be asked to translate the interview/focus group discussion questions to the participant and back translate his/her answers to the researcher. During both the performance of the study and after the development of the instrument, there might be a need for English translations of some of the project materials such as transcription of tape-recorded sessions and so on. To prevent problems related to Persian-English translations all documents will be translated to the US English independently by two members of the research team who are fluent in English and controversies will be solved with consensus. Data interpretation will be performed on English documents and at the end the findings will be back translated to Persian.

3. Logistics: As it was described in the section 5.2., this study needs a considerable number of travels to endemic areas. Some instruments from those needed for laboratory examination to stationary, relevant forms, tape-recorders and so on should be carried to the fields. The places for interviews and focus group discussions should be ready at the appropriate time. In addition, local personnel including drivers should be available when field studies are running. To address such problems close cooperation with local officials is crucial and hopefully will help the research team considerably.

4. Change in incidence of the disease: CL is an infectious disease and getting the disease can result in strong immunity [11]. This may result in significant changes in the number of new cases in some areas. Suggested study sites have been selected according to the available data at the beginning of 2006 (A. Firooz, personal communications).
5. Qualitative research data analysis: It might look reasonable that to get the most homogenous results the whole data collection and interpretation be done by one investigator, but it will limit the data interpretation because of this fact that all data are interpreted by one person. As it was mentioned under the section 5.5.9, it is planned that data collection including transcribing of the recorded materials in each of the selected areas done by a member of research team who is responsible for the research in that particular area. Quality control methods for increasing the validity of the obtained data were discussed under section 5.5.8. As has been mentioned previously, coding and interpretation of the collected data of the qualitative study will be done by the PI. This approach might provide a wider diversity of findings because several individuals are involved in data collection methods, but finally data interpretation will be done by one person. Another alternative approach is to ask the responsible member of each area to do the analyses independently and then discuss the findings with the PI. This approach may be advantageous because it can potentially detect some codes/constructs that might be overlooked if the whole analysis process is done by a single person. This is the rational behind the delegation of some parts or whole data collection and analyses procedure to a co-investigator sometimes after the commencement of the study.

5.9. Psychometric Evaluation

After development, the instrument has to be assessed for its psychometric properties. This assessment will be done in the same field areas where the qualitative study is to be done and the eligibility criteria for participants in the survey are the same as what have mentioned under section 5.5.5. The validity, reliability and responsiveness of the instrument will be assessed according to the methods suggested by Chen et al. and Anderson et al. [22, 32]. Methods for these assessments are summarized in Table V. To evaluate the discriminat validity of the instrument, it will be run in parallel with the Persian version of DLQI, which has been validated by Aghaei et al. [33].
Table V. Methods for psychometric evaluation of the developed instrument.

<table>
<thead>
<tr>
<th>Psychometric property</th>
<th>Method for Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Validity</strong></td>
<td></td>
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<tr>
<td>Face and Content</td>
<td>Expert and patients checking*</td>
</tr>
<tr>
<td>Construct</td>
<td>Factorial analysis</td>
</tr>
<tr>
<td>Discriminant</td>
<td>Running the developed instrument in parallel with a previously validated instrument</td>
</tr>
<tr>
<td><strong>Reliability (Reproducibility)</strong></td>
<td></td>
</tr>
<tr>
<td>Interrater</td>
<td>Patient’s vs. physician rating of the severity of diseases</td>
</tr>
<tr>
<td>Internal consistency</td>
<td>Calculation of Cronbach’s alpha</td>
</tr>
<tr>
<td>Test-retest</td>
<td>Re-administration of the instrument to the same patients 72 hours after the first administration†</td>
</tr>
<tr>
<td><strong>Responsiveness</strong></td>
<td>Assessment of patients with different severity of the disease, assessing patients whose severity of the disease has changed over time‡</td>
</tr>
</tbody>
</table>

* After expert checking a pilot study on 30 patients will be done to finalize the number of constructs and items and wording. † For this purpose validated Persian version of DLQI will be used. ‡ For this purpose the instrument will be re-administered to a sample of patients after 30 days of the first administration.

The total required sample for psychometric evaluation depends on the total number of items in the developed questionnaire. Patient recruitment will be done according to a computer generated random list. In order to collect data on age, sex, occupation, place of residence, marital status, socio-economic status, symptoms related to and clinical characteristics of the AOWCL lesions of participants, besides the instrument itself, a copy of the same CRF which has been described under section 5.5.6. will be handed in to each participant and will be collected after being filled. All participants will be examined and clinical characteristics of their lesions will be recorded on the same CRF. All data analysis for psychometric evaluation as will be done using SPSS software version 13 (SPSS Inc., IL, USA).
5.10. Timetable

The estimated time for this study is 48 months. Details of planned activities and their time schedule are displayed in tables VI to IX.

**Table VI.** Timetable of planned activities for months 1 to 12

<table>
<thead>
<tr>
<th>Planned Activity</th>
<th>Month</th>
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</thead>
<tbody>
<tr>
<td>Final operationalization and determination of study sites</td>
<td>1</td>
</tr>
<tr>
<td>Coordination with MoH and local officials</td>
<td>4</td>
</tr>
<tr>
<td>Training of the research team members at the CRTSDL</td>
<td>2</td>
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<tr>
<td>Recruiting and training of supporting staff</td>
<td>7</td>
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<tr>
<td>Recruiting patients*</td>
<td>11</td>
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<tr>
<td>Data collection†</td>
<td>12</td>
</tr>
<tr>
<td>Data analysis‡</td>
<td>1 2 3 4 5</td>
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</tbody>
</table>

* Recruitment of participants for in-depth individual interviews, focus group discussion and free listing.
† Data collection methods are in-depth individual interviews, focus group discussion and free listing.‡ As recommended for qualitative research, data analysis will be done during the same time that data collection. This will help the researcher to make necessary changes to the collection methods according to the findings in data analysis.
**Table VII.** Timetable of planned activities for months 13 to 24

<table>
<thead>
<tr>
<th>Month</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
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<th>21</th>
<th>22</th>
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<td>Data collection</td>
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<tr>
<td>Data analysis</td>
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<tr>
<td>Development of the instrument</td>
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<tr>
<td>Report writing*</td>
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<tr>
<td>Report dissemination†</td>
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* Includes writing the drafts of the relevant scientific papers. † Includes submission of the written manuscripts to the scientific journals.

**Table VIII.** Timetable of planned activities for months 25 to 36

<table>
<thead>
<tr>
<th>Month</th>
<th>25</th>
<th>26</th>
<th>27</th>
<th>28</th>
<th>29</th>
<th>30</th>
<th>31</th>
<th>32</th>
<th>33</th>
<th>34</th>
<th>35</th>
<th>36</th>
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<tbody>
<tr>
<td>Report dissemination*</td>
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<tr>
<td>Expert checking for validity</td>
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<tr>
<td>Preparation for psychometric evaluation</td>
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<tr>
<td>Pilot study for psychometric evaluation</td>
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<tr>
<td>Making necessary changes to the instrument</td>
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</table>

* Includes submission of the written manuscript(s) to the scientific journal(s).
Table IX. Timetable of planned activities for months 37 to 48

<table>
<thead>
<tr>
<th>Month</th>
<th>Planned Activity</th>
<th>37</th>
<th>38</th>
<th>39</th>
<th>40</th>
<th>41</th>
<th>42</th>
<th>43</th>
<th>44</th>
<th>45</th>
<th>46</th>
<th>47</th>
<th>48</th>
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<tbody>
<tr>
<td>37</td>
<td>Recruitment of patients to psychometric evaluation</td>
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<td></td>
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<tr>
<td>38</td>
<td>Psychometric evaluation</td>
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</tr>
<tr>
<td>39</td>
<td>Data analysis</td>
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* Includes writing the draft(s) of the relevant scientific paper(s). † Includes submission of the written manuscript(s) to the scientific journal(s).

5.11. Budget

Four main categories of expenses are considered:

1. Salaries: include the sum of salaries of the PI, co-investigators, consultants, research assistants, and local staff.
2. Services: include road and air transportation expenses, laboratory fees and catering.
3. Equipment: include required equipment for fieldwork such as tapes and tape-recorders.
4. Writing and publication expenses: include expenses for stationery, printing, and copying of the required forms, study documents and materials that are needed for writing reports and dissemination.

The estimated budget will be presented in Euro.
6. EXPECTED RESULTS

6.1. Expected Constructs

Based on clinical manifestations of AOWCL and literature review, it seems that AOWCL could adversely affect physical, mental and social aspects of life of patients who suffer from [1, 8, 20, 21], so at least 3 constructs are expected to be found.

6.2. Expected Instrument

The expected instrument will be a questionnaire which will be developed according to the found constructs in the qualitative research. Multiple items will be used for scaling purposes. Each item will be scaled using a five score Likert scale and will be scored from 0 to 4.

6.3 Expected publications

It is expected that results of this research as well as its proposal be published in scientific journals. Four papers are expected to be published. The planned publications are:

1. Study design (1 paper)

2. Results of the qualitative study (2 papers)

3. Results of the psychometric evaluation of the developed instruments (1 paper)
7. DISCUSSION

7.1. Need for Development of a Disease-Specific QoL Instrument for AOWCL

Due to some characteristics of AOWCL, neither generic health-related QoL instruments such as SF-36, SIP, and so on nor dermatology specialty QoL instruments like DLQI, DSQL and Skindex are appropriate for evaluation of QoL in AOWCL patients. Evidence includes:

1. AOWCL is limited to the skin and lacks systemic presentations like fever
2. It shares some characteristics of skin diseases like an impact on QoL as a result of visibility of lesions and stigmatization.
3. Unlike most of other skin diseases that either has been studied with dermatology-specific QoL instruments [34] or for which disease-specific QoL instruments have been developed, AOWCL is a self-healing disease in the majority of cases.
4. AOWCL has a relatively rapid course in comparison with other skin diseases such as psoriasis and eczema.
5. Absence of some common skin symptoms such as pruritus limits the use of those instruments that have questions regarding those symptoms.
6. Absence of some common cutaneous signs like scaling which is present in other skin diseases also reduces the validity of those instruments for assessing QoL in AOWCL patients.
7. Being a potential source for transmission of the diseases in ACL cases may be of particular importance that is not covered in currently available generic, dermatologic-specific or diseases-specific QoL instruments
8. No outcomes measure is available to reflect patients’ perspective concerning their disease
9. No universally outcome measure is available for evaluation of AOWCL changes overtime in clinical trials
Anderson and Rajagopalan and Finlay and Khan in their articles on development of DSQL and DLQI explained some deficits of application of generic health-related QoL instruments in patients with skin diseases [19, 20]. They pointed to the absence of many of the salient factors that are associated with skin diseases, and lack of close resemblance to needed conceptual models of QoL in generic instruments [20] as well as their length that make them unsuitable for routine use in busy dermatology clinics [19].

Doward et al. considered inclusion of some items that are inappropriate for the specific health problem as one of the major disadvantages of the generic health status instruments [35]. Accordingly, missing of some areas of importance in such instruments is another disadvantage [35]. General characteristics of HRQoL and needs-based QoL instruments are demonstrated in table IX.

**Table X.** HRQoL vs. needs-based QoL instruments.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type of the instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HRQoL</td>
</tr>
<tr>
<td>Fundamental assumptions</td>
<td>Health is the major influence on QoL, no interaction between health and other determinants of health</td>
</tr>
<tr>
<td>Emphasis on</td>
<td>Symptoms and functions</td>
</tr>
<tr>
<td>Main value(s)</td>
<td>Health</td>
</tr>
<tr>
<td>Role of patient</td>
<td>Patient-completed</td>
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<tr>
<td>Interest of</td>
<td>Experts/physicians</td>
</tr>
<tr>
<td>Cultural issues</td>
<td>Culture-bond</td>
</tr>
<tr>
<td>Irrelevant questions</td>
<td>Yes</td>
</tr>
<tr>
<td>Assessment of patient adaptation to illness</td>
<td>No</td>
</tr>
<tr>
<td>Responsiveness</td>
<td>Limited reliability and responsiveness in clinical trials</td>
</tr>
</tbody>
</table>
Table X. (continued)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type of the instrument</th>
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<tbody>
<tr>
<td></td>
<td>HRQoL</td>
</tr>
<tr>
<td>Valuable for</td>
<td>Clinical assessments</td>
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<tr>
<td>Drawbacks</td>
<td></td>
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<tr>
<td></td>
<td>Focus on fulfillment of normal roles</td>
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<tr>
<td></td>
<td>Devaluation of unemployed and disabled individuals</td>
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<tr>
<td></td>
<td>Requires some insight and expertise on behalf of respondents</td>
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</table>

Lack of responsiveness of generic instruments such as SF-36 and SIP has been described by Doward et al. [35]. The rational for assuming of shortcomings of dermatology-specific in evaluation of QoL follows the same logic. For example in DLQI there are questions about itch, pain, and so on that are generally not relevant to AOWCL patients. Similarly, parts of the questions which include patient’s gardening, messy treatments and sexual difficulties may not appropriately understood and answered by patients in most CL areas both in Iran and in the region. The disease (condition)-specific QoL instruments are developed to measure QoL in patient with specific diagnosis and do not allow for comparison of patients in different diagnostic groups [12].

7.2. Defining a Patient-Concerned Outcome Measure

Khatami et al. in their recently published systematic review of randomized controlled trials of treatments for AOWCL found that in different trials a diverse spectrum of outcomes was used to assess the efficiency of treatments and to define “cure” [10]. All of those outcomes were based on clinical or clinical plus parasitological criteria and none of them reflected patients’ perspective about their disease and the administered treatment. [10]. The planned instrument can be used in routine practice to assess patients’ perspective about their disease and to provide more patient-centered health care. In addition, Doward et al. have discussed the effectiveness of several needs-based QoL
measurement instruments in the assessment of changes over times in clinical trials. [14]. Development of a disease-specific instrument for QoL measurement in AOWCL patients not only could provide a patient-concerned outcome measure for use in clinical trials but also could be used as a between study comparable outcome measure.

7.3. Qualitative Study vs. Survey

Development of a QoL instrument for AWOCCL which has a combination of clinical manifestations of a skin disease with its own specific impacts on QoL like visibility, stigmatization, and so on; and a self-healing nature in a relatively short time is quite specific [8, 36]. Unfamiliarity of the subject as well as a need for an exploratory research and finding meanings rather than frequencies suggests choice of a qualitative approach with enough flexibility to allow for detection of unexpected and in-depth study of specific topics [31]. Development of a needs-based QoL measurement instrument requires in-depth individuals with relevant patients [12].

7.4. Rationale for Choosing Sampling Method

To develop a needs-based QoL instrument it is crucial to understand patients’ perspective about their disease or condition. For this reason, patients from both endemic and non-endemic areas who will predictably provide a wide spectrum of clinical disease and demographic background will be recruited. This sample will not only include cases due to both L. major and L. tropica but also covers geographically different foci of AOWCL in Iran, including two endemic foci in central as well as one focus in each south-west and north-east Iran which are close to Iran’s border with Iraq and Afghanistan, respectively. This sample provides an opportunity to be aware of patient’s perspectives from different cultural background. Choosing these areas may increase the generalizability of the developed instrument and facilitate its future validation for use in Afghanistan, Iraq and other Arab countries.

7.5. Rationale for Selection of Data Collection Methods

To increase the credibility of the study through triangulation, use a combination of different data collecting methods is planned.

1. In depth individual interviews:
a. Interviews are appropriate methods when the researcher is looking for belief and attitudes. [31]

b. In-depth interviews are considered as the main material for Grounded Theory.[30]

2. Focus group discussions:
   a. Similar to in-depth interviews with individuals, focus group discussions are valuable to address questions about people’s beliefs and attitudes. [31].
   b. In addition, they reflect groups’ points of view rather than individual perspectives [30, 31]
   c. They can be used to collect considerable amount of information about a focused topic in a short time [30].

3. Free listing: is another way for assessing patients’ beliefs and attitude toward their disease and is relatively easy to use. [30].

They are appropriate for answering almost all research questions.

7.6. Rationale for Choosing Grounded Theory for Data Interpretation

Dahlgren et al have counted several characteristics of Grounded Theory [30]. Some of these characteristics are:

1. Clinically AOWCL is quite different from other dermatoses for which QoL measurement instruments have been already developed. The cultural setting in which the current instrument is presumed to be developed is different, so looking for new ideas and constructs is essential and the Grounded Theory is appropriate for this objective.

2. The Grounded Theory can be used effectively for developing constructs.

3. Generalizability from concrete to abstract is another advantage of Grounded Theory.

4. In comparison with other qualitative research methods, Grounded Theory is relatively easier to teach.
7.7. Rationale for Developing the Instrument as a Questionnaire

A needs-based approach is used and the patient perspectives will be elaborated through a qualitative research. A review of current dermatology- or disease (condition)-specific QoL instruments in dermatology shows that all of them have been developed as questionnaires. This might be caused by: easy administration, possibility for different types of administration like self-administration, interviewer-administration and so on according to needs, reducing of missing data, convenience for reviewing for detection of errors, and provision of an objective easy scoring.

7.8. Rationale for Choosing Lickert Scale

Davey et al compared adequacy of a single-item question with a five-point Likert Scale response and a Visual Analogue Scale (VAS) in random order, by assessing their correlations with a demographic questionnaire, the State Trait Anxiety Inventory (STAI). They found that despite both the VAS and the Likert Scale measures were adequate predictors of the STAI score and their correlations with STAI were 0.78 (95% confidence interval [CI] 0.73-0.82) and 0.75 (95% CI 0.70-0.79), respectively, 11% of women incorrectly completed the VAS which limited its usefulness [37]. In addition, a five scale Likert provide more choices for the participant in comparison with a yes/no scoring system.

7.9. Generalizability

As K.J. Rothman has mentioned in his book *Epidemiology: an Introduction* “in epidemiologic science, just as in laboratory science, we move away from specific toward the general: we hope to generalize from research finding, a process based more on scientific knowledge, insight, and even conjecture about nature than on statistical representative of actual participants” [38]. Because of clinical characteristics of AOWCL most patients attend health care facilities to receive treatment. In addition, the population that this instrument will be used for are not significantly different from the sample that is used to develop that instrument. There is no evidence for a significant difference among those patients who attend and who do not attend health care facilities (A Firooz, personal communication).
7.10. Conclusion

Development of an instrument for evaluation of QoL in AOWCL patients has many advantages from provision of patients’ perspective about their disease which can promote the health care delivery to these patients to the possibility of using the developed instrument in research such as an outcome measure in clinical trials.
8. REFERENCES


APPENDICES

Appendix I. Case Report Form (CRF) for Background and Clinical Data Collection

Project title:

Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients: A Study Protocol

Project's ID number:

Sponsor:

Principle investigator:

Institute: Center for Research & Training in Skin Diseases & Leprosy, Medical Sciences/ University of Tehran

Address: No. 79, Taleqani Avenue, P.O. BOX 14155-6383, Tehran, 14166, Iran

Phone: +98 (0) 21 8897 0657, Fax: +98 21 (0) 8897 0658

Email address: akhatami@tums.ac.ir

Site:

Patient's initials: [___] [___] [___] [___] [___] [___]

Patient's identification number: [___] [___] [___]
Case Report Form (CRF)

**Project title:** Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients: A Study Protocol

**Participant’s Initials:**

**Date:** (YYYY/MM/DD)

**Eligibility Criteria**

**Inclusion criteria:**

1. Parasitologically confirmed cases of cutaneous leishmaniasis based on positive smear and/or culture

2. Age 18 years or more

3. Willingness to participate in the study and sign the informed consent

All the answers should be **Yes** to include the participant.

**Exclusion criteria:**

1. Duration of lesions more than 6 months

2. Significant mental disorder according to medical records

3. Significant chronic physical illness or disability that can have and influence on the possible AOWCL-related QoL or to communicate

All the answers should be **No** to include the patient.

**Date of birth:** (YYYY/MM/DD)

Sex: 

Current Job: 

Job before getting AOWCL:

Socio-economic status (according to participant): Low/ Average/ High
Case Report Form (CRF)

**Project title:** Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients: A Study Protocol

**Participant’s Initials:** [Redacted]

**Date:** [Redacted] (YYYY/MM/DD)

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Appendix II. Informed Consent Form

Participant’s Initials: |___|___|___|___|___|___| Patient's identification number: |___|___|___|

1. Research Project Information

**Project Title:** Development of a Disease-Specific Instrument for Evaluation of Quality of Life in Patients with Acute Old World Cutaneous Leishmaniasis in Adult Iranian Patients

**Project ID Number:**

PI: (first name and last name) Location:

**Contact Address:** Center for Research and Training in Skin Diseases and Leprosy, No. 79, Taleqani Avenue Tehran 14166 I.R. IRAN

**Phone:** +98 (0) 21 8897 0657, **Fax:** +98 21 (0) 8897 0658 **Email:** akhatami@tums.ac.ir

2. General Information about the Project

Cutaneous leishmaniasis (CL) has been reported from almost all provinces of Iran and is a major health problem in several regions in our country. CL can affect patients’ life through different ways. This research project is performed to find out how life of patients with acute Old World CL can be affected by their disease and what is their point of view about their disease which the research team belief that will result in better care of AOWCL patients.

Please read this consent form and if you want to participate in this study sign it. If there is any question please do not hesitate to ask who handed this form to you. If you can not read this consent form please ask the research member team that has handed it to you. (s)he will explain its content to you completely and if you wish to participate you can use your fingerprint instead of signature.

3. Procedures

In this project you will be asked to participate in an in-depth interview/ a focus group discussion /a survey which is a type of study in which you will be asked to complete a questionnaire. In each of these sections you will be asked to provide your personal
experience and opinions about your disease. In-depth interviews and focus group discussions will take about 60-90 minutes and 2 hours, respectively.

4. Confidentiality

Your identity in this study will be considered as confidential. The results of the study, including any data, may be published for scientific purposes but will not give your name or include any identifiable references to you.

5. Authorization

Taking part in this study is voluntary and you can discontinue your participation whenever you decided. This act will not result any change in the routine local health care services you receive for your diseases.

I (first name and last name of the participant) have read/listened to above mentioned information and understand it completely. I wish to participate in this study.

Date and place          Signature/Fingerprint of Participant

Date and place          Signature of who has obtained the informed consent

Date and place          Signature of Principle Investigator