The rough journey to access health care
The case of leishmaniasis in the Bolivian rainforest

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To my dear father. You always believed in me, even more than I do. My confidence to face life’s challenges, I owe to you.

To my dear mommy. You were always taking care of me and my future, demanding to never stop.

To my brothers and my sister, you were always available to listen and comfort me when I felt alone. Contacting them, home didn't feel so far.

To my loved sons who allowed me to discover my greatest happiness, being a father.

To my little daughters, “las niñas de mis ojos”. Seeing them every day makes me feel the most privileged person for being able to witness their joys and innocence.

To my beloved Ana. Owner of my heart and my main support in this long journey when I no longer had strengths... just to tell you, we did this together!
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Abstract

Background

Leishmaniasis is a parasitic infectious disease transmitted by vectors that cause three main clinical syndromes: cutaneous (CL), mucosal (ML), and visceral (VL). Since VL is not relevant to this thesis, only CL and ML will be further discussed. Leishmaniasis is present in 98 countries, with more than 350 million people at risk of infection. Leishmaniasis disproportionately affects poor countries and, in particular, remote areas where health services are weaker. Bolivia, a lower-middle-income country, is the fifth country with more cases in Latin America, and case detection and management is the main control strategy of the National Leishmaniasis Control Programme (NLCP). The NLCP provides free treatment to patients, which consists of systemic pentavalent antimonials (SPA) for 20 days. This treatment is highly toxic for patients and costly for the government, resulting in long periods of shortage of the drug. A good alternative to SPA is the use of intralesional pentavalent antimonials (ILPA), which are safer and have similar efficacy to SPA in treating CL. Case detection and management depend on a well-structured health-care system, and the primary level of care is responsible for this task in Bolivian endemic areas. It is well known that health-care access for leishmaniasis patients is limited but the extent and the determinant factors of this problem are unknown. The aim of this thesis is to assess health-care access among patients with leishmaniasis in a Bolivian rainforest rural area, addressing four specific questions: Who is most vulnerable to CL?; What is the extent of their lack of access to health care?; How do the dimensions of access and the quality of care influence health-care utilization in a context of vulnerability?; and how can a change in NLCP policy related to the treatment of CL improve the level of access to health care?

Methods

This thesis is based on four studies that use quantitative and qualitative methods. Data collection was conducted through surveys, in-depth interviews and revision of official documents. Sub-study 1 was based on a cross-sectional study conducted in two communities of Cochabamba and assessed risk factors for CL using multivariate analysis. Sub-study 2 used the method of capture–recapture to assess the level of under-reporting of the national register for the period of 2013–2014, using Chapman’s formula. Sub-study 3 was conducted through in-depth interviews applied to 14 participants, using thematic analysis. Sub-study 4 was an economic evaluation that used data from surveys with physicians, official documents and key informants and compared the costs of systemic pentavalent antimonials (SPA) and intralesional pentavalent antimonials (ILPA) from the
perspective of the Ministry of Health (MoH) and society. Additionally, a budget impact analysis of the implementation of ILPA in hypothetical scenarios of increasing level of demand was carried out.

Main findings

Sub-study 1 showed that gender/sex was the only statistically significant factor associated with CL, with men being the most affected group. Other classical factors, such as animal ownership, house materials and protective measures were, however, not related to CL. Sub-study 2 revealed a high level of under-reporting (73%) of CL in the study area, and this under-reporting was higher among men compared to women. Sub-study 3 showed that the lack of availability, accessibility, affordability and quality of care were the main factors that limited the access to care of CL and ML patients. In sub-study 4, the economic analysis pointed out that the use of ILPA was cost-saving for the MoH and society, and the budget analysis confirmed that the implementation of ILPA as first-line treatment was not only cost-saving for the MoH, but it would also increase the number of patients accessing the treatment.

Conclusions

The predominance of a sylvatic pattern of transmission, with men as the most affected group, demands new approaches to prevention related to occupational activities. The NLCP policy related to case management has been essential to reducing economic barriers for patients with leishmaniasis; however, there are still a considerable amount of cases who do not have access to the treatment. Lack of health services, equipment and drugs, as well as difficulties in reaching health services, the high costs of seeking health care and the low quality of care are important factors that must be addressed to fulfil the right to health care for these patients. Finally, new therapeutic alternatives, such as ILPA, must be considered to reduce problems of affordability, adherence, as well as side effects to the treatment. This information can be used to develop targeted interventions aimed at increasing the access to health care of people with leishmaniasis in the rainforest of Bolivia.
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CL</td>
<td>Cutaneous Leishmaniasis</td>
</tr>
<tr>
<td>CTMSSU</td>
<td>Center of Tropical Medicine of San Simon University</td>
</tr>
<tr>
<td>DME</td>
<td>Direct Microscopic Examination</td>
</tr>
<tr>
<td>ILPA</td>
<td>Intra Lesional Penta Antimonials</td>
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<tr>
<td>INT$</td>
<td>International Dollars</td>
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<tr>
<td>ISNP</td>
<td>Isiboro Secure National Park</td>
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<tr>
<td>LIC</td>
<td>Low Income Countries</td>
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<tr>
<td>ML</td>
<td>Mucosal Leishmaniasis</td>
</tr>
<tr>
<td>MoH</td>
<td>Ministry of Health</td>
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<tr>
<td>MST</td>
<td>Montenegro Skin Test</td>
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<tr>
<td>NLCP</td>
<td>National Leishmaniasis Control Program</td>
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<tr>
<td>PHC</td>
<td>Primary Health Center</td>
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<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>SPA</td>
<td>Systemic Penta Antimonials</td>
</tr>
<tr>
<td>UMCHI</td>
<td>Universal Maternal and Child Insurance</td>
</tr>
<tr>
<td>VL</td>
<td>Visceral Leishmaniasis</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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The thesis is based on the following papers:


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Prologue

Introducing myself

I completed my training as a medical doctor in the Faculty of Medicine at San Simon University in Cochabamba, Bolivia in 2004. Then I had the opportunity to continue my professional career in a research project with an indigenous group, the Tsimane, who live isolated in the deep rainforest of the Bolivian Amazon. For 13 years, I worked collecting epidemiological data and providing primary medical care to this population. In the first years of my work, I learnt from the Tsimane's lifestyle the exquisiteness of the simple and natural, and the value of living with the bare minimum. However, even though I was convinced that their lifestyle was very much better than mine in the city, it was clear they were full of unattended medical needs. It was very sad to witness how people died from easily preventable and curable diseases. As part of my job, I had to manage complicated medical cases, organizing the logistics needed for transferring patients and providing them adequate attention in centres of a higher level of care. During this period, we signed many collaboration agreements with non-governmental organizations, church institutions, and public services to facilitate this process, reducing direct and indirect costs of medical attention. However, this task was not sustainable and, currently, support to the indigenous people has been reduced substantially. Independent initiatives do not solve health problems because, usually, they are not sustainable over time.

That is why, the main responsibility must be taken by the government, generating conditions to ensure the fulfilment of people’s right to health, with a health system that ensures the quality of care and in which health facilities, goods and services are available and affordable to all.

In 2014, I had the opportunity to participate in a public invitation from San Simon University and the Swedish International Development Agency (SIDA) to enrol in a PhD in public health. This PhD gave me not only the opportunity to be part of the research team of the Centre of Tropical Medicine at the medical school of San Simon University but also to meet Miguel, Isabel and Anna-Karin, who since from then have become my supervisors at Umeå and my support in this journey.

I chose leishmaniasis as my topic for this thesis because it is a problem that enables the portrayal of the conditions of marginality, the limited options to accessing health care and the little attention that people receive from the national health authorities in the remote rural areas of the Bolivian rainforest. In this sense, I believed the investigation of leishmaniasis control in Bolivia would allow
me to portray the problem of inequity in health-care access in tropical rural areas and hopefully contribute to its improvement.

What is this thesis about?
This thesis is about the challenges that patients with leishmaniasis in the Bolivian rainforest experience when trying to access health care. Four main questions guide this thesis: Who is most vulnerable?; What is the extent of the lack of access to health care?; How do the dimensions of access and quality of care influence health-care utilization in settings of limited livelihood assets?; and can a change in the National Leishmaniasis Control Programme policy related to the treatment improve the level of access to health care?

The thesis begins with a brief background about the disease, its epidemiology and control methods, with emphasis on diagnosis and treatment as part of the case management strategy. Additionally, the difficulties and limitations of epidemiological surveillance systems are described, as well as those related to access to treatment. A chapter about the context of the study continues with a brief description of Bolivia, its health system, the situation of leishmaniasis in Bolivia and the approach used by the National Leishmaniasis Control Programme (NLCP). Next, the justification, objectives and the conceptual framework of the thesis are presented. The methods applied to achieve all the objectives, as well as the results, are described separately in the subsequent chapters. There follows a chapter that includes the discussion of the results, organized in relation to the conceptual framework, including the methodological considerations. Finally, the conclusions, the implications for practice of the findings and future research needed are described.
Background

What is leishmaniasis?
Leishmaniasis is a treatable and curable parasitic infectious disease transmitted by sandflies when they bite humans. Leishmaniasis is considered a complex disease due to the wide variety of different species involved in the transmission chain among Leishmania parasites, reservoirs, and vectors. There are more than 70 animal species, including humans, identified as reservoirs; more than 30 different species of phlebotomine sandflies identified as vectors; and more than 20 species of Leishmania parasites pathogenic to humans [1]. Humans are infected when being bitten by a sandfly, which carries the parasite from its natural reservoir. In Latin America, the human is an accidental host when invading the vector and parasite’s ecosystem for occupational reasons – this mechanism of transmission is called ‘sylvatic’. In other cases, when there is a process of deforestation and colonization of rainforest areas, vectors and parasites become adapted to these new environments and find new reservoirs close to the houses; this mechanism of transmission is known as peridomestic (Figure 1).

Source: Constructed by the author.

Figure 1. Transmission chain of leishmaniasis infection.
The clinical syndromes caused by the infection depend on the species of Leishmania parasite involved [2]. The three main clinical syndromes are: cutaneous, mucosal and visceral. Cutaneous leishmaniasis (CL) is the most frequent syndrome, characterized by chronic skin ulcers that can take months to years to heal, leaving scars for life (Photo 1). CL affects patients’ quality of life in addition to work and school activities [3]. CL scars produce loss of self-esteem, depression, anxiety and stigma and are an obstacle to their social integration [4, 5]. Mucosal leishmaniasis (ML) is characterized by chronic ulcers of the mucous membranes in the nose, mouth and larynx that can evolve to partial or complete destruction of underlying structures. This destruction affects the ability to speak, and in severe cases, vital functions can be compromised as well, such as breathing or feeding, leading to death (Photo 1). Visceral leishmaniasis (VL) is characterized by irregular episodes of fever, weight loss, hepatosplenomegaly, and anaemia. Since VL is not relevant to this thesis (only 10 cases have been reported during the last 40 years in Bolivia), only CL and ML will be discussed hereafter.

Photo 1. Cutaneous ulcer in the face and mucosal ulcer in the nasal septum


Epidemiology of leishmaniasis

Globally, leishmaniasis is among the top ten neglected tropical diseases with more than 12 million infected people. Leishmaniasis is endemic in 98 countries, with more than 350 million people at risk of infection (Figure 2). There are 1.5 to 2 million new cases of CL, with an average of 66,900 cases of CL and ML recorded each year in Latin America alone [6]. In this region, CL has been recorded in 20 countries, and is endemic in 18 of them (Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, French Guyana, Guyana, Honduras, Nicaragua, Mexico, Panama, Paraguay, Peru, Suriname, and Venezuela). Of the 10 countries in the world with the highest number of cases of CL, three are in Latin America (Brazil, Colombia, and Peru).
Leishmaniasis prevention and control is a complicated task due to the diverse ecology of the parasite’s transmission and the different clinical expressions of the disease. However, three main strategies are applied for leishmaniasis control: 1) reservoir control; 2) vector control; and 3) case detection and management.

**Reservoir control strategy**
Reservoir control includes those methods used to limit or eradicate reservoirs involved in the leishmaniasis transmission. This strategy is especially difficult when the transmission occurs in a sylvatic environment, as usually happens in Latin America, due to a large number of wild reservoirs and vectors involved in the process. However, during the last decades, there has been a strong process of deforestation and urbanization of Latin American rainforests that has forced vectors to adapt to new environments and find new domestic reservoirs. In this regard, dogs have been the study target in settings of peridomestic transmission; however, their role in CL is not clear due to contradictory results found in several studies [8-11]. In any case, the attempts to control the spread of the disease in settings of peridomestic transmission, by eliminating or treating infected dogs, have not been effective because reinfections are frequent.
**Vector control strategy**

Environmental management, chemical control, and personal protection are a group of strategies commonly applied to control vector exposition.

Among the environmental management methods, the destruction of breeding sites, such as attacking rodents’ burrows, has been an effective strategy in central Asia [8] and Africa [12, 13] for CL and VL control. Other options, such as using plastered bricks for building walls, rather than straw or mud, have been used in India [14]. In areas of peridomestic transmission, those vulnerable dwellings, which are constructed with non-durable materials, allow the formation of cracks through which the vectors can enter into the houses [15-17].

As part of chemical control measures, the insecticide residual spraying (IRS) of both houses and animal shelters, has proven to be effective in the reduction of peridomestic transmission of leishmaniasis [18]. However, IRS has proved to be useless when transmission occurs in sylvatic environments or when people remain exposed to vectors outside of their dwellings due to their work activities, as is usually the case in Latin America.

Insecticide-treated nets have shown contradictory results in terms of their protection capacity. Their effect on reducing VL is not yet clear due to conflicting findings among studies [19-22], while in Latin America, bed nets impregnated with pyrethroids have been effective for CL prevention in community trials [15, 23, 24].

Finally, the use of repellents, as an alternative for personal protection, has limited impact as a public health intervention because it requires multiple applications during the day (the protective effect lasts a maximum of 10 hours).

**Case detection and management**

Nowadays, most of the endemic countries have prioritized the detection and treatment of cases as the main control strategy, given that in sylvatic environments, the strategies of vectors and reservoirs control are not feasible.

**Leishmaniasis Diagnosis**

There are highly accurate diagnostic methods available for the diagnosis of CL and ML, such as parasite culture and parasite DNA detection by molecular biology [25-28]. Nevertheless, due to their elevated costs and complicated requirements for use, direct microscopic examination (DME) is the most widely used diagnostic method. However, the lack of equipment needed to perform DME is a common problem in primary health centres (PHCs) in rural areas.
Other methods such as the Montenegro Skin Test (MST), an immunological method, are not used routinely for CL or ML diagnosis but are commonly applied in clinical and epidemiological studies to capture exposure to the parasite [29-34].

**Leishmaniasis Treatment**
The most widely used treatment for CL is based on antimony (Sb), which has a long history since Vianna published the use of trivalent antimonials for the treatment of CL for the first time in 1913 [35]. Some years later, it was replaced by the current treatment based on systemic pentavalent antimonials (SPA), discovered by Brahmachari in 1920 [36]. Although there has been great progress in VL treatment with the implementation of liposomal amphotericin B and miltefosine, very little progress has been achieved for the treatment of CL. The first-line treatment for CL is still based on SPA, which are administered intravenously or intramuscularly for 20 days. Several adverse effects have been described with this treatment, which can be so intense that it requires treatment interruption. In some individuals, SPA toxicity can be fatal due to the risk of pancreatitis and cardiac arrhythmias [37-40]. For these reasons, it is contraindicated in patients with renal, cardiac, hepatic and pancreatic diseases, as well as in pregnant women and infants. In addition, the evaluation of renal, hepatic and pancreatic function, as well as electrocardiogram to detect conduction disorders, is highly recommended, before and during the treatment administration, to recognize the occurrence of life-threatening complications [41]. However, due to the lack of equipment in health centres in remote areas of Latin America, these tests are rarely performed.

In 2010, the World Health Organization (WHO) encouraged researchers to work on alternative treatments for leishmaniasis [2]. Currently, there are several treatments proposed, such as allopurinol, azithromycin, topical and systemic use of aminoglycosides (paromomycin), imidazole drugs, immune compounds, carbon dioxide laser, cryotherapy, thermotherapy and intralesional pentavalent antimonials (ILPA) [42, 43]. However, only ILPA and thermotherapy have been included in the recommendations of the Pan American Health Organization (PAHO) Experts Committee on leishmaniasis as alternatives to treating CL. Experiences with thermotherapy are recent but very promising, showing a similar efficacy compared to SPA but with fewer adverse effects and greater adherence since the treatment consists of a single application [44-46]. The main limitation with this treatment is the high cost of the equipment, which is still under patent and difficult to implement in health centres with limited economic resources. Conversely, experience with ILPA dates back many years and is abundant in several Latin American and Asian countries [47-53]. Photo 2 shows the application technique of ILPA therapy in a cutaneous ulcer due to CL. The studies performed with ILPA have shown similar efficacy to SPA without its related
toxicity, with almost no adverse effects and high adherence to the treatment [54, 55]. Regarding the risk of mucosal complications, one study of 5-years of cases-follow-up in Brazil showed no cases of mucosal complications with ILPA [52].

*Photo 2. Intralesional pentavalent antimonials treatment*

![Image](image.png)

Source: Extracted from Duque 2016 [56].

**Leishmaniasis surveillance and access to treatment**

Leishmaniasis surveillance is still a pending task in many endemic countries. Only two-thirds of them have presented incidence reports from the last five years [57]. Furthermore, it is well known that registers have a significant level of under-reporting. For instance, studies from Brazil [58], Argentina [59], India [60], Jordan [61] and Guatemala [62] have observed under-reporting ranging from 4 to 40 times the real figures. Several reasons can explain this phenomenon: i) leishmaniasis surveillance is not a priority in many endemic countries, the reporting of the disease is mandatory only in 32 of the 88 endemic countries; ii) civil wars, droughts and migration, which have, at the same time, both contributed to the spread of leishmaniasis and restricted access to health care; iii) many people affected by leishmaniasis try to keep it hidden due to the facial deformities and social stigma caused by the disease.

Under-reporting portrays a severe picture of lack of health-care access. Leishmaniasis is considered one of the most neglected tropical diseases and mostly affects the poorest people in rural areas and urban slums [63]. Compared with other diseases, treatment for leishmaniasis is very expensive, ranging from 30 to 1,500 U.S. dollars (USD) in drug costs alone, which is considered a major contributor to the poverty of the affected individuals [64]. Even though treatment is provided for free in some Latin American countries, leishmaniasis patients’ income is usually low, which makes it difficult for them to afford the additional
costs related to treatment seeking, such as transportation to health centres, food and lodging [65-67]. This care-seeking process can sometimes be catastrophic to households’ weak economies, a situation that is impaired due to the income loss related to work absence. One study from Ecuador described the impact on the capacity to work among men due to the illness [68], and in Paraguay another study showed that travelling to health centres meant 8 hours of work lost, which over 20 days implied an important monthly salary loss, in addition to the risk of losing the job [67]. All these factors create a vicious cycle between poverty and leishmaniasis that limits the patients’ health-care access [69].
The research context

The country setting

Bolivia, located in South America, is a country with an estimated population of 11,052,000 inhabitants (Figure 3). Bolivia is divided politically, economically and administratively into nine departments, which are subsequently divided into municipalities, and those into communities. Even though its geography includes valleys, mountains and high plateaus, most of the country is a tropical rainforest. The main source of income in the country are natural gas and oil, followed by mining, agriculture and forestry. Over one-third (68.5%) of the population live in urban areas. The life expectancy at birth is 70.2 and 63.84 years for women and men, respectively, 31.4% of the population is under 15 years old and 8.7% is over 60 years old [70]. Bolivia belongs to the group of lower-middle-income countries with a gross domestic product per capita of 3,076.8 USD. In general, 39% of the population is considered poor according to the poverty line and the Gini index of inequality is 0.47, indicating an inadequate income distribution [71].


Figure 3: Map of Bolivia.
The Bolivian health system
The Bolivian health system is organized into three sectors:

The public sector. This sector is directed at the national level by the Ministry of Health (MoH), which organizes, plans and executes the health policies at the central level. In 2008, Bolivia had registered 3,233 health-care establishments, of which 90% were primary posts and health centres, 7% were basic hospitals that provided second-level care and 3% were hospitals that provided third-level care. The public sector is financed 80% from taxes and 20% with external funds and donations [72]. In this sector, the government subsidizes the costs related to medical staff salaries, diagnostic exams, hospitalization and surgeries but no costs of drugs, which are totally paid for by patients.

The social security sector. This sector, financed by workers and employers, is organized on nine social security funds and university insurances providing medical attention to salaried employees who are affiliated to them. The last information about the national social security coverage was published by the National Institute of Social Security in 2010, reporting that 32.4% of the Bolivian population were covered by this sector.

The private sector. This sector includes non-profit and for-profit organizations, which are financed by out-of-pocket payments. The role of non-profit non-governmental organizations (NGOs) is more important in marginal urban and rural areas, particularly those managed by the Catholic Church. Traditional medicine providers, such as yatiris, healers, natural healers, who have greater importance in rural areas, are also included in the private sector.

Health programmes. Given that most of the population had been traditionally excluded from the Social Security, the Bolivian government began in 1996 to implement a series of reforms aimed at improving health-care access, such as public health insurances and specific disease control programmes. The public insurances were the Universal Maternal and Child Health Insurance (UMCHI) and the Social Insurance for Elderly (SIE). UMCHI provides free care to all children under 5 years of age and women in reproductive age. UMCHI was implemented with the aim of reducing maternal and infant mortality by decreasing the financial accessibility barriers. Following the same idea, SIE was created to provide health care to elderly people who were not covered by the social security. Since 2012, UMCHI and SIE have been merged into the Unique Health Insurance (UHI). Additionally, in the last 10 years, some municipal and departmental governments have implemented public health insurances for their own populations, focusing on the age groups not covered by the UHI (Tarija and Beni in 2007, Chuquisaca in 2014, Cobija and El Alto in 2011 only for children of school age).
In addition to public insurance, the MoH provides programmes to control endemic diseases such as the ones for Chagas, tuberculosis, leishmaniasis and HIV. These programmes are financed mainly by external collaboration funds. All these programmes depend on the resources and infrastructure of the public sector of the health system.

Although these health reforms and programmes have greatly improved health care during the last 30 years in Bolivia, still most of the health expenses rely on out-of-pocket payments because most of the population does not have health insurance and they can only resort to the public or the private sector. In addition, the public sector has severe problems related to the management of human and economic resources. The number of physicians per 1,000 inhabitants is 0.5 and there is a large gap in physicians’ availability among municipalities, with fewer physicians in poorer municipalities [73]. PHCs work in precarious conditions with a very limited capacity for resolving problems due to the lack of investment. One revision of UMCHI’s impact on maternal and child mortality in Bolivia exemplifies the influence of the previously mentioned problems in the performance of national health policies and programmes. From 1996 to 2015, the maternal mortality rate was reduced from 375 to 206 deaths per 100,000 live births; child mortality from 97 to 36.9 deaths per 1,000 live births; and infant mortality from 76.15 to 38.79 deaths per 1,000 live births. However, nowadays Bolivia still has one of the highest maternal and child mortality rates outside sub-Saharan Africa, especially in newborns. A recent report by the Economic Commission for Latin America and the Caribbean showed that public health insurances mostly benefited people living in urban areas with greater economic resources, while those who live in rural areas – and to a larger extent, people from indigenous groups – are marginalized, [74].

**Leishmaniasis in Bolivia**

In Bolivia, CL is the most common form of leishmaniasis followed by ML. VL is rare, with only 10 cases described during the last 30 years in one single area [75]. From 1983 to 2014, 522,444 cases of CL were reported, showing an increasing trend with time. In 1985, the incidence rate per 100,000 was 4.1, reaching 16.6 in 1993 and 32.7 in 2006 (Figure 4) [76]. Even though there is limited information about the current epidemiological profile of leishmaniasis in Bolivia, given its small population size it is among those countries with higher incidence rates in Latin America [6]. ML is also an important problem in Bolivia, which has the greatest ratio (i.e., up to 20% of all cases) of ML compared to localized CL cases in America [77]. Bolivia also has the highest frequency of ML in Latin America (20%) compared to Ecuador (7.7%), Colombia (2.3%), Brazil (2.7%) and Venezuela (0.4%) [78].
CL cases are caused by several species of Leishmania parasite, with *Leishmania Vianna braziliensis* being responsible for most of the cases (up to 85% cases) [80]. Seven sandfly species are incriminated as vectors and several non-human mammal hosts have been identified. Transmission is associated mostly with forest-related activities, with farmers and indigenous groups being those most affected by CL and ML [77]. However, in some areas of the country, peridomestic transmission patterns have also been described [81].

**Leishmaniasis surveillance and control in Bolivia**

Leishmaniasis surveillance and control in Bolivia is responsibility of the National Leishmaniasis Control Programme (NLCP) and its activities are focused on reducing morbidity and mortality, as well as providing free treatment to all those cases who are detected through passive surveillance.

The national leishmaniasis surveillance system is based on reports constructed from registers of cases who receive the treatment provided by the NLCP. The NLCP’s reports do not include additional case information of those who were
diagnosed clinically, or by laboratory methods when those cases do not receive the treatment.

NLCP guidelines demand parasitological laboratory confirmation of the diagnosis of leishmaniasis in order to provide free treatment for patients. The diagnostic methods available in Bolivia are the DME, which is performed in first- and second-level hospitals, and parasite culture, Polymerase Chain Reaction (PCR) diagnostic, and the MST, which are carried out only in research centres. The NLCP’s activities are restricted to the public health sector and, in consequence, the NLCP depends on its resources and infrastructure to assist patients with leishmaniasis. In general, health centres in remote areas are precarious and do not have laboratory services with which to perform DME. This situation forces patients to travel in search of these services, usually available only in urban settings. Due to the difficulties of the patients in accessing the treatment, which is also the base of the register, NLCP national reports are underestimated and are of low quality. Hence, the scope of the passive surveillance system of leishmaniasis in Bolivia is limited and does not allow the real burden of this disease to be known.

The treatment accepted and provided in Bolivia by the NLCP is based on the use of antimonial drugs, specifically Meglumine antimoniate at a dose of 20 mg/kg over 20 days for CL and 30 days for ML. The second-line treatment in case of therapeutic failure is amphotericin B deoxycholate. All health centres that belong to the public sector are authorized to administer anti-leishmanial treatment, as long as they fulfil the indispensable requirement of parasitological confirmation of the cases.

Anti-leishmanial drugs are distributed in capital cities of the department where the NLCP offices are located. When a case of CL or ML is confirmed, the personnel of the health centre where the cases are presented must travel to these offices to complete administrative procedures and personally collect the drugs. When the drugs arrive at the health centre, the medical staff contact the patient and are responsible for the treatment application. Sometimes, the patient is the one that goes to pick up the drugs with the commitment to deliver them to the health centre, always after coordination with the medical staff where the treatment will be applied.

In addition to the delays caused by these bureaucratic proceedings, patients must often wait for long periods to receive the treatment due to the drugs shortage, because of the limited national budget and the high costs of the drugs.

Given that in Bolivia the main transmission mechanism is sylvatic and there are no effective control measures for reservoirs and vectors of the Leishmania
parasite in rainforest environments, the NLCP does not undertake activities for the reduction of the disease’s transmission.
Rationale of the study

Access to health care is a major concern and a global commitment included in the sustainable development goals. Under the slogan of ‘Universal health coverage for all’, the WHO aims to ensure that all people obtain the health services they need without financial hardship when paying for them [82]. Health-care services are considered not only to be structures where technically specialized services are provided, but rather they are key social institutions to ensure the respect and exercise of the human right to health [83]. Health-care services are also considered key elements for leishmaniasis control. In the Sixtieth World Health Assembly in 2007, member states were encouraged to strengthen the capacity of the health centres to deliver primary and secondary care, so that they could provide appropriate diagnosis and treatment, as well as acting as sentinel surveillance sites [84]. However, despite the importance of and commitments made to this issue, very little attention has been paid to research on access to health care among patients with leishmaniasis. In Bolivia, even though leishmaniasis research has undergone important development in the last decades, it has mostly focused on basic science related to the parasite and vectors involved in the transmission chain [85-101] and on clinical trials for CL treatment [55, 102-105]. However, research from a public health perspective is scarce [81, 106] and no studies about health-care access among patients with leishmaniasis exist.

It is well known that leishmaniasis disease affects disproportionately the poorest of the poor, those who live in precarious settlements and work in disease-endemic environments without adequate protective measures [107, 108]. It is therefore important to identify the characteristics of the population affected by leishmaniasis. In this context, there have been many studies that have tried to identify the relationship between housing, lifestyles and work conditions with leishmaniasis. However, the vast majority of these studies have been conducted in Asia and Africa and mainly focused on visceral leishmaniasis [109-124], while research on this topic is limited in Latin America [29, 125-132]. In Bolivia, a few epidemiological studies have been conducted; however, they are very old and have studied this problem tangentially [81, 106].

Although leishmaniasis treatment has been provided for free by the government in Bolivia since 2007, it is well known that many patients are not able to access the treatment, and in consequence the Bolivian surveillance reporting system in leishmaniasis underestimates the real burden of this disease. Globally, leishmaniasis surveillance systems have been criticized for the poor quality of their reports. In fact, it has been described that a fifth of the endemic countries do not have updated incidence data and very few studies have measured the
severity of this problem [6]. While some of these studies have been carried out in Latin America [58, 59, 62], the potential under-reporting of leishmaniasis in Bolivia is unknown. Under-reporting is linked to difficulties in health-care access. In Latin America, there is still a huge part of the population without access to health care for financial, geographical or cultural reasons, especially in remote areas of the tropical rainforest. Overall, little is known about barriers to access to health care among patients with leishmaniasis in Latin America [67, 133-137], and more specific information about the Bolivian context is needed.

Leishmaniasis treatment is the core of the control strategy of the NLCP. The high costs of the standard treatment with SPA involve a large investment both for the Bolivian government who pays for the drugs, and for the patients who have to manage the additional costs related to this treatment. Even though economic constraint is probably one of the main problems for leishmaniasis control, not only in Bolivia, surprisingly there are very few studies in the world that provide information about the economic implications of implementing therapeutic alternatives to CL in real scenarios [138-140]; none of them has been carried out in Bolivia or is relevant to the Bolivian context.
**Aims**

To investigate the health-care access among patients with leishmaniasis and to explore alternatives to improve the access of those patients in the poverty context of the Bolivian rainforest.

**Specific objectives:**

1. To assess the relationship between context and the risk of CL (sub-study 1).
2. To estimate the under-reporting level of the NLCP registers in order to capture the lack of health-care access among patients with CL and ML (sub-study 2).
3. To explore the experiences of accessing and using health services among people affected with leishmaniasis (sub-study 3).
4. To evaluate economically the implementation of ILPA as first-line treatment for CL and its potential effect on health-care access (sub-study 4).
The conceptual framework: access to health care

Health-care access definitions and conceptual models

Access to health care is an important concept when planning health policies in order to achieve their objectives effectively and respecting the principles of equity. Implementation of health policies without considering elements related to access leads to exclusion of some groups from the impact of these policies.

Although the concept of access has been widely used, there is no a standard definition and many models and theories have been developed in the attempt to explain and operationalize it. Two main elements present in all definitions of access are those related to the characteristics of the population (family income, insurance coverage, attitudes towards medical care) and those related to health systems (characteristics, organization and distribution of health services) [141]. In this sense, some authors have defined access as: ‘The use of qualified health care for the need for care’ [142] or as ‘Providing the right service at the right time in the right place’ [143]. Gulliford elaborated on the concept by making a distinction between having access, which is the possibility of using the services if being required, and gaining access, which is the use of the service itself. In this sense, having access is related to the availability of services or the existence of resources for service provision; while gaining access is focused on organizational, financial and sociocultural barriers that influence the use of medical care by the population [144].

While Gulliford’s model addresses the ability or willingness to enter into the health-care system, Penchansky and Thomas defined access as: ‘The degree of fit between the user and the service’, reflecting the dynamic features of the process and the interaction of the elements involved. In this model, the access concept was optimized for evaluation by accounting for five dimensions of access: accessibility; availability; acceptability; affordability; and adequacy in terms of service design, implementation and evaluation [145].

Frenk modified Penchansky and Thomas’s model. He noticed the problem of using not a clearly defined but interchangeably terms such as ‘access’, ‘accessibility’, ‘availability’. Frenk defined access as ‘the ability to utilize health care given a need or desire to obtain it’ and accessibility as ‘the degree to which a person needing and seeking care actually receives it’ [146].

Afterwards, Levesque proposed a model that organized the access-related factors into three elements: the supply and demand side features and the process factors
that determine the way these features interact to get access realized (utilization of care) [147].

However, Andersen’s model has been the most frequently used to guide research and evaluation studies on access. Andersen’s model is characterized by including five components in its structure: 1) health policies; 2) the characteristics of the population at risk; 3) the characteristics of the health delivery system; 4) the use of health services; and 5) the satisfaction of the population [141, 148].

The conceptual framework of this thesis

Recently, Obrist et al. developed a conceptual framework of access that includes the broad scope of factors involved in Andersen’s model, as well as the operational dimensions of access described by Penchansky and Thomas, with the added value of incorporating a perspective of livelihood assets, which make the model more suitable to use in low-income settings [149](Figure 5).

![Figure 4. The Health Access Livelihood Framework, adapted from [149].](image)

This livelihood assets approach emphasizes that the social and material resources used in the search for medical attention are the same needed for subsistence, which, at the same time define a vulnerability context of families. In conditions of economic hardship, as usually is the case among patients with leishmaniasis, other factors that interact with this vulnerability context in limiting health-care
access are those related to the health system, including services’ features, health policies and institutions. At the end of the chain are the care utilization and health status of the people, which result in being seriously affected by these health-care access conditions.

**Linking the objectives to the framework**

For this thesis, the Obrist framework has been chosen as it is considered the most appropriate to understand the complex phenomenon of health-care access in the context of poverty in rural areas of the Bolivian rainforest (Figure 5). The importance of the inclusion of the vulnerability context in the analysis of health-care access is based on the principle that poverty is not simply a lack of income. There is a trade-off between patients’ livelihood assets that determine the decision to seek medical care. In a vulnerability context, productive activities aimed at improving their economic capital usually mean putting their health status at risk. On the other hand, the medical care-seeking process to recover their health puts their financial capital at risk, and therefore subsistence. In this sense, the population of rural areas in the Bolivian rainforest must figure out how to manage their livelihood assets in their context of vulnerability to overcome and balance their needs of health and subsistence.

The first sub-study assesses the contextual factors that may increase the risk of CL, including variables such as house construction materials, basic services and sociodemographic characteristics of the population at risk.

In Obrist’s framework, utilization of care affects directly to health status. Leishmaniasis has received little investment from the governments to control it. In Bolivia, NLCP registers are designed for administrative purposes of drugs delivery rather than for disease surveillance. However, this reporting system can be a good indicator of the level of access to health care among patients with leishmaniasis. The second sub-study, trying to capture the magnitude of lack of health-care access, fits in Obrist’s framework dimension of health services utilization.

The access dimensions, as well as the quality of care, are key health services-related elements that determine health services utilization. PHCs, which are the operative arm of the public health system in rural areas, usually work in precarious conditions. The remote location of communities in rainforest areas is one of the main reasons why primary care is not well implemented. The NLCP’s policy for case detection and management must be performed in this context. The third sub-study aims to provide an insight into how different dimensions of access and quality of care are influencing the utilization of care in this vulnerability
context, through the exploration of patients’ experiences related to health services access and utilization of care.

Health policies define the conditions for health services’ functioning. The NLCP must be able to adapt to PHC conditions and evolve their strategies to facilitate access to leishmaniasis treatment. The standard treatment for CL with SPA has very high costs, and it is often unaffordable for both the government and patients, limiting health-care access. The fourth sub-study is an economic evaluation of the ILPA implementation as first-line treatment for CL, focusing on its benefits related to health-care access measured in terms of treatment utilization and the impact on the MoH’s budget.

The objectives and their connection to the different dimensions of the framework are presented in Table 1.

*Table 1. Study objectives and the focus within the framework to access health-care*

<table>
<thead>
<tr>
<th>Study Objectives</th>
<th>The framework of access to health care</th>
</tr>
</thead>
<tbody>
<tr>
<td>To assess the relationship between context and the risk of CL (sub-study 1)</td>
<td>Vulnerability context</td>
</tr>
<tr>
<td>To estimate the under-reporting level of the NLCP registers to capture the lack of health-care access among patients with CL and ML (sub-study 2)</td>
<td>Health-care utilization access</td>
</tr>
<tr>
<td>To explore the experiences of accessing and using health services among people affected by leishmaniasis (sub-study 3)</td>
<td>Dimensions of access Quality of care Vulnerability context</td>
</tr>
<tr>
<td>To evaluate economically the implementation of ILPA as first-line treatment for CL and its impact potential effect on health-care access (sub-study 4)</td>
<td>Health policy Health-care utilization Quality of care</td>
</tr>
</tbody>
</table>

Methods

Study setting: Villa Tunari

Villa Tunari is a municipality located in the northern part of Cochabamba Department (Figure 6), with 11,095 square kilometres and a population density of 5 inhabitants per square kilometre. Villa Tunari is a rainforest area of the Bolivian Amazon; its climate is mainly humid with a mean annual precipitation of 2800 to 5400 mm$^3$ in the wettest areas and a mean annual temperature of 24ºC (maximum of 41.5ºC).

![Figure 5. Map of Villa Tunari municipality.](image)

The Isiboro Securé National Park (ISNP) is located in Villa Tunari. The park is a protected area for fauna and flora and for sustainability of native communities settled in it since ancient times. The ISNP geography is characterized as being mostly primary forest, while the rest of Villa Tunari is mainly secondary forest. This consideration is remarkably important because Leishmania parasite wild reservoirs are found mostly in primary rather than in the secondary forest.

The colonization of Villa Tunari is an ongoing process that started in the 1980s, highly criticized by its environmentally destructive nature. From 1992 to 2012, its population increased by 52% from 48,477 to 73,914 inhabitants. Nowadays, more than 400 communities are registered in the area and 90 of them are in the
national park. Villa Tunari’s population is mainly young (75% are below 40 yrs) and almost 44% of them are migrants from the western high lands, who came to work in agriculture. In 2012 it was estimated that 95% of the population lived below the poverty line and 22% of them in extreme poverty in terms of unsatisfactory basic conditions [150].

Villa Tunari is an area affected by seasonal flooding with rapid and unpredictable changes in river courses. However, besides the difficulties in establishing perennial cash crops, agriculture has flourished with coca farming in the deep rainforest. The lack of access to the communities is the major factor in the difficulty of trading agricultural products, but at the same time, it is the main factor facilitating coca trading in illegal markets as a cocaine precursor.

**The Tsimane population**
The Tsimane are one of the 33 indigenous groups inhabiting the rainforests of Bolivian Amazon. Its wide territory covers the protected area of three departments: La Paz, Beni and Cochabamba in the ISNP. They comprise more than 100 small communities, settled mostly close to the shores of the rivers. It is estimated that there are about 12,000 inhabitants dispersed in 1.35 million ha, giving an overall population density of 1 individual per square kilometre [151]. The Tsimane economy is based on small-scale agriculture for subsistence, hunting and fishing. Most communities lack roads and there is no public transportation. Some communities are only accessible by river. These conditions make it extremely difficult to get their products out to the markets or to access health services.

Tsimane health conditions are precarious. The only one study published about Tsimane mortality using data from the year 2002 showed a high level of neonatal mortality (178 per 1,000 births) and under-five mortality (18 per 1,000 individuals) in the farthest communities. The total fertility rate is 9.1 children per woman. Their life expectancy in 2002 was 54 years, which was lower than the national level of 64 years. The main causes of mortality are preventable diseases such as gastrointestinal and respiratory infections in children under 5 years; complications related to pregnancy, childbirth and puerperium in women of reproductive age; and infections in adults [152]. There are only three primary care posts close to the indigenous communities; however, the limited capacity of these services [to function effectively] forces patients to travel to larger urban centres searching for health services of a higher level of care. This implies in some cases trips of up to 5 days by the river for the most remote communities and two days of walking for the communities without river access.
Leishmaniasis in Villa Tunari

Villa Tunari was the municipality chosen for this study due to its high leishmaniasis endemicity, this being responsible for 60% of CL cases in Cochabamba department.

There are 33 health services in the municipality, of which 18 are in the ISNP. The NLCP analysis of the municipality of Villa Tunari records for the period of 2011 to 2016 gives an idea of the health services use and treatment demand among patients with leishmaniasis. Although the greatest risk area is the ISNP due to the presence of Leishmania vectors and wild hosts (429 cases), more than half of the demand for treatment in Villa Tunari corresponds to cases from the area outside the park (503 cases). Focusing on the ISNP cases, 66% of them (282 cases), were treated in health centres of the park, 24% (106 cases) travelled more than 100 km from the park and 10% (41 cases) travelled more than 200 km from the park to receive treatment in health centres with a higher level of attention in urban settlements or in the capital city of Cochabamba. Another interesting finding is that from the total number of cases attended in health centres located in the park, 41% were carried out in three health centres with laboratory diagnostic services for leishmaniasis and this rises to 99% when six centres near these laboratories are included. The remaining nine health centres in the ISNP that are far from the laboratories did not reported hardly any treatment delivered.

Another fact that is striking is the little demand for treatment from indigenous communities, with only 4% of the total cases of ISNP and 2% of all cases in the whole department of Cochabamba (in health centres located not too far from health services with laboratory diagnosis for leishmaniasis). This is an unexpected finding considering that indigenous’ peoples’ exposure to the disease is greater than among the farmers. Exposure to leishmaniasis is constant among indigenous peoples and it is not necessarily associated with their work activities, as is the case among colonizing farmers. Indigenous communities are settled deepest into the rainforest and their lifestyle consists mostly of hunting and fishing as subsistence activities.

All these data illustrate the difficulties of health-care access related mainly to laboratory diagnosis, which is a compulsory requirement to receive treatment, but also for the delivery of treatment. Although some communities located near the main roads have good public transport conditions to reach these health services for diagnosis and treatment, in most of them the public transport is scarce, there are no roads, or they are in poor condition; in addition, during the rainy season, many of them become inaccessible (Photo 3).
Data collection and analysis

Sub-studies 1 and 2
A leishmaniasis screening-based study was conducted to identify current and past cases of CL and ML in the communities of Ichoa, Chipiriri and Tacopaya in the municipality of Villa Tunari y, in August 2015 and August 2016 through medical campaigns, with 6 days spent in each community. Multiple invitations were made to the population living in these communities by their local authorities, the medical staff of the health centre and the researchers. During the medical campaigns, all the participants received a physical examination of their skin and mucous membranes, looking for present or past CL and ML. A group of senior researchers from the Centre of Tropical Medicine of San Simon University in Cochabamba conducted all the examinations and whenever a skin ulcer was present in the participants, a sample was taken for DME. In a similar way, whenever a skin scar with a history of skin ulcers that lasted more than two weeks before healing was present, the MST was performed. The antigens used for the MST used were produced by the Institute of Tropical Medicine at the Cayetano Heredia University, Peru.

The criteria used to identify CL were: 1) presence of skin ulcers on which Leishmania parasite was identified through DME; or 2) skin scars with a history of skin ulcers that lasted more than two weeks before healing and which had had a positive reaction to the MST. The criteria used to identify ML were: 1) ulcers in mucosal membranes of nose, pharynx, palate or upper lip; 2) presence of Leishmania parasite in the lesions confirmed by DME or culture methods.
For sub-study 1, an additional questionnaire was applied to participants from the communities Ichoa and Chipiriri. The questionnaire was adapted from the Demographic and Health National Household Survey and included information related to 1) sociodemographic characteristics (age, gender, farming activity, schooling level, and mother tongue); 2) household construction materials (wall, roof); and 3) basic services (electricity, gas, drinking water networks and sewer system) [153]. In addition, information related to forest exposure and use of protective measures against mosquito bites, such as the use of bed nets, use of repellants and household fumigations, was collected. All these factors were used as independent variables in the analysis. For this sub-study, only the presence of CL was included as the dependent variable. For the data analysis, descriptive statistics were conducted and the risk to CL was evaluated in two steps using logistic regression: first, univariate analyses were performed with all the variables included in the study; and second, those variables with p-values less than 0.2 were included in the multivariate analysis. The variance inflation factor test was used to show that there was no collinearity among the variables included in the multivariate analysis. Statistics analyses were conducted with the SPSS software.

For sub-study 2, the capture–recapture method was applied to estimate the unknown total number of patients with CL and ML. This method was initially developed to measure species populations in biology, and it has been used more frequently in epidemiology to estimate the number of cases for specific illnesses, such as tuberculosis [154-157], cancer [158], HIV-infected patients [159-162], drug users [163], injury cases [164-167] and also visceral leishmaniasis [58]. This method is based on the comparison of two incomplete sources of data (lists of patients) of the same population during the same period of time [168]. In this sub-study, the selected communities were Ichoa and Tacopaya and the period of comparison was from 2013 to 2014.

The first source of data corresponded to the list of patients registered through passive surveillance by the NLCP. This list included identifier information, such as full name, age, sex, year of infection, the community of residence and health centre where the treatment was delivered. All the cases included in this list of the NLCP were confirmed by parasite identification using DME.

The second source of data corresponded to the list of patients with CL or ML identified through the leishmaniasis screening-based study who were from the communities of Ichoa and Tacopaya for the period 2013–2014. This list included personal identification data such as name, age, sex, year of infection, the community of residence, in addition to the health centre name with those participants who got access to medical treatment.
The lists were indexed and sorted to identify duplicated cases. Subsequently, a new list that contained the cases captured by the NLCP and those that were recaptured by the study was created, adding new variables that allowed us to recognize the presence of the case in each of the information sources.

To estimate the total number of cases, the Chapman formula was applied. Figure 7 illustrates the method of capture–recapture using two data sources and the Chapman formula for the analysis [58]. This formula allows the calculation of the unknown size of the population (N), the variance and the confidence interval at 95%.

\[
N = \frac{(M+1)(n+1)}{(m+1)} - 1
\]

Where:
- \(N\) is the estimated number of cases;
- \(M\) is the number of cases in the first source;
- \(n\) is the number of cases in the second source;
- \(m\) is the number of cases in common.

Source: Extracted from Maia-Elkhoury, Carmo et al. 2007.

Figure 6. Two-sample capture–recapture method diagram and Chapman’s formula.

Finally, to evaluate the level of completeness of the NLCP registers, the proportion of cases found by the NLCP in relation to the total cases estimated by Champan’s formula was calculated and expressed in percentages.

Given the NLCP’s surveillance system is based on registers of cases of CL and ML that receive treatment, the capture–recapture method allows the measurement
of the level of coverage of cases of leishmaniasis found by the health system as well as the utilization of health care by patients.

**Sub-study 3**
For this study, semi-structured interviews with participants who lived in different regions of the country, who had different ethnic and cultural backgrounds, as well as, different types and severities of the disease were conducted. The sample consisted of 14 participants (11 men) between 17 and 45 years old. Interviews were performed in the office of the Centre of Tropical Medicine of San Simon University (CTMSSU) and in Tsimane indigenous communities (3) during medical campaigns of the Tsimane Life and History Project. In the CTMSSU, the interviews were performed in Spanish while in the Tsimane communities, the interviews were performed in Tsimane with the collaboration of a Tsimane interpreter. All the interviews were conducted in a private and comfortable space. Each in-depth interview lasted between 30 and 45 minutes. At the beginning of the interview, the aim and the main topic of the research were explained, and the participants were encouraged to express their experiences and opinions freely. Questions with some key topics were used to guide the interview, such as (1) perception of illness threat; (2) coping response to the disease; (3) experiences with traditional and Western medicine; (4) economic, social, emotional and productive consequences. All the interviews were digitally recorded; when interviews were conducted in Spanish, they were transcribed verbatim, and for Tsimane interviews, the translations performed by the interpreter were transcribed.

Interviews were analysed using thematic analysis [21, 22]. Two interviews were analysed first looking for recurring concepts that were codified. NVivo 10 software [23] was used to organize the information and retrieval of text chunks that corresponded to similar codes. Then, codes with similar information were arranged and collated into groups. Afterwards, the other 12 interviews were analysed using these groups as a guide. After the analysis of the next 12 interviews, the new list of groups was refined and grouped into four themes.

**Sub-study 4**
An economic evaluation was performed in the municipality of Villa Tunari, calculating the cost-per-patient treated with SPA and ILPA from the payer’s perspective (Ministry of Health) and from a societal perspective in which patients’ direct and indirect costs were included.

Additionally, the budget used to treat the average annual number of CL cases reported in the department of Cochabamba was calculated using the cost analysis results. This budget was compared with four hypothetical scenarios of increased
treatment demand and ILPA implementation as a first-line treatment to evaluate the budget impact of the use of ILPA.

The target population for the cost analysis was all patients diagnosed with skin ulcers due to CL who were eligible for ILPA according to the PAHO−WHO guidelines [20], which are: 1) lesion size up to 900 mm²; 2) no more than one lesion; 3) lesions not located on face, joints or genitals; and 4) an absence of immunosuppression. The target population for the budget impact analysis consisted of all CL patients, of whom a proportion would be eligible for ILPA and the remainder would receive SPA, regardless of the sex or age of the patient, or the duration of the ulcers.

Cost analyses included direct costs of drugs, in addition to patients’ out-of-pocket expenses such as transportation, food and productivity loss. The costs of complementary examinations, usually recommended for toxicity evaluation, were not considered since these are not carried out in the primary care centres in rural areas due to lack of equipment.

SPA treatment consists of doses of 20 mg/kg for 20 days according to WHO’s recommendations; while for ILPA, five applications with a maximum dose of 10 ml per application were considered based on the average number of applications of the studies included in the ILPA meta-analysis used in this sub-study [54].

Drug costs and salary scale were obtained from official documents of the MoH and the Ministry of Economy and Public Finance. To calculate the out-of-pocket expenses paid by patients, information collected from a survey carried out in the medical services of Villa Tunari and from key informants was used (Table 2).
Table 2. Resource use quantities and unit costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Quantity</th>
<th>Unit price</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(sensitivity analysis values)</td>
<td>(INT$)</td>
<td></td>
</tr>
<tr>
<td>SPA</td>
<td>ILPA</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Costs for MoH</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Staff time use</strong></td>
<td>16 min per application</td>
<td>1670 per month</td>
<td>Health facility survey and Ministry of Economy and Public Finance</td>
</tr>
<tr>
<td></td>
<td>(48min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Drug applications</strong></td>
<td>20</td>
<td>5</td>
<td>---- Meta-analysis [169] Systematic review [54]</td>
</tr>
<tr>
<td></td>
<td>(1-10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Costs for patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Drug ampoules</strong></td>
<td>3 per application</td>
<td>4.1 per ampoule (2.1–12.4)</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td></td>
<td>2 per application</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Surcharges for supplies</strong></td>
<td>One-off</td>
<td>1.0</td>
<td>Health-facility survey</td>
</tr>
<tr>
<td><strong>Drugs administration fee</strong></td>
<td>20 times</td>
<td>5 times</td>
<td>Health-facility survey</td>
</tr>
<tr>
<td></td>
<td>0.7 per application</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Transport</strong></td>
<td>20 round trips</td>
<td>5 round trips</td>
<td>Key informants</td>
</tr>
<tr>
<td></td>
<td>3.5 per round trip (1.8–10.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Meals</strong></td>
<td>20 meals</td>
<td>5 meals</td>
<td>3.2 per meal</td>
</tr>
<tr>
<td><strong>Productivity loss</strong></td>
<td>20 days (5 days)</td>
<td>21.5 per day</td>
<td>Ministry of Economy and Public Finance</td>
</tr>
<tr>
<td></td>
<td>5 days (0 days)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SPA: Systemic pentavalent antimonials; ILPA: Intralesional pentavalent antimonials; MoH: Ministry of Health; INT$: International dollars.

To evaluate the effect of the uncertainty on the incremental cost of ILPA, a sensitivity analysis was carried out from the perspective of the MoH and society.
The parameters included in this analysis were the number of infiltrations with ILPA, staff time, drugs and transport costs.

For the budget impact analysis, initially, the annual average incidence of CL cases in Cochabamba department from the period 2011 to 2016 was calculated, then the proportion of not eligible cases for ILPA was estimated. Afterwards, the number of cases to be treated with each therapeutic scheme and the budget needed to pay for it was calculated regarding the next four hypothetical scenarios: 1) an increment in treatment utilization of 20% of reported cases using only SPA; 2) current treatment utilization using ILPA as first-line treatment; 3) an increment in treatment utilization of 20% of reported cases using ILPA as first-line treatment; and 4) an increment in treatment utilization to 80% of total expected cases using ILPA as first-line treatment. The last scenario considers the total cases expected, not only those reported. This distinction is important because due to the low levels of access to treatment (26.6%), the reported cases could not be considered as the total expected cases. The total expected cases estimated in Cochabamba based on these figures was 654 per year, which resulted from adding 74.4% to the reported cases by the NLCP (n=237).

Finally, the number of cases that could be treated with the current budget in case of ILPA implementation as a first-line treatment was estimated.

All costs in the study were initially calculated in bolivianos, the local currency of Bolivia (BOB) and later converted to international dollars (INT$) using the purchasing power parity adjusted exchange rate for 2017 (3.102 BOB=1 INT$) [170]. Cost calculations were expressed in Int$ because they better represent the purchasing power and inflation of the local currency.
A summary of the four studies with objectives and methods is presented in Table 3.

Table 3. *Overview of the methodology applied in the different sub-studies*

<table>
<thead>
<tr>
<th></th>
<th>Sub-study I</th>
<th>Sub-study II</th>
<th>Sub-study III</th>
<th>Sub-study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>To assess the relationship between context and the risk of CL</td>
<td>To estimate health-care utilization among patients with CL</td>
<td>To explore health services access and utilization of care among patients with leishmaniasis</td>
<td>To evaluate economically the implementation of ILPA as first-line treatment for CL and its benefits related to health-care access</td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
<td>Community-based cross-sectional study</td>
<td>Capture–Recapture study</td>
<td>Qualitative study</td>
<td>Economic study</td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td>274 participants</td>
<td>743 participants</td>
<td>14 interviews</td>
<td>12 health facilities</td>
</tr>
<tr>
<td><strong>Study Setting</strong></td>
<td>Villa Tunari</td>
<td>Villa Tunari</td>
<td>Cochabamba and Beni</td>
<td>Villa Tunari and Cochabamba</td>
</tr>
<tr>
<td><strong>Analysis</strong></td>
<td>Multivariate logistic regression</td>
<td>Chapman’s Formula analysis</td>
<td>Thematic analysis</td>
<td>Cost analysis and budget impact analysis</td>
</tr>
</tbody>
</table>

CL: Cutaneous leishmaniasis; ML: Mucosal leishmaniasis; ILPA: Intralesional pentavalent antimonials

**Ethical considerations**

The doctoral project with the four studies was approved by the research ethics boards of the Faculty of Medicine of San Simon University in March 2015. For sub-studies 1 and 2, the research team attended monthly community meetings organized by the board of the Local Farmers Union. During these meetings,
researchers provided information on leishmaniasis, as well as the nature and importance of the study to the community members (Photo 4). The researchers asked for permission from the population to proceed with the study. For sub-study 3, respondents were informed that they could avoid answering any question and that they could withdraw their participation at any time, with no need to explain their reasons and without negative consequences. None of the interviewees chose this option. For the four studies, the participation was voluntary, no incentives were provided to participants. Clinical exams, as well as treatment, were free of charge. Participants with parasitological confirmation of active CL were assisted with diagnosis and treatment free of charge. Participants with skin scars due to past chronic skin ulcers that resulted positive in the MST were assessed looking for signs of reactivation of CL and mucosal complications. Given that none of the participants showed these problems, they were advised to contact the researchers in the case of any sign or symptom suggestive of these problems appearing. In addition, in all the studies individual written consent was signed by each participant, and for children, written consent was also sought from their parents. Finally, all data were anonymized to guarantee the confidentiality and privacy of the participants.

*Photo 4. Presentation of the project to a community*
Results

Sub-study 1

The sample consisted of 274 subjects from Ichoa community (n=200) and Chipiriri community (n=74). Of the total sample, 119 participants (43.4%) had CL and of them, 116 cases (97.5%) corresponded to past infections, while 3 cases (2.5%) corresponded to active skin ulcers. The majority of CL cases were men (69.7%) and the median age was 35 years old. Most of the cases were from the Ichoa community (79.8%) compared to the Chipiriri community (20.2%). A greater proportion of cases were migrants from highlands (58.0%), with Quechua and Aymara as their mother tongue (87.4%). More than half of the cases worked in agriculture (64.7%) and most of the cases were literate (89.0) (Table 4).

Table 4. Sociodemographic characteristics of the participants expressed in percentages

<table>
<thead>
<tr>
<th>Variable</th>
<th>CL Positive N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36 (30.3%)</td>
</tr>
<tr>
<td>Male</td>
<td>83 (69.7%)</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
</tr>
<tr>
<td>Mean (min–max)</td>
<td>35 (14–73)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>Chipiriri community</td>
<td>24 (20.2%)</td>
</tr>
<tr>
<td>Ichoa community</td>
<td>95 (79.8%)</td>
</tr>
<tr>
<td>Years of residence</td>
<td></td>
</tr>
<tr>
<td>Below 10</td>
<td>54 (45.8%)</td>
</tr>
<tr>
<td>More than 10</td>
<td>64 (54.2%)</td>
</tr>
<tr>
<td>Migrant from highlands</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>50 (42.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>69 (58.0%)</td>
</tr>
<tr>
<td>Mother tongue</td>
<td></td>
</tr>
<tr>
<td>Spanish</td>
<td>15 (12.6%)</td>
</tr>
<tr>
<td>Quechua or Aymara</td>
<td>104 (87.4%)</td>
</tr>
<tr>
<td>Farmer</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>42 (35.3%)</td>
</tr>
<tr>
<td>Yes</td>
<td>77 (64.7%)</td>
</tr>
<tr>
<td>Literate</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13 (11.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>105 (89.0%)</td>
</tr>
</tbody>
</table>
Regarding the households’ characteristics, there was a greater proportion of cases who used wood as wall material compared to concrete (78.2% and 21.8%, respectively), who had a cesspool or nothing (88.2%) as a drainage system and used wood (81.4%) instead of gas (18.6%) as cooking fuel. Additionally, the majority of cases lived in households with less than 3 rooms (71.4%). Finally, there were more cases who had hens (92.0%) and less who owned dogs (38.6%) (Table 5).

**Table 5. Participants’ household characteristics expressed in percentages**

<table>
<thead>
<tr>
<th>Variable</th>
<th>CL Positive N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wall material</strong></td>
<td></td>
</tr>
<tr>
<td>Brick or concrete</td>
<td>26 (21.8%)</td>
</tr>
<tr>
<td>Wood and others</td>
<td>93 (78.2%)</td>
</tr>
<tr>
<td><strong>Drainage system</strong></td>
<td></td>
</tr>
<tr>
<td>Septic tank</td>
<td>14 (11.8%)</td>
</tr>
<tr>
<td>Cesspool or nothing</td>
<td>105 (88.2%)</td>
</tr>
<tr>
<td><strong>Cooking fuel</strong></td>
<td></td>
</tr>
<tr>
<td>Wood</td>
<td>96 (81.4%)</td>
</tr>
<tr>
<td>Gas</td>
<td>22 (18.6%)</td>
</tr>
<tr>
<td><strong>Number of rooms</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 3</td>
<td>85 (71.4%)</td>
</tr>
<tr>
<td>Three or more</td>
<td>34 (28.6%)</td>
</tr>
<tr>
<td><strong>Persons per room</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.9 (1.8%)</td>
</tr>
<tr>
<td><strong>Dog ownership</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>62 (61.4%)</td>
</tr>
<tr>
<td>Yes</td>
<td>39 (38.6%)</td>
</tr>
<tr>
<td><strong>Hens ownership</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8 (8.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>92 (92.0%)</td>
</tr>
</tbody>
</table>

CL: Cutaneous leishmaniasis

In the case of protective measures, almost all participants referred to always using bed nets (92.4%); however, most of them always slept with the windows open (66.7%). The majority of the cases fumigated their household sometimes (54.2%) or always (23.7%) and never used repellent (78.0%) (Table 6).
Table 6. Protective measures of the participants expressed in percentages

<table>
<thead>
<tr>
<th>Variable</th>
<th>CL Positive N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of bed nets</td>
<td></td>
</tr>
<tr>
<td>Sometimes</td>
<td>9 (7.6%)</td>
</tr>
<tr>
<td>Always</td>
<td>109 (92.4%)</td>
</tr>
<tr>
<td>Use of repellent</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>92 (78.0%)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>25 (21.2%)</td>
</tr>
<tr>
<td>Always</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Household fumigations</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>26 (22.0%)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>64 (54.2%)</td>
</tr>
<tr>
<td>Very often or always</td>
<td>28 (23.7%)</td>
</tr>
<tr>
<td>Sleeping with windows open</td>
<td></td>
</tr>
<tr>
<td>Sometimes</td>
<td>35 (33.3%)</td>
</tr>
<tr>
<td>Always</td>
<td>70 (66.7%)</td>
</tr>
</tbody>
</table>

CL: Cutaneous leishmaniasis

In the univariate analysis, to be male, a farmer, or living in a village close to primary forest (Ichoa community) was significantly associated with an increased vulnerability to CL. Other variables related to the households’ characteristics such as wall materials, sewage system, number of rooms in the house, number of persons per room and ownership of hens were significantly associated with an increased vulnerability to CL. However, in the multivariable analysis, only sex/gender remained statistically significantly associated with CL, where men had 3.2 times increased odds of being infected with CL compared to women (Figure 8).
Figure 7. Multivariable regression analysis of sociodemographic and housing conditions factors associated with CL. Adjusted odds ratios and their 95% confidence intervals.
**Sub-study 2**

The sample size of this sub-study consisted of 512 participants, 200 of whom were from Ichoa and 312 from Tacopaya corresponding to a participation rate of 41.3% and 40.2%, respectively, based on data from the municipality census collected in 2016.

The number of cases captured by the NLCP registers was 23, while the CL and ML screening-based study captured 50 of which 13 were also present (recaptured) in the NLCP registers (Figure 9).

![Venn Diagram]

**Figure 8. Distribution of CL cases after linking both data sources.**

The total number of cases estimated (N) with the Chapman formula was 86.4, which corresponds to a level of under-reporting of 73% (Table 7). Comparing by sex, place of residence, age and year of notification, it was possible to notice that differences inside the groups were minimal, ranging between 64% to 80% in all groups.
Table 7. Capture–recapture analysis and NLCP under-reporting estimation

<table>
<thead>
<tr>
<th></th>
<th>Notified† (M) No.</th>
<th>Medical Campaigns (n) No.</th>
<th>Common (m) No.</th>
<th>Aggregated registry</th>
<th>Ascertainment-corrected estimate (95% CI) ( \dagger N = (M+1)^{n+1}/(m+1)+1 )</th>
<th>Estimated under-reporting (95%CI) % = ( 1-(N/M) \times 100 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(a) Overall registers comparison</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>50</td>
<td>13</td>
<td>60</td>
<td>86.4 (62.1–110.8)</td>
<td>73.4% (63.1%–81.5%)</td>
</tr>
<tr>
<td><strong>(b) Disaggregated registers comparison</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>11</td>
<td>27</td>
<td>5</td>
<td>33</td>
<td>55.0 (29.0–81.0)</td>
<td>80.0% (67.6%–88.5%)</td>
</tr>
<tr>
<td>Women</td>
<td>12</td>
<td>23</td>
<td>8</td>
<td>27</td>
<td>33.7 (24.2–43.1)</td>
<td>64.4% (47.9%–78.5%)</td>
</tr>
<tr>
<td>Ichoa</td>
<td>15</td>
<td>38</td>
<td>9</td>
<td>44</td>
<td>61.4 (41.9–80.9)</td>
<td>75.6% (63.3%–84.5%)</td>
</tr>
<tr>
<td>Tacopaya</td>
<td>8</td>
<td>12</td>
<td>4</td>
<td>16</td>
<td>22.4 (12.6–32.2)</td>
<td>64.3% (43.0%–80.3%)</td>
</tr>
<tr>
<td>&lt;15</td>
<td>3</td>
<td>9</td>
<td>2</td>
<td>10</td>
<td>12.3 (6.9–17.8)</td>
<td>75.7% (46.8%–91.1%)</td>
</tr>
<tr>
<td>&gt;15</td>
<td>20</td>
<td>41</td>
<td>11</td>
<td>50</td>
<td>72.5 (50.4–94.6)</td>
<td>72.4% (61.4%–82.0%)</td>
</tr>
<tr>
<td>2013</td>
<td>14</td>
<td>27</td>
<td>8</td>
<td>33</td>
<td>45.7 (30.6–60.7)</td>
<td>69.3% (55.2%–80.9%)</td>
</tr>
<tr>
<td>2014</td>
<td>9</td>
<td>23</td>
<td>5</td>
<td>27</td>
<td>39.0 (22.8–55.2)</td>
<td>76.9% (61.7%–87.4%)</td>
</tr>
</tbody>
</table>

†Cases notified by NLCP.
‡ Chapman’s formula used to calculate the estimator.
Sub-study 3
Two main topics were identified in the analysis of the interviews: 1) the therapeutic journey between traditional and Western medicine; and 2) caught between a rock and a hard place. They portray the experiences of patients with CL and ML regarding what they have to overcome in health services to cure their disease in terms of availability, accessibility, affordability and quality of care.

The therapeutic journey between traditional and Western medicine

Traditional medicine was usually the first therapeutic option for CL in communities. The participants resorted to medicinal plants to try to heal the wound in addition to a series of dietary practices to prevent the growth of the ulcer. For instance, medicinal plants such as *japainiqui*, tobacco, and pepper were applied as poultices to the wound, in addition to restricting the intake of salt and oil in food. More dangerous treatments were also tried, as one of the participants described:

> When I had the disease, my grandmother used fire to treat it. She put fire directly on the wound of my face. I was a child, and it hurt me a lot. She also used a poultice with *japainiqui* (traditional plant). Additionally, she forbade me to eat food with salt and oil. (Informant 9, Tsimane indigenous man with CL)

The use of traditional medicine very often resulted in superinfections of the ulcers, which became disabling due to the pain. This pressed patients to seek for other remedies within the formal health-care sector, as another participant expressed:

> I put tobacco on it, and the wound became very infected. My leg was very swollen. I put more tobacco on it and the wound filled with more pus. I also noticed that the wound was growing. It was getting worse. At that moment, I stopped using medicinal plants and I went to the hospital. (Informant 1, mestizo man with CL)

However, getting to the health centres in the communities did not suppose the end of the search for a cure, but more the beginning of a long pilgrimage. Since health-care centres in the communities where the patients lived lacked laboratory equipment and/or drugs, informants were often referred to health centres of a higher level of care in big cities. A participant shared his experience:

> First, I went to a private doctor in Shinaota community who gave me an injection that did not help me in anything. He told me I had...
leishmaniasis and that I had to save money to make me heal. He sent me to the town of Villa Tunari, but when I arrived, they told me that they could not attend me and that I had to go to Cochabamba city. (Informant 2, mestizo man with CL)

Even though many of the participants were satisfied with the quality of care received, some of them mentioned going on a pilgrimage around health services due to the lack of experience and knowledge of the medical staff about the disease. This pilgrimage led them to undergo what participants perceived as unnecessary examinations and treatments, as illustrated by one participant in the following comment:

> I visited many hospitals. They ran many tests on me, but everything was negative. They believed I had cancer. It's cancer, it is cancer, they said, but the results were negative as well. They thought it was tuberculosis, but that was negative too...
> (Informant 13, mestizo man with ML)

These negative experiences created loss of trust in Western medicine and were their motivation to continue the pilgrimage by going back to traditional medicine solutions. The participants mentioned going to healers who gave them strange and expensive recipes that did not work. One participant commented on his experience:

> After several attempts with hospitals, I didn’t go any more. I waited almost a year for it to heal itself, but it was getting worse. So, I went to a traditional healer. He put ants’ poop on my neck and gave me herbal tea to drink. I spent more than 600 BOB (100 USD) on those treatments. It made me feel a little better, but it didn’t cure me. (Informant 14, mestizo man with ML)

Similar experiences were referred to by participants with CL when resorting to traditional healers, but they also commented on the fact that the dangerous, harmful and painful treatments given by traditional healers were worse than the disease itself. One participant shared his experience:

> I put one remedy on my wound that the traditional healer sold me. I don’t know what it was. It was extremely painful. I couldn’t stand it. It was awful... It was like an acid. It made my leg swell. That is why I stopped using it... (Informant 12, mestizo man with CL)
Caught between a rock and a hard place

Because patients could not find a solution in their pilgrimage between traditional and Western medicine at PHCs in their communities, they were forced to choose between travelling looking for health services of a higher level of care or to remain at home and suffer the complications of the disease. A situation that can be compared with being ‘caught between a rock and a hard place’. On the one hand, travelling means an investment of their limited livelihood assets and endangers their household economies, while on the other hand, staying at home could compromise their income source in the future, and in some cases their life as well.

Many participants remarked on the difficulties related to reaching these health centres of a higher level of care. Long distances, bad roads and expensive travel costs were mentioned as important limitations to accessing adequate medical treatment, as illustrated by the experience shared by one of the participants:

*I have to travel from Yungas community in La Paz to Cochabamba city (380 km) to receive medical attention. It is very far, expensive and dangerous. I've already had one traffic accident... In my community there are many people with the same disease, but they can’t pay for the travel.* (Informant 11, mestizo mother of a child with CL)

In addition to these high expenses, participants commented that the lack of income due to the loss of work during the time spent searching and undergoing the treatment put their family’s economy at risk. A mestizo participant reflected:

*The doctor told me that I need to stay 28 days to receive the treatment. I see this as something impossible. It is a long time without working. Who is going to work for me? If I am not working, how can I get the money to live?* (Informant 12, mestizo man with CL)

On the other hand, those participants who delayed the search for health care suffered the complications of the disease, as is the case of patients with ML, in which the disease produced the destruction of oral and nasal structures affecting basic functions such as eating and sleeping. As one participant commented:

*I visited the hospital one and a half years after I had started feeling the problem. I didn’t go before because I didn’t have the money...Mucosal leishmaniasis is very severe. I started to cough during the nights, and I couldn’t sleep well... I couldn’t eat. If I ate*
something that was a bit hot, it hurt me a lot! The pain got to the roots of my teeth. (Informant 14, mestizo man with ML)

Sub-study 4
The standard treatment based on systemic pentavalent antimonials (SPA) demands great economic effort from both the government and from patients. These demands are usually not completely met so there are long periods of shortage of medicines from the side of the government, as well as, under-utilization or abandonment of treatments on the side of the patients. The use of intralesional pentavalent antimonials (ILPA) is a promising alternative not only from an economic but also from a clinical point of view, since ILPA are less toxic and safer to use. ILPA would also have important consequences in terms of health access for patients with CL.

In the economic sub-study, the cost of treating a patient from the MoH perspective was 303.4 Int$ with SPA and 55.2 Int$ with ILPA, which represents a net difference of 248.2 Int$. From the societal perspective, the cost was 889.5 Int$ for SPA, and 201.7 Int$ for ILPA, which represents a net difference of 687.8 Int$. From the perspective of the MoH, the main contributor to the difference was the number of drugs used (83%); while from the perspective of society the most important factor was the reduction in productivity loss (47%), being drugs costs reduction less important (30%) (Table 8).

Table 8. Costs per patient treated in Int$

<table>
<thead>
<tr>
<th>Selected cost parameters</th>
<th>SPA</th>
<th>ILPA</th>
<th>Incremental cost of ILPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff time cost</td>
<td>55.7</td>
<td>13.9</td>
<td>-41.7</td>
</tr>
<tr>
<td>Drug cost</td>
<td>247.8</td>
<td>41.3</td>
<td>-206.5</td>
</tr>
<tr>
<td><strong>Sum MoH perspective</strong></td>
<td><strong>303.5</strong></td>
<td><strong>55.2</strong></td>
<td><strong>-248.2</strong></td>
</tr>
<tr>
<td>Drugs administration fee*</td>
<td>14.8</td>
<td>3.7</td>
<td>-11.1</td>
</tr>
<tr>
<td>Surcharges for supplies</td>
<td>20.6</td>
<td>5.2</td>
<td>-15.5</td>
</tr>
<tr>
<td>Meals</td>
<td>64.5</td>
<td>16.1</td>
<td>-48.4</td>
</tr>
<tr>
<td>Transport</td>
<td>70.9</td>
<td>17.7</td>
<td>-53.2</td>
</tr>
<tr>
<td>Productivity loss</td>
<td>430.0</td>
<td>107.5</td>
<td>-322.5</td>
</tr>
<tr>
<td><strong>Sum societal perspective</strong></td>
<td><strong>889.5</strong></td>
<td><strong>201.7</strong></td>
<td><strong>-687.8</strong></td>
</tr>
</tbody>
</table>

* Excluded from societal perspective costs.

SPA: Systemic pentavalent antimonials; ILPA: Intralesional pentavalent antimonials; MoH: Ministry of Health
Sensitivity analysis from the MoH perspective showed that ILPA remained cost-saving compared to SPA despite the variation of all parameters, including the number of applications with ILPA, drug costs and the staff time (Figure 10).

SPA: Systemic pentavalent antimonials; ILPA: Intralesional pentavalent antimonials; MoH: Ministry of Health; INT$: International dollars

Figure 9. Tornado diagram of one-way sensitivity analyses of basic assumptions’ effects on the incremental cost of ILPA expressed in INT$ from the MoH perspective.

From the societal perspective, the sensitivity analysis showed ILPA remained more cost-saving compared to SPA with the variation of all the parameters as well. The most influencing parameters were the number of applications of ILPA, the drug costs and the loss of production time (Figure 11).
SPA: Systemic pentavalent antimonials; ILPA: Intralesional pentavalent antimonials; INT$: International dollars

Figure 10. Tornado diagram of one-way sensitivity analyses of basic assumptions’ effects on the incremental cost of ILPA expressed in Int$ from a societal perspective.

The budget used for treating the current incidence of 237 cases of CL with SPA only was 71,906 Int$. A modest increase to 20% the current demand would suppose an additional expense of 14,381 Int$ (Scenario 1). Assuming the treatment utilization remains at the current level, changing to ILPA would result in a saving of 45,529 Int$ to the current budget (Scenario 2). The same increase on demand as Scenario 1 but using ILPA as first-line treatment would save 37,854 Int$ (scenario 3); while an increase in demand to 80% of the expected cases would still represent a saving of 9,262 Int$ (Scenario 4). Finally, retaining the current budget but with ILPA implementation would allow increasing access to treat 601 patients, which is 2.5 times more patients than the current scenario (Table 9).
Table 9. Budget impact analysis from the MoH perspective. Costs expressed in Int$

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>Number of cases treated</th>
<th>MoH perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SPA</td>
<td>ILPA</td>
</tr>
<tr>
<td>Current Practice</td>
<td>237</td>
<td>0</td>
</tr>
<tr>
<td>1) 20% increase in utilization on reported cases†</td>
<td>284</td>
<td>0</td>
</tr>
<tr>
<td>2) Current level of treatment utilization*</td>
<td>62</td>
<td>175</td>
</tr>
<tr>
<td>3) 20% increase in utilization on reported cases*</td>
<td>74</td>
<td>210</td>
</tr>
<tr>
<td>4) Increase in treatment utilization to 80% of total expected cases*</td>
<td>136</td>
<td>387</td>
</tr>
<tr>
<td>Total patients can be treated with the same budget*</td>
<td>156</td>
<td>444</td>
</tr>
</tbody>
</table>

† Current practice, SPA only.
* Using ILPA as first-line treatment.

SPA: Systemic pentavalent antimonials; ILPA: Intralesional pentavalent antimonials; MoH: Ministry of Health; INT$: International dollars
Discussion

The findings of this thesis offer a broad perspective on the challenges of access to health care faced by patients with leishmaniasis in the rainforest areas of Bolivia. These results allow an analysis of the access to health care from different angles based on these four research questions: Who is most vulnerable? What is the extent of the lack of access to health care? How do the dimensions of access and quality of care influence health-care utilization in a context of vulnerability? Can a change in the NLCP policy related to first-line treatment improve the level of access to health care?

Who is most vulnerable?

The remote areas of the Bolivian rainforest represent a vulnerable context due to the precarious living conditions of the people settled there. This context is defined by poverty and characterized by a low educational level of the people, the use of precarious construction materials in houses, the absence of basic services, scarce public transport, bad roads, and precarious and weak medical services.

The first sub-study, aimed at identifying the characteristics of those who are more vulnerable, showed that the only factor significantly associated with CL was sex/gender, the risk for men being three times higher than for women. This risk pattern is common in areas where the transmission mechanism is sylvatic. Even though there are few studies about risk factors in Latin America with which to compare, some of them showed similar results regarding the gender impact in Bolivia [106], Ecuador [16] and Brazil [171-173]. In addition, the results of the study are consistent with the epidemiological profile of CL in Bolivia and the Americas. In the latest national report published in 2015 by the NLCP [174], 70% of the total cases reported in Bolivia during the last 6 years were men; similarly, in the last epidemiological report published by PAHO and WHO, men represented 67.2% (32,886) of the total cases reported in 2106 in the 18 endemic countries of America [175].

The association between sex/gender and the risk of CL can be better understood using a gender approach. According to the concepts and the theory of eco-social-epidemiological perspective of diseases developed by Krieger in 2003 [176], leishmaniasis cannot be considered just a sex-related disease because there are no biological differences in terms of the risk of being affected by the disease. At the same time, in sylvatic contexts, the occupational gendered activities require men to enter into the primary forests, which are the ecological niche of wild reservoirs, vectors and parasites, increasing their exposure. This situation fits well with a gender-related disease pattern.
In addition, leishmaniasis can also be understood as a mirror of the social constructionism of masculinity. Men experience high social pressure to endorse gendered social prescriptions, such as that men are strong, self-reliant and tough. To demonstrate these features, men engage in activities that might require the dismissal of fear, and feats such as demonstrations of physical strength and endurance that often put them at risk of injuries and death [177]. The rainforest is a context where a demonstration of masculinity requires men to adopt risky behaviours, such as hard work, constant exposition to injuries, the use of dangerous tools, as well as hunting and fishing activities, all them starting from a young age. In contrast, the construction of femininity among women is related to safer and healthier-promoting behaviour compared to men, working at home and child-rearing leading to a lesser exposition to leishmaniasis.

This pattern of risk associated with gender tends, however, to disappear when the mechanism of transmission is peridomestic, which occurs when urbanization of tropical forests occurs and both the vector and the parasite adapt to new environments and find new reservoirs, as has been shown in studies conducted in Brazil [178] and Colombia [179].

The presence of animals inside the house is also a common risk factor when the transmission mechanism is peridomestic. In our study, no association was found between possession of hens and CL, which is different to the findings in studies conducted in Brazil [171, 180], where poultry tenure increased the risk of CL. However, due to the wide range of the confidence intervals in this result, it is possible that the effect is hidden due to the small sample size. The association found in other studies has been explained by the attraction of vectors to peri- and intra-domiciliary environments looking for birds’ blood [181, 182]; however, there is also evidence that birds cannot be reservoirs because their blood does not allow the development of the parasite [183].

In our study, dog ownership was not associated with CL. In Latin America, the role of domestic dogs as a reservoir for CL has been well studied. One systematic review of more than 90 studies concluded that the association between dogs and CL is only circumstantial [11]. Experimental studies have not found evidence of the infectiousness of dogs to sandfly vectors of CL, either [10].

The lack of association between households’ characteristics and CL risk was similar to studies from Brazil, where transmission was also mainly sylvatic [184]. However, in areas where transmission is mainly peridomestic, the association between vulnerable housing and CL is usually present. Studies carried out in Argentina [132] and Brazil [180] have shown that when houses are built with non-durable material there is a greater risk of infection. This is explained by the fact
that non-durable materials, with time, allow the formation of cracks in the walls, which are the entry point for vectors inside the houses.

The use of bed nets was not significantly related to CL in our study, probably because of the small variation in its utilization, since most of the people mentioned that they used them all the time; however, studies conducted in Colombia and Venezuela have shown that the use of bed nets per se does not provide enough protection for CL and bed nets impregnated with insecticides such as deltamethrin [23] or lambda-cyhalothrin [24] are required to reduce the risk of vector bites.

**What is the extent of the lack of access to health care?**

Sub-study 2 showed that the passive surveillance system of leishmaniasis in Bolivia has a high level of under-reporting (73%) in one of the most endemic and remote areas of the country. The high level of under-reporting uncovers the problem of access to health care among patients with leishmaniasis, since only 26% of them could access the treatment. Undoubtedly, the support offered by the NLCP to patients with leishmaniasis through the provision of free treatment is a breakthrough, since the high costs of drugs have been described as a major limitation to patients accessing treatment [66, 67, 185]. However, the dependence of the programme’s activities on the limited infrastructure and the scarce resources of public health services greatly influences the efficacy of this disease control strategy. In Bolivia, the high toxicity of systemic pentavalent antimonials and its elevated costs demand the confirmation of the presence of the parasite by laboratory methods, which are only available in big urban centres, distant from the small communities in rainforest areas. Although the NLCP’s policy of case detection and management is based on international standard criteria, they are difficult to meet in the precarious contexts of PHCs in these remote settings. In consequence, health-care access is restricted to patients’ capability to travel and reach health centres of a higher level of care.

On the other hand, epidemiological surveillance of leishmaniasis is a global problem and there is a major concern regarding the attempt to control leishmaniasis worldwide. A multinational study assessing the incidence of leishmaniasis in the world in 2012, revealed that a third of the endemic countries did not have updated information for the last 5 years [57]. In general, it is believed that there is an important level of under-reporting, which prevents the real burden of the disease worldwide from being known. Even though there are few international studies that have evaluated the level of under-reporting of the national surveillance data of leishmaniasis, the results show alarming figures, which suggest that the real incidence figures may be up to 40 times higher than the actual numbers [186]. There are only three studies published in Latin
America, these being from Guatemala [62], Argentina [59] and Brazil [58]. Compared to them, the levels of under-reporting found in our study were higher than in Argentina (55%) and Brazil (45%) but lower than in Guatemala (97.5%).

How do the dimensions of access and quality of care influence health-care utilization in a context of vulnerability?

In the third sub-study, four main elements related to health services that limit access to health care could be recognized from the experiences of the patients seeking health care: availability; accessibility; affordability; and quality of care. No problems related to acceptability were mentioned.

Regarding availability, three main problems were identified. First, laboratory services for diagnosis were not available in remote rural communities; second, most indigenous communities did not have primary health centres; and third, antimonial drugs were not available in health centres. Similar findings have been described in Colombia [133] and Ecuador [137], where understaffed medical facilities and lack of medications were the main impediments in receiving adequate treatment.

Accessibility was probably the greatest determining factor influencing access due to long distances, long travel time and lack of transportation to health services. Lack of accessibility was worse among indigenous participants. In the Tsimane area, the nearest hospital is located further than one day of travel from most of the communities, preventing participants from using health-care services. This accessibility issue has severe consequences on Tsimanes’ health; for instance, one study showed that the communities located farthest from the main town, where the regional hospital is located, had higher infant and neonatal mortality rates compared to the closer communities [152]. Participants from non-indigenous communities too, where a PHC exists, often must travel searching for health centres with a higher level of care where they can find the service of laboratory diagnosis confirmation required to receive the treatment. Similar situations have been described in other Latin American countries. In Paraguay, patients commented that they had to travel between 1 to 3 hours to reach the nearest health centre and distance was one of the main reasons for not seeking medical attention [67]. In Suriname, long distances between towns and capital cities were one of the main access barriers. This is because long trips to seek medical attention would result in work absenteeism causing them to lose their job [66]. Similarly in Sudan, where the treatment is provided for free by the government but there is a lack of drugs and laboratory diagnostic services, patients are forced to travel to the higher level of care services in the big cities [187]. Travel times to reach health centres can range from 3 hours to 1 day during the dry season and
these times increase up to 1 and 4 days for the same areas during the rainy season [185].

Even though in Bolivia the treatment for leishmaniasis is free for patients and the costs of the drugs are paid for by the government, affordability is still a problem due to the indirect costs related to transportation, food, accommodation and loss of work. This situation needs to be considered in the context of poverty, in which these expenses often become catastrophic for the poor family’s economies. In our study, participants mentioned the high costs related to the process of seeking health. Similar results have been found in Suriname and Paraguay, where costs equated to one month’s salary, with the additional damage of not being able to work during that time and the risk of losing their job [66, 67]. Likewise, examples from Nepal, Bangladesh and India, where many families had to sell part of their livestock or take loans to pay these costs, resulted in catastrophic economic consequences [187-191]. In Sudan, a study showed in detail the impact of high indirect costs on the decision to seek medical attention. This study showed how during the rainy season, transport costs increased greatly because only private transport was available. Furthermore, if someone in the family became ill during the harvest time, they could not be taken to the medical centre because the harvest was their main source of income.

Patients also reported experiences related to poor-quality medical care. The lack of experience of some doctors in the recognition of the disease led to inadequate treatment, as well as unnecessary examinations. These experiences resulted in a loss of trust, which led patients to make a pilgrimage between traditional medicine and Western medicine, delaying the provision of an adequate treatment, with additional costs that further affected their family economies, in addition to the risks related to the use of traditional medicine. Low-quality medical care has also been described in two studies conducted with medical staff in endemic areas from Ecuador [192] and Honduras [193]. In these studies, the level of knowledge about leishmaniasis was insufficient, with shortcomings in the recognition of the lesions as well as in the therapeutic schemes to treat them. The problem of the continuous movement of medical staff in rural areas was also mentioned as one of the causes, leaving medical services in charge of personnel without adequate experience and training on the national protocols for the management of leishmaniasis.

Although the national health policies aim to provide health-care access for all through primary health care, its implementation has not been adequate, and in many cases, it has been limited to the construction of infrastructure without providing minimal resources for its operation, such as medicines, equipment or means of transport to reach the communities. In addition, the organization and infrastructure of the public health system still have strong roots in a hospital-
based model, which is centralized in large urban areas and receives most of the economic investment. On the other hand, since the beginning of the implementation of the primary health care policy, there has been very little investment in human resources and equipment for primary care centres, particularly in rural areas. Furthermore, the implementation of primary care does not currently have a system that guarantees the quality of care with continuous training and evaluation of the medical staff.

Another problem related to accessibility is that the NLCP administrative offices are located in the capital cities of the departments, from where antimonial drugs are managed and distributed. This centralization creates a further delay in the provision of treatment for patients, who depend on the availability of the PHCs’ medical staff to travel to big cities to pick up the drugs.

Can a change in the NLCP policy related to the treatment improve the level of access to health care?

A key element for health-care access is related to the current standard treatment of CL, which is based on the use of SPA. The treatment is highly toxic and its use implies risks to life in several vulnerable groups, such as patients with underlying pathologies or those who are over 50 years old [37, 39, 41, 194]. Additionally, it is quite expensive for the government because it implies an expenditure of 60 ampoules on an average adult patient. One of the most feasible alternatives is the use of ILPA, which has similar efficacy to SPA, but with the benefit of not being toxic to the patient and having minimal adverse reactions. Regarding the economic issues related to SPA, our study showed that ILPA implementation was highly cost-effective for both the patient and the government. On the one hand, from the patient perspective, it meant a significant reduction in non-direct costs such as transportation, food and loss of work. These additional costs have been mentioned in other studies as important elements that limit access to health care. Studies conducted in Paraguay and Suriname described how the difficulty of absenting themselves from their work activities for 20 days and the risk of losing their job prevented patients from accessing medical care [66, 67]. From the MoH perspective, there was a substantial reduction in drugs costs and medical staff time.

In addition, its implementation would remain sustainable in hypothetical scenarios of increasing its use by up to 2.5 times more than the current demand. Currently, 75% of the cases are eligible for ILPA, a figure that would increase if the population’s confidence is gained and they decided to search for medical attention in the early stages of the disease. This initiative needs to go hand in hand with a decentralization process of drugs delivery supported by municipal pharmacies, which would reduce even more the drugs delivery barriers, at the
same time as they could collaborate in controlling the adequate use of the medicaments.

Paradoxically, although affordability is one of the main problems for leishmaniasis control, very few economic studies have been conducted. To my knowledge, only two studies have been conducted in Colombia but neither of them about ILPA. The first study compared thermotherapy with SPA from an institutional perspective, showing that thermotherapy was highly cost-effective by reducing the high costs of the required tests for the follow-up of adverse reactions that could occur with SPA [138]. However, these results are not applicable to the Bolivian context for two reasons: first, examinations are rarely carried out in PHCs due to the lack of personnel and equipment; and second, the equipment for thermotherapy is still under patent, making its implementation expensive. Although a positive experience has been described with a cheap thermotherapy device manufactured by a group of researchers in Peru, more field experiences are still needed to consider its implementation [195]. The second study compared the use of miltefosine in children with SPA and showed that although miltefosine was more expensive from the government’s perspective, when patients’ costs were added it became more cost-effective [139].
Methodological considerations

Two main limitations related to the sample size and the sampling process have to be considered when interpreting the results of sub-studies 1 and 2, due to the difficulties of accessing the communities. Additionally, it was not possible to rule out a selection bias between the members of the community who considered themselves healthy and refused to participate in the study. Furthermore, most of the participants in these studies were men, probably because they were the group at highest risk and the most affected ones.

Another specific limitation for sub-study 1 was related to the different methods used to register the incident cases. The NLCP captured new cases using the DME method, while the screening-based study used the MST in addition to DME. The method of the MST identified CL cases even when the participants themselves did not know they had the disease; in consequence, the NLCP had a lower probability of capturing cases in comparison with the screening-based study. In addition, despite 2013 and 2014 being a short time ago in terms of remembering and even though the screening-based study was conducted in 2015, the possibility of recall bias cannot be rejected regarding the specific year of CL infection among the participants captured by this study.

For sub-study 3, some methodological considerations related to the qualitative approach need to be mentioned. According to Lincoln and Guba, in order to enhance trustworthiness qualitative studies should fulfil the criteria of credibility, dependability, confirmability and transferability [196]. Credibility refers to the ability of the study to capture the phenomenon under study. Several measures were taken to meet this requirement. Firstly, I spent year and a half visiting the study area to become familiar with the medical services and the patients, but also with their experiences with the disease and their search for medical attention, which relates to the strategy of prolonged engagement. Secondly, the researchers who participated in the analysis of the data provided a combination of outsider and insider perspectives. Dependability refers to following an emergent design guided by emerging findings, which allows adapting to the changing circumstances of the phenomenon being studied. To fulfil this requirement, the sub-study adopted an emergent design throughout the research process; i.e. new emerging relevant topics from previous interviews were further explored in the subsequent interviews. In order to fulfil confirmability, there is a need for the results to be grounded in the data, notes were taken throughout the process, and in order for the reader to assess that our analysis remained grounded in the data, quotes were provided from the participants to illustrate and expand our interpretations. A naturalistic transferability was aimed for, letting it be up to the reader to assess whether our findings could be applicable to other settings. In
order to enhance naturalistic generalizability, a detailed description of the study context has been provided.

As previously mentioned, it must also be acknowledged that some limitations in this sub-study related to the fact that most of the participants were men. Women might have other experiences that the study might not have captured fully. It is also possible that some information may have been lost during the translation of interviews performed among indigenous participants. Finally, another limitation was related to the acceptability dimension of health services among indigenous participants, which did not come out in the interviews probably because most of them could not get access to health-care services.

For sub-study 4, three limitations regarding the assessment of ILPA as first-line treatment for CL should be mentioned. First, although the PAHO recommended ILPA as an alternative treatment for CL, they do not include it in the standard scheme recommendations. The schemes included in the meta-analysis that was the basis of our study varied in regimens, volumes, periodicity and administration dosage [54]. However, it is worth mentioning that in Brazil, where they have the same species of parasite as in Bolivia and with a long experience of using ILPA, they use a scheme of three doses once a week. The parameters included in the scheme defined by the Brazilian MoH coincide with those used in our evaluation. Second, the analyses did not include additional treatment costs related to the toxicity of SPA, or the costs of complementary examinations. This decision was taken because the primary care centres do not usually have the equipment to perform these examinations and the means to treat the potential side effects. However, the inclusion of these parameters would only increase the costs of SPA, making our results more robust and the ILPA alternative more cost-effective. Third, the specific susceptibility of the different species of Leishmania for each therapeutic scheme was not considered because it was not available in the meta-analysis. However, in vitro tests have shown that the species braziliensis, which is the most aggressive and responsible for 85% of the cases of CL in Bolivia, has a very good response to pentavalent antimonials drugs.
Conclusions

Men were the most vulnerable group affected by CL, which reflects the predominance of a sylvatic pattern of transmission in this rainforest area. Other factors related to the characteristics of the dwellings and the presence of animals in the house were not significantly associated with the risk of CL. These findings reinforce the importance of case detection and management as the main strategy to control leishmaniasis in these settings.

The passive surveillance system for leishmaniasis control in Bolivia highly underestimates the burden of the disease in remote rural areas of the Bolivian rainforest, which are at the same time, the most endemic. The high level of under-reporting of the NLCP registers reflects another very relevant problem, related to the lack of health-care access among patients with leishmaniasis in these areas.

Lack of health services, equipment and drugs, as well as the difficulties in reaching health services, the high costs of seeking health care and the low quality of care are important factors that limit health-care access among patients with leishmaniasis.

A change in the NLCP’s policy related to the treatment of CL can improve health-care access, reducing some affordability barriers. In this sense, the use of ILPA would be cost-saving for both patients and the MoH, and its implementation would greatly increase the number of patients who can be treated without a negative impact on the MoH’s budget.
Implications for practice

Activities promoting occupational safety must be carried out in endemic areas, including education about the vector’s habits and how to prevent vector bites. Additionally, the identification of risky habits and the promotion of safe work practices should be implemented.

The high levels of under-reporting found in our study should alert health authorities to the problem of access to health care in these areas. In addition, the system used for registering cases by the NLCP should be reviewed to achieve its objective of an adequate epidemiological surveillance that responds in a timely fashion to geographical and temporal changes.

There is a need to search for alternatives to improve the performance of the NLCP adapted to the limited conditions of the PHCs in remote rural areas. The capacity of the medical staff in primary care level to solve problems must be strengthened, developed and empowered regarding clinical diagnostic activities. A task-shifting strategy implementation by the NLCP in a well-planned way, with standardized training, supporting supervision, certification and permanent evaluation to ensure its quality, would extend the scope of the NLCP, and thus it could improve laboratory diagnosis and access to treatment.

In parallel to the research sub-studies of this thesis, different activities have been conducted throughout these years to strengthen the capacity of health services in the field. Training activities on clinical and laboratory diagnosis as well as in the treatment of CL and ML were carried out. As a result, the service of laboratory diagnosis of CL and ML was incorporated into the activities of seven more PHCs. One of them was Ichoa, a small community located deep in the rainforest where the general physician learnt how to perform laboratory diagnostic procedures in the absence of a laboratory technician, showing that task-shifting can be a feasible and efficient strategy for these settings.

The implementation of ILPA should be considered as a first-line treatment for CL. However, for the successful implementation of ILPA it is indispensable to establish an efficient system of drugs delivery from the NLCP. During this project, I facilitated the coordination between the departmental offices of the NLCP and the municipal pharmacies of the main health centres in the study area to store the drugs, improving greatly the timely delivery of treatments to those patients who had had their diagnosis confirmed.
Future research

Research is needed to better understand the role of sex/gender in the occurrence of CL in sylvatic environments. Such research should focus on the relation between gender and the chronicity of the lesions, the severity of the disease, and how the use of medical services takes place.

This research was conducted mostly among farmers in the tropical rainforest area of Cochabamba. Future research needs to be carried out to evaluate risk factors in other areas of the country among other ethnic groups with different lifestyles. This will allow domestic patterns of transmission to be identified and opportunities for the implementation of primary prevention measures among different cultural and ethnic groups.

More evaluations about the level of under-reporting of the NCLP are needed in other endemic areas of the country to develop more efficient plans to provide improved medical attention to patients with leishmaniasis in Bolivia.

The nature of the problems related to lack of health-care access among patients with leishmaniasis has revealed two questions in need of further investigation: how people cope with other diseases and how these accessibility problems affect different groups of the population in these settings.

This research used health economic methods to assess the costs and the budget impact of ILPA implementation. However, further research needs to be done to establish whether new diagnostic alternatives are cost-effective as well, given that laboratory diagnostics is another important barrier that must be addressed in order to improve access to health care.

I hope that the findings of my thesis and the recommendations based on them serve to improve the health-care access and the quality of care among patients with leishmaniasis in Bolivia.
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