



# Integrated Analyses of Human Dimensions and Policy Implications of Cross-Border Migration on Vector-Borne Neglected Tropical Diseases (NTDs) in the Andes-Amazon Region

## Executive Summary



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### **Abstract**

The recently constructed Transoceanic Highway has facilitated increased cross-border migration between Brazil and Peru in the Southwestern Amazon. The objective of this research was to determine whether migrants are at greater risk for the endemic vector-borne American Cutaneous Leishmaniasis (ACL) than non-migrating populations, and to explore the emergence of Bartonellosis in Acre, Brazil and Madre de Dios, Peru. Residence and employment in forested and deforested areas, such as those often frequented with migration in the region is a known risk factor for vector-borne diseases. Social drivers, experiences and patterns of migration were explored among cross-border and internal migrants. An interdisciplinary approach was utilized that captured the migrants' experiences and disease risks through qualitative, epidemiological and biological investigations.

Drivers for migration included employment and familial relationships. Consular services in Acre Brazil facilitated residence while Brazilians in Peru remained largely confined to 'tourist' status. Migrants were familiar with local term for ACL, but not with transmission risk. ACL was associated with migration and sleeping outdoors in Peru where illegal gold mining and Brazil nut harvesting are primary sources of informal work in forested and deforested areas, known risk factors for ACL. Distance, cost and cultural variations hindered access to health services. This research provided the first multidisciplinary investigation into ACL and Bartonellosis in the Southwest Amazon and provides key insights for prevention and early intervention among vulnerable and migrating populations.

### A. Research Plan

The Southwestern Amazon is an area of internal and cross-border population movement and transit due to the newly paved Transoceanic Highway, connecting Atlantic ports in Brazil with Pacific Ports in Peru. The last part of the highway – crossing the Peruvian Amazon – was only opened 5 years ago. As the highway crosses through forested and deforested jungles endemic for vector-borne diseases (VBDs), there is increased concern about the (re)emergence and increased distribution of diseases to non-endemic areas. Environmental destruction due to increased agriculture, farming, and illegal gold mining operations has expanded deforested areas in the Southwestern Amazon in Brazil and Peru, a known risk factor for vector-borne diseases (VBDs). Satellite images show the evolution of deforestation along the Transoceanic Highway that has affected this region (see Annex 1, **Figure 1**). Increased residence in forested and deforested areas are environments where vectors breed and sylvatic animals act as hosts for zoonotic VBDs such as American Cutaneous Leishmaniasis (ACL) and Bartonellosis, the focus of our research.

ACL is a disfiguring parasitic disease which causes ulcerative cutaneous lesions on the skin leading to secondary infections, while the mucosal form can cause complete destruction of the nasal cavity. There are more than 1.5 million new cases of cutaneous leishmaniasis (CL) globally [1], with New World *American* Cutaneous leishmaniasis counting for a third of all cases globally [2] (Annex 1, **Map 1**). Madre de Dios, Peru and Acre, Brazil are highly endemic areas for ACL, with incidence rates 34 (713/100,000) [3] and 12 (144/100,000) [4] times the national average of ACL respectively. Non-immunity to cutaneous leishmaniasis is considered to be a risk factor for migrants arriving from non-endemic to endemic areas [5] and length of time (>6 years) has been shown to increase immune response to the disease [6]. Thus recent migrants are considered at higher risk for ACL infection, particularly when employment activities are in areas of high environmental exposure. ACL differs from the Old World leishmaniasis in the diversity of vectors (more than 30 sandflies of the species *Lutzomyia* spp) circulating in the Americas, making vector and disease control and treatment more complex. Also, access to health centres may be more difficult for migrants than for residents given that they tend to work further away from urban centres.

Bartonellosis is a highly fatal bacterial disease, thus far confined to Peru, and also transmitted by *Lutzomyia* spp. The disease causes haemolytic anaemia and can evolve to organ and systems failure in the first phase, the second phase is distinguished through the presence of chronic blood-filled nodules, often referred to as “Peruvian Warts”. Bartonellosis is considered a possible emerging disease in the Southwest Amazon. Centered in the Cajamarca, Ancash, and Piura departments increased distribution of Bartonellosis in Madre de Dios is a possibility through migration from endemic regions [7].

This research sought to determine, through a mixed method qualitative and quantitative approach, whether migrants are at higher risk for American Cutaneous Leishmaniasis (ACL) and Bartonellosis than the non-migrating population. Research also included the collection and species identification of *Lutzomyia* sandflies on the border between Brazil and Peru, to identify local vector species infected and associated with ACL and Bartonellosis, as well as the collection of tissue samples for the identification of leishmaniasis disease species. Importantly, migrants in both Peru and Brazil have been interviewed to capture their migration history knowledge and risk of disease exposure, as well as their health seeking behaviors. As policy for cross-border migration can influence health access and experiences, we reviewed literature and spoke with migrants about regional policy and process of documentation and residency.

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The research was guided by the following research questions and objectives:

| Research Questions  | Objectives  |
|---|---|
| What are the links between disease transmission and migratio)? Are migrants at higher risk for American Cutaneous Leishmaniasis (ACL) and Bartonellosis than non-migrant populations?   | To describe social, environmental and behavioral context and patterns of cross-border migration between Brazil and Perú   |
| What are the patterns and determinants of population movement between Brazil and Perú?  | To conduct health centre-based studies and cross-sectional surveys to evaluate socioeconomic, behavioral, and environmental risk factors for ACL/Bartonellosis and cross-border migration |
| What are the key insights into determinants of migration, social and environmental migrant risk for ACL and Bartonellosis, health access, disease exposure, management and basic health strategies to mitigate risk, enhance service utilization and reduce barriers to access? | To map the distribution of ACL/Bartonellosis, environmental risk, and patterns of migration between Perú and Brazil   |
| What are the specific policies in Brazil and Perú that influence migration and ACL/Bartonellosis risk? Do existing policies influence migration, access to health services and disease transmission?  | To review policies to assess possible influences on migration patterns, health service access and ACL/Bartonellosis risk, and identify potentially conflicting policies                   |

### **Methodology**

The research was conducted in highly endemic states for ACL identified by the Ministries of Health in Acre, Brazil and Madre de Dios, Peru, and where Bartonellosis distribution was considered a risk through migration. Acre, Brazil (population 790,101) [8] and Madre de Dios, Peru (population 130,876) [9] have the highest incidence of ACL infection nationally, and Bartonellosis has thus far been limited to Peru.

### **Interdisciplinary Study Design**

*Qualitative Study Design:* The qualitative study was designed to investigate links between ACL and Bartonellosis transmission and migration. We explored insights into drivers of migration, prevention behaviors and social and environmental risk as well as health seeking behaviors and barriers to healthcare access among Peruvian migrants in Acre, Brazil and Brazilian migrants in Madre de Dios, Peru. We also wanted to identify patterns of population movement between Brazil and Peru, experience in cross-border migration, the process of documentation for residency and policies in effect that influence migration and residency. A primary objective was also to identify sites in Madre de Dios, Peru and Acre, Brazil of high population movement in which the epidemiological portion of the project would be conducted, and locally relevant disease risk among migrants to include in the epidemiological surveys.

*Epidemiological Study Design:* The epidemiological study was designed to determine if migrants are at higher risk for ACL in an endemic area for the disease, and Bartonellosis, an emerging disease, in the Southwestern Amazon of Acre, Brazil and Madre de Dios Peru. The study explored biosocial, behavioral, clinical factors that may influence disease risk, including migration.

The ACL study compared those positively diagnosed with ACL by microscopy conducted through the Ministries of Health in Acre, Brazil and Madre de Dios, Peru, compared to an uninfected control population matched by age, sex and geographic location of diagnosis. The Bartonellosis study was designed to confirm freedom of disease in Madre de Dios, Peru and Acre, Brazil through a hospital based cross-sectional study whereby blood samples from individuals were randomly collected in areas with high migrant movement. Freedom of disease is an approach to investigating absence of disease in

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veterinary epidemiology but has hardly been used in public health despite similar epidemiological questions. Migration was defined as living in another municipality at least 3 months or longer within the past five years. Finally, qualitative and epidemiological interviews and migration data was mapped to explore population flow between endemic and non-endemic areas for ACL and Bartonellosis.

Blood samples were collected to assess the presence of Bartonellosis, and tissue samples were collected among ACL cases to determine parasite and leishmaniasis species associated with active infection by PCR. Sandfly species were collected to identify *Lutzomyia* spp. species and the presence of Bartonellosis and leishmaniasis and their species in the environment.

### Data Collection

*Qualitative Study:* Data collection was conducted among cross-border migrants with residency between 3 months and 5 years in April and June, 2013 among Brazilian migrants in Madre de Dios and among Peruvian migrants in April, June and October, 2013 in Acre, Brazil. Internal Peruvian migrants living in Madre de Dios were interviewed in April and May 2014. Key informant interviews with Ministries of Health and Departments of Immigration and Federal Police in Madre de Dios, Peru and Acre, Brazil identified areas with high population movement between the two countries. Additionally, we surveyed cities along the Transoceanic Highway in Acre and Madre de Dios for the presence of cross-border migrants.

Purposive sampling was based on selecting migrants from a variety of drivers of migration including occupation, familial arrangements and risks for ACL and Bartonellosis such as proximity to forested and deforested areas. A semi-structured interview guide was used to conduct in-depth interviews among 25 migrants in Madre de Dios and 21 migrants in Acre. Topics explored included past five year migration patterns and drivers of migration, border and documentation process and experience, access to health services, employment, knowledge of ACL and Bartonellosis and vector prevention activities, as well as regional policy surrounding migration and its application among cross-border migrants.

*Epidemiological Study:* Data collection for the epidemiological study was conducted between September, 2013 and April, 2015 in Madre de Dios and December 2014 to January, 2015 in Acre, Brazil. Data collection was coordinated with the Ministries of Health through the local health centers in 8 sites identified in the qualitative study. Study participants were recruited through public health centers located in each site, and interviewed by trained health professionals at the local health care centers. ACL cases were confirmed through the Ministries of Health in Madre de Dios and Acre, ACL controls were matched to ACL case based on age, sex and geographic location, and Bartonellosis participants were randomly selected in local public health centers. Information on demographics, socioeconomic status, access to health services, prior infection for ACL or Bartonellosis, vector prevention behavior, migration, biosocial environment and employment were collected through structure questionnaires. Clinical data were also collected through patient medical records.

Whole blood samples were collected from participants for the Bartonella investigation and stored in tubes containing EDTA anticoagulant. Lancets used during tissue sample extraction was stored in tubes for ACL. Tissue and blood samples were stored at -70c. Sandfly samplings were performed using miniature CDC light traps and a Shannon trap with protected human attractant, the methods and devices were described in Perez et al., 1988. Both types of traps were placed in secondary forest approximately 300 m from houses, the traps were operated from 18:00 to 24:00.

### Data Analysis

*Qualitative Study:* Interviews were recorded and transcribed in their original language and translated into English entered into Microsoft Word. Data from Brazil and Peru was imported separately into MaxQDA software version 11 (VERBI Software Consult, Berlin, Germany) for analysis. Text

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segments were coded using thematic analysis to identify multiple domains for migration and relationships between migration and biosocial and environmental risk for ACL and Bartonellosis, risk mitigation, health access, and policy influencing migration.

*Epidemiological study:* Data were entered using Microsoft Access 2013. Data analysis was conducted using STATA version 12 (Stata Corporation, College Station, USA). We conducted bivariate analyses comparing cases and controls in the two countries using Fisher's exact test for explanatory variables to investigate associations with ACL infection and socioeconomic status, clinical factors (exposure to others, prior infection), healthcare access and health seeking behavior, prevention behavior, environmental and household risk, past 5 year migration patterns, and occupation.

For Bartonella samples, two smears were stained with Giemsa stain and cultures were obtained on blood agar (Columbia agar base medium). The whole blood DNA was purified according to HENRÍQUEZ *et al.* (Rev Med Hered 13 (2), 2002). DNA extraction methods used ZOL® BD (lysis solution with guanidine detergent). An extraction protocol was followed for DNA extraction from whole blood which made a first lysis step through the guanidine detergent BD ZOL® DNA, purification and subsequently subjected to PCR using primers 16S and 23S for the Intergenic Transcribed Spacer (ITS). Heat lysis was performed as *Brucella mellitensis*, species phylogenetically related to *Bartonella*, amplified a product of Bartonella smaller than the bacilliformis, comparable to discriminate between other bacteria and even among other Bartonella species.

### **Ethics Statement**

This research was formally approved by the Ethikkommission beider Basel, the Comité Institucional de Ética (CIE) de Universidad Peruana Cayetano Heredia (three times – twice for cross-border migrants [annual renewal requested in Peru] and an additional one on internal Peruvian migrants as this came up as major research topic), and in Brazil clearance was obtained for the qualitative work (CEPE-UNIFRAN 112/08). In Brazil, permission to conduct the research was also obtained from the local Ministries of Health. Informed written consent to participate in the survey and sample collection was obtained from study participants, who were also provided with information on ACL and Bartonellosis in the language of the participant.

### **Workshops**

The first bi-national Peruvian and Brazilian workshop took place in June 2013 (see mid-term report). We have contacted the University of Acre and the Ministry of Health of Rio Branco, Acre to host a larger tri-national (Peru, Brazil and Bolivia) workshop on the health of migrants in the Andes-Amazon region.

### **Innovations**

Lack of information on tropical diseases and their prevention among migrants, particularly among internal Peruvian migrants arriving from the Andes mountains into the tropical forest, was identified as a major constraint to reduce exposure and improve treatment of migrants. A significant barrier among this population is isolation from public health facilities (for diagnosis) and outreach staff (for educational and communication campaigns on risk reduction). A proposal on how to engage taxi-drivers and farm concession owners in dissemination of tropical disease (with special emphasis on ACL) prevention, education and information and distribution of insecticide treated bednets (ITNs) and personal repellents, was proposed to the Geigy Foundation. Development of networks between these non-traditional actors and local public health facilities supports prevention, while engaging those in direct contact with high risk migrants in active surveillance and early diagnosis.

### **Partner institutes**

We present below the joint efforts of partner institutes, Swiss Tropical and Public Health Institute (SwissTPH, Basel, Switzerland), Universidad Peruana Cayetano Heredia (UPCH, Lima, Peru), Universidad de Franca (UNIFRAN, Franca, Brazil) and NGO AIAOASSCA (Franca, Brazil), and an interdisciplinary research team from University of Zurich (Zurich, Switzerland) and the Federal University of Goias (Goiania, Brazil),

## **B. Results**

### **Site selection**

Based on qualitative interviews with migrants and key informants, and preliminary surveys as described in the method's section, in the Peruvian department of Madre de Dios, seven sites in areas of high ACL transmission and high population movement in the gold mining cities of Mazuko, Huepetuhe, and Laberinto, and in the Brazil nut harvesting cities of Iberia and Planchon were selected, as well as the commercial center, Puerto Maldonado and the border town Inapari. Both mining and Brazil nut harvesting areas bring in circular internal migrants from other areas of Peru, while the commercial center of Puerto Maldonado is a primary destination of cross-border migrants from Brazil (see Annex 1 **Maps 2-4**). In the bordering Brazilian state of Acre, the capital city of Rio Branco and the border town of Assis Brasil were chosen for cross-border migrants from Peru.

### **Migration and American Cutaneous Leishmaniasis in Madre de Dios, Peru**

#### **a. Characteristics of migrants in the cross-border study region**

During the qualitative study, in-depth interviews were conducted among 25 Brazilian cross-border migrants with ages ranging from 19 to 56 years, 17 females and 13 males, and 9 internal Peru migrants, ages 20 to 44, 5 males and 4 females. There were three confirmed ACL cases and two suspected cases among Peruvian migrants, and one confirmed and one suspected among Brazilian migrants. In the epidemiological study, preliminary results are shown for 56 ACL cases and 27 controls. There were 41 males (73%) and 15 females (27%) among the cases, and 15 males (56%) and 12 females (44%) among the randomly selected controls ( $p=0.01$ ). The mean incomes were 1184 PEN and 1184PEN (~377 USD) for cases and controls respectively, and without statistical difference.

#### **b. Migration and Population Flow**

Through our qualitative research we identified patterns of cross-border population movement that drew primarily from the border adjacent Brazilian state of Acre, Brazil, and secondarily from other non-contiguous Brazilian states, and lastly from inside Peru and from other international locations. There were important internal population movement primarily between Peruvian departments of Ucayali and Loreto, followed by Cusco, Ayacucho, Arequipa, Lima and Junin. (Annex 1, **Map 2**), which was unexpected

Brazilian migrants in Peru concentrated in the urban Madre de Dios capital of Puerto Maldonado (Annex 1, **Map 3**). Family relationships were among primary drivers for cross-border migration due to the proximity of the border between the two countries. Brazilians were from bi-national parents, were married to Peruvians and/or had children born in Peru, or had family members residing in Madre de Dios.

Other drivers of migration for Brazilians included employment in Madre de Dios, with respondents citing benefits from niche markets for Brazilian foods and products – both informal street vendors selling Brazilian “churrasco” or barbecue, Brazilian beauticians, and informal investment for the sales of Brazilian soft drinks, beer and food products..

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*“Here the people don’t know this type of BBQ that we do in Brazil and they like to eat different things” (Brazilian street vendor, male)*

Origin unemployment was also an incentive for migration from the border areas of Assis Brazil. Many of these respondents maintained cross-border relationships and were sometimes recruited to work in hotels, restaurants and as household help through family relationships or other contacts. Brazilians also arrived to Madre de Dios for ministry work supported through evangelical ministries in Brazilian Churches.

*“in Peru there ‘s a lot of witchcraft, sorcery, terrible things...and we came to help and show them Jesus Christ” (Brazilian missionary, female, 32)*

Internal migrants were largely attracted to employment in gold mining and Brazil nut or “*castana*” harvesting, a seasonal activity with circular migration between cities in the Andes and other Departments in Peru. Both Brazilian and Peruvians migrated in search of a better life for themselves and family.

*“We came here because of the children, right? For them to study here” (Brazilian who migrated from Japan with Peruvian wife, male, 35)*

*“I was looking for a better life, better opportunities for my family” (Peruvian harvester, male, 45)*

While internal Peruvian movement was largely for temporary settlement, Brazilians sought stable residency despite inaccessibility to visas available through the South American *Mercosur* accord, a multi-country agreement promoting free movement of goods and people. Typically, Brazilians were issued ‘tourist’ visas for 90 days upon entry and with 30-day renewals thereafter, requiring most to undertake a 6-hour round trip to the Brazil-Peru border from Puerto Maldonado.

*“they always want to give me [only] 30 days...it’s a headache and expensive going back and forth” (Brazilian, cleans Brazil nuts, married to a Peruvian, 39)*

Investors were issued 2 year residency visas, however benefits were often not extended to family members. Missionaries were required to be from a church established for at least 7 years and with >10,000 members.

Barriers to the documentation process for Brazilian migrants were unfamiliarity with the *Mercosur* policy, Federal police in Peru who were neither familiar with *Mercosur* policy nor guided migrants on available options, and costly documentation. A significant issue for Brazilians in Madre de Dios in accessing documentation was the absence of Brazilian consular services. Details of the *Mercosur* accord will be discussed in the section on Policy and Migration.

*“it costs about 600 soles and it’s not only that...there’s the travel too” (Brazilian married to Peruvian minister, female, 36)*

### **c. Knowledge of American Cutaneous Leishmaniasis, risk and prevention in Madre de Dios**

Knowledge of ACL was explored in detail in the qualitative study among Brazilian and Peruvian migrants. Half of respondents were able to identify ACL from a photo of a lesion, primarily using the local terminology “*ferida brava*” (bad sore) by Brazilian migrants and “*Uta*” by Peruvian migrants. Other respondents knew of ACL, primarily by the local term, when prompted by the interviewer, and 12% had never seen nor heard of ACL. When correctly identified, respondents described symptoms, “*it begins and grows*”; treatment, “*strong injections, he couldn’t be in the sun and couldn’t work*”; the ACL vector, “*Uta I know is a lesion from a mosquito that puts larvae*”; and risk “*I watched a news report that said it’s transmitted by dogs*”. However, while identifiable by a photo or when prompted, the majority of those interviewed were unaware of the risks for the disease.



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Misunderstanding included incorrect examples of disease etiology, “*I got it from my sister in law*”, vector misidentification such as the triatomine or ‘kissing’ bug for Chagas Disease and botfly larvae, “*this is UTA...no it’s not a mosquito, it’s a little animal that’s like a sponge that walks on wood*”; and geographic risk “*I didn’t know that the disease was common here....I’ve never heard anyone talk about it...I thought it was more common in Brazil than here*”. Additionally, if not from an endemic area, migrants may not be aware of ACL until arrival in the migration destination or may not have any knowledge of the disease.

*“Before that, I hadn’t heard about it. Over there (Ucayalli – another department in the Peruvian Amazon), it’s rare someone would have that, unlike here, it’s very popular. Over there I would hear about Dengue”.* (Peruvian logger, male, 39)

The epidemiological study showed that neither ACL cases nor controls used repellents consistently, with only 7 cases (13%) and 4 controls (15.4%) using repellents and only one in each group using repellents “always”. There was no significant difference in repellent use comparing cases and controls.

*“We don’t use repellent...it doesn’t work, we put (detergent) powder o our clothes and we’re fine...that’s the repellent when we’re in the field”* (Peruvian Brazil Nut Harvester, female, 42)

Protective clothing was more often used by respondents working in mining and harvesting areas of Peru, although there was no significant difference between ACL cases and controls. Bednets were regularly used in Peru by both ACL cases (92.5%) and controls (81.5%), citing daily use during nighttime hours or when sleeping, although it appeared from observation in the camps that these nets were untreated with insecticides. Other prevention measures included using household insecticides and smoke from fires or cigarettes. There were no Brazilian cases in Peru during the study period, however during qualitative interviews, Brazilians did not use bednets frequently, and cited instead the use of household insecticides, fans, and cleaning to reduce environmental exposure to vectors. Many Brazilians, however, didn’t use any protective measures.

The primary significant risks identified by the epidemiological study in Peru was migration in the past five years (OR: 3.4; 95% CI 1-12 p value=0.05) and sleeping outside (OR: 2.8; CI 95% 1.1-7.4; p-value 0.037). As mentioned in the previous section, internal migration is to forested areas for mining, brazil nut harvesting and logging that are highly endemic for ACL. As such, internal migrants in the qualitative study cited sleeping in encampments in Madre de Dios for the purpose of these occupational activities, or visiting a rural “chacra” or forested residence used for weekends and holidays. Temporal periods of heightened outdoor sleeping were January through May, with February, March and May times most frequently cited. These months are also the harvest season for Brazil nut harvesting when more ACL cases were engaged in nut collections and living in forest camps for multiple months.

**Photo 1:** Brazil nut harvesting camp. Alerta, Madre de Dios (photo by Christine Murto).



### d. Access and Use of Health Services and ACL

Brazilian cross-border migrants in the qualitative study sought health services in Madre de Dios for illnesses such as prenatal and delivery care, dengue, accidents, surgery, oral health and pediatric care. Overall, these migrants were content with service delivery, and language generally was not problematic during consults. As public health services are free of charge in Brazil, a primary complaint was cost of services in the public health system in Peru, which was more expensive for non-residents, the majority of migrants in our study.

*“to do your record you pay 3 soles, for a consult you pay 8 soles, and for an IV you pay 8...you pay for everything” (Brazilian food stall operator, female, 36,)*

*“put it this way, it’s public, but you also have to pay for the service” (Works with father, male, 21)*

Despite non-residency, healthcare access in the public system was available to cross-border migrants, however many Brazilians also sought private healthcare, primarily due to expedience of service delivery.

*“there’s always a long line so I paid a private physician, because otherwise I wouldn’t have time” (Brazilian manicurist, female, 25)*

Specialist services, such as urology and allergy, etc., were not generally available in Madre de Dios, with the closest specialty services available in Cuzco in the Andes mountains. For these services, and more complicated health problems, many cross-border migrants returned to Brazil for medical care.

*“there was no option...because of the surgery, so he had to go to Sao Paulo” (missionary, female, 32)*

Additionally, Brazilians returned to Acre, Brazil for general checkups and vaccines, as these were already recorded in the electronic medical records through the national Brazilian health plan.

*“The vaccine card is there...all of it is there then I can do the health schedule for vaccines for all of them there” (Brazilian mother of 3, female, 39)*

One barrier was discomfort with facility hygiene and perceptions from narratives told by other migrant experiences.

*“it was cluttered, right? Trash, trash seen in the hallway ...very dirty, like really dirty, you know?” (Married to Peruvian, male, 35)*

In the epidemiological study, ACL cases had more difficulties reaching health care services than those without the disease (OR: 4.3; 95%CI: 0.9-20.6; p-value=0.07). Reasons for difficulty in accessing healthcare services primarily were related to distance and cost of transport, with the many cases (43%) walking to the healthcare center on the day of the interview.

More than three-fourths (78%) of cases took a month or more after symptom onset to seek diagnosis, the mean time to diagnosis was 56 days. Reasons for delays in diagnosis were often related to unfamiliarity with ACL (17.9%), thinking it would heal (14.3%), distance to health services for diagnosis (10.7%) in addition to other reasons such as mistaking the disease for fungus, work, time and using alternative or antibiotic self-treatment. Seeking diagnosis in non-endemic areas also delayed diagnosis, reflecting likely that Peruvian doctors are not trained or conscious or time-limited to ask patients about past travelling.

*“In Lima, they didn’t diagnose me with anything... it started to heal after 3 yrs. I had the wound 4 years ago, but last year it barely started to heal” (Brazil nut harvester, male, 21)*

Many (42%) cases with ACL self-treated prior to seeking diagnosis with both pharmaceuticals and alternative folk remedies. In the epidemiological study, antibiotics were used by 41 % of ACL cases who treated themselves prior to diagnosis. In fact, pharmacies were often a first attempt at treatment.

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*“A [pharmacy] in Puerto Maldonado told him it was not Leishmaniasis. They sold him an ointment. This ointment only helped to close the wound superficially, but the inside of the wound was not healing” (Brazil nut harvester, female, 42)*

Herbal and medicinal plant, creams, tobacco and battery acid were additionally sought as remedies.

*“No I didn’t get treatment....I usually cure it with Cocona leaves, lime and salt. Boil everything, and then use that water to rinse the wound (logger/Brazil nut harvester, male)*

Some migrants recounted stories of purchasing ACL treatment (Pentavalent Antimonial) injections through the local ‘botica’ or pharmacy. ACL treatment in Peru is dispensed only through the public healthcare system, and offered free of charge, with referrals required from private physicians as ACL is a reportable disease under surveillance by the national Ministry of Health. However, Brazilian *Glucotime* is considered more efficacious for treatment than that offered through the Peruvian public health system.

*“but here everyone talks about vaccines, and they know it by the Peruvian injection. The hospitals have the Peruvian injection and the pharmacies carry the Brazilian injections for 35 soles (12 USD)” (Brazil nut harvester/logger, male, 39)*

ACL caused loss of days of work for cases in our study (38.9%) from 1 day to three months. Approximately one-third (27.8%) lost at least two weeks of employment.

We investigated several biosocial factors, such as household and employment contact with others with ACL. While there were no significant differences between ACL cases and controls, cases tended to have had someone at home or work infected with ACL compared to controls. It is unlikely that household presence of ACL can be explained by poor housing, as there were no significant differences in housing materials or flooring between ACL cases and controls. Having a need to go to a health centre during the past year, but could not was a significant prophylactic for ACL (OR: 0.2 95% CI: 0.1-0.6; p value=0.003), which can be explained possibly because ACL cases that were interviewed sought services for their diagnosis. This finding should be interpreted with caution given that the respondents were from a hospital-based sample.

### **Migration and American Cutaneous Leishmaniasis in Madre de Dios, Peru**

#### **a. Study Population Characteristics**

We conducted 21 in-depth interviews among Peruvian cross-border migrants in Assis Brasil and Rio Branco, Acre, Brazil. Respondents ranged in age from 21 to 61 years, with 5 females and 16 males. There were two confirmed and one suspected case among Peruvian migrants in Acre.

Preliminary results are shown for 13 ACL cases and 13 controls from Assis Brasil, Acre. There were 7 males (50.0%) and 7 females (50.0%) among the cases, and 9 males (69.2%) and 4 females (30.8%) among the controls.

#### **b. Migration and Population Flow**

Cross-border migration to Acre, Brazil was primarily travel to the State capital city of Rio Branco from origin Departments of Lima, followed by Madre de Dios (Puerto Maldonado and Inapari), Pucallpa, Cusco, Chiclayo, and other departments. Peruvians also migrated from neighboring Bolivia (Annex 1, **Map 4**). Past 5 year migrants were less likely to be situated on the border, and perhaps this is related to drivers of migration for this population, which were almost solely employment and higher education, and occasional marital separations.

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In some cases relatives and friends living in Rio Branco facilitated movement, however in many cases Peruvians developed social networks on arrival. The Brazilian higher education system offers financial resources to support higher education, and many Peruvians took advantage of the opportunity to study at the Federal University of Acre (UFAC). Acre also has a large open air marketplace that draws self-employed and entrepreneurial Peruvians to make a living selling goods in rented or purchased vending ‘stalls’. Other Peruvians interviewed worked in a family business (carwash) as Spanish language teachers, or in formal businesses such as hotels.

Most Peruvians were familiar with the *Mercosur* policies on residency and had procured legal 2-year residencies at the time of our interviews, or had progressed from two year residencies to permanent residence in Brazil. The Brazilian Amnesty for foreign residents was also mentioned as a means to permanent residence for respondents.

*“I entered illegally and within 10 days the Brazilian government was giving an amnesty for all illegals...so now I have residence” (carwash worker, male)*

As student visas required yearly renewals, many opted to apply for the *Mercosur* visa instead. The *Mercosur* process for Peruvians was facilitated through the Peruvian Consulate in Rio Branco, a notable difference in comparison to Brazilians in Madre de Dios, who lived for years with monthly renewable ‘tourist’ visas, and where no Brazilian consular services were present to facilitate documentation for residency. Because most Peruvians had documentation, return migration to visit family was common.

*“thank God everything has changed, because Peru entered the Mercosur and then all was wonderful...now everything is easier...I have work papers....everything” (Student, male, 39)*

### ***c. Knowledge of ACL, risk and prevention behaviors among in Acre***

The majority of Peruvians who participated in qualitative interviews were able to identify leishmaniasis or the local term in Peru “*uta*” from a photograph. The remaining were able to identify the disease through verbal prompting by the interviewer. Knowledge of ACL and other vector borne diseases (ie dengue) and particularly nuisance of insect bites were factors in the use of bednets and screens in the household by the majority of respondents. Others used fans, repellents and insecticides. Only one respondent did not use any protection.

The risk for ACL was small in the capital city of Rio Branco where the majority of past 5-year Peruvian migrants were located, most respondents did not cite specific personal risks with the exception of being in rural areas. However, some Peruvians were aware of transmission dynamics from a “mosquito” and symptoms, but detail on ACL was otherwise limited in relation to diagnosis and treatment for the disease, with the exception of those previously infected.

The epidemiological study showed that migration was not a significant risk on in the border town of Assis Brasil where the investigation was conducted. While Peruvians were not among cases that were realized during the study period, important risk behavioral risk was identified among Brazilians living in proximity to the border. There was inconsistent use of repellents and protective clothing among both ACL cases and controls. Bednets were significantly *more* likely to be used by ACL cases (OR: 7.3; 95% CI: 1.2-46.2; p value=0.03), with users citing daily use of nets. As some cases were interviewed during the time of treatment, this may indicate successful health promotion of prevention measures by healthcare staff in Assis Brasil, Brazil. Alternatively, bednets may have been used in outdoor camps, however transmission may have occurred through other (ie. occupational) exposure, or bednets were not sufficiently protective. Few Brazilians had significant occupational exposure to forested and deforested areas that was evident in the Madre de Dios, Peru data.

### **d. Access and Use of Health Services and ACL in Acre**

Brazil's Sistema Unico de Saude (SUS) was introduced into the constitution in 1988 as a human rights issue whereby Brazil's federal government is mandated to provide free medical services for all, regardless of nationality or status. Generally, Peruvians used health services in Brazil without needing documents of residency, although many had the SUS number and were registered in the SUS system. Free healthcare was often highlighted in the in-depth interviews with Peruvian migrants, in contrast to fee-for-service requirements in Peru.

*"in Peru they charge..here it's free" (Peruvian vendor, male)*

Most Peruvians in the qualitative study were located in Rio Branco and used the *Unidad Protóna Atendimento*) or UPA, the public Urgent Care Centers. UPA facilities are part of the national health system, and were preferred over the neighborhood "Postos" or health posts. The perception was that services through UPA were faster, although the primary complaint in general was slow attendance.

*"it was crowded, I waited a long time. Wow! I waited about three hours or more" (Student, female, 33)*

*"I was surprised because a child should have priority...and we waited and waited...we arrived at 10 and were seen at 2pm" (Tour agent, female, 28)*

The majority of Peruvian respondents used healthcare services for problems such as flu, skin infections and fungus, prenatal care and children's vaccines and checkups. Language did not appear to be a barrier to receiving services, according to respondents. Infrequently, Peruvians sought health services in Peru as part of general healthcare with familiar physicians

No ACL positive recent Peruvian migrants were encountered in Rio Branco during the qualitative study period. ACL transmission in Rio Branco is low, according to health officials who were interviewed as key informants, rather is related to distant outpost referrals from rural areas in Acre. Additionally, few Peruvians interviewed were from high incidence areas for ACL.

The epidemiological study was conducted in the highly endemic border area of Assis Brasil, a small town with 6610 residents, one health center and a public hospital. Services were easily accessible with the mean time to reach services 10.0 minutes for ACL cases and 12.5 minutes for controls. As services were within close proximity to the city center, most cases (90.0%) and controls (88.89%) walked. ACL cases used healthcare services more often, with an average of 16.58 visits in the past 12-months compared to controls (2.54 visits), perhaps also as a result of treatment requirements for ACL.

For these ACL cases, The mean time to seek diagnosis was 27.6 days, with some respondents citing to treatment at home (61.5%) as reason for delayed diagnosis. Cases treated themselves primarily with creams "pomade" prior to seeking diagnosis at the local healthcare center. The majority (76.9%) did not lose work due to ACL. The majority of cases (78.6%) and controls (84.6) never had ACL prior to the survey, and case presence in the home or work was not significant.

### **An Ecohealth -Health Approach to Human and Vector surveillance of Bartonellosis and ACL**

An Ecohealth approach was used to assess the connection between human health and environment, and the relationship to distribution of disease through migration. An entomological and a human sample investigation was conducted to identify species of ACL in humans and *Lutzomyia* vectors, and explore whether Bartonellosis exists in either population. A total of 21,564 vectors were captured, 11,655 females and 9909 males have been identified. Vectors are currently being biologically tested for disease through PCR to identify *Lutzomyia* spp. species and ACL species strains, 1,126 vectors have been classified by species from among the more than 30 *Lutzomyia* vectors present in the Southwestern Amazon that may transmit disease. Where no human cases exist, infected vectors may

## Executive Summary

be used as an early warning system for disease control before a disease transmission cycle emerges in a new region.

In Peru, 131 human serum samples for Bartonellosis were collected and 67 tissue samples were collected for ACL. Among Madre de Dios samples tested by PCR (Annex 2, **Figure 2** and **Table 3**) thus far, there is no presence of Bartonellosis. In Brazil, 310 human serum samples were collected for Bartonellosis and 13 samples were collected for ACL.

The entomology team in Peru captured a total of 1,126 female and 134 male *Lutzomyia* sandflies in the mining area of Mazuko and border area of Inapari, Peru. Species identification of female vectors is shown in **Table 1**.

**Table 1** Species of *Lutzomyia* sandflies

|                                | %   | Vector-species associated with ACL in Madre de Dios |
|--------------------------------|-----|---|
| <i>L. yuilli</i>               | 54  |   |
| <i>L. davisi</i>               | 24  |   |
| <i>L. carrerai</i>             | 6   | <i>L. braziliensis</i>                              |
| <i>L. trichothoromyia, spp</i> | 0.6 |   |
| <i>L. llanosmartinisi</i>      | 14  | <i>L. braziliensis</i>                              |

The entomology team in Brazil captured *Lutzomyia spp.* on the border cities of Assis Brasil, Brazil and Inapari, Peru with 17 CDC light traps monthly, throughout a year-long period (**Table 2**).

**Table 2** *Lutzomyia* sex of captured and identified for the cross-border region

|        | Assis Brasil | Inapari, Peru |
|--------|--------------|---------------|
| Female | 10,233       | 296           |
| Male   | 9525         | 250           |

An additional 500 sandflies were collected in and outside of sentinel domiciles in Inapari and 1500 male sandflies collected in and outside of sentinel domiciles in Assis Brasil are currently being classified. All vectors and human samples are in the process of PCR for the identification of disease species.

### **Migration Policy and cross-border migration**

The Treaty of Asuncion established the *MERCOSUR* in 1991 with the primary objective of facilitating free trade between countries in South America. (Brazil, Argentina, Uruguay, Paraguay, Bolivia, Chile, and Peru). Within the *MERCOSUR*, The agreement for Free Movement and Residence provides for a temporary 2-year residency permit for cross-border migration between member countries, after which time it can be renewed or transformed into permanent residency in the host country. The 2200km Transoceanic Highway has paved the way for increased migration between the two countries.

We have shown throughout the research that the experience of cross-border migration and documentation processes are imbalanced when considering migration between Brazil and Peru. Availability of consular services for Peruvians in the capital city of Rio Branco in Acre, in most cases, facilitated access to the two year residency visas and permanent registry as is available through the *Mercosur* accords. Close proximity of Rio Branco to the Peruvian border (330KM) facilitated access, where solicitation of documentation (such as documentation exonerating criminal activities) required for residency could be procured and applications submitted. Conversely, the majority of Brazilian migrants who were living in Madre de Dios for the past 5 years continued to live with 30-day ‘tourist’ visas, requiring monthly renewal. Consular services were available to Brazilians only in the capital of

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Lima, Peru which required costly travel that was not feasible for most Brazilian migrants living precariously as unskilled informal workers. For Brazilian missionaries, access to visas to conduct ministry activities was not viable for small churches without large memberships established in Peru. For investors, residency was not extended for immediate family members, requiring a separate application process. Most Brazilians were not knowledgeable about the requirements of residency offered through the *Mercosur* accords, and in particular were not aware that national identity cards were sufficient in the documentation process.

One effect of inaccessibility to residency for Brazilians, was increased cost of medical services for foreign nationals. While the Peruvian Ministry of Health provides a fee for service based on income, services for foreign nationals have a premium attached that appeared to be a barrier to healthcare access for Brazilians. Secondly, inability to secure residency also precluded access to formal employment documentation for Brazilians, while Peruvian migrants interviewed were more likely to have secured formal employment, scholarships for higher education and free health services with access to the Brazilian Sistema Único de Saúde (SUS), Brazil's publically funded public health system. One exception was for Peruvians engaged in small stall product vending who were unable to secure vending stalls without a Brazilian national as a 50-percent partner.

### **C. Correspondence of results to those expected**

We hypothesized that ACL was associated with migration in the Southwestern Amazon and this finding was confirmed in Peru. However we did not expect that there would be a dearth of past 5-year migrants on and close to the border regions in both Peru and Brazil, rather migrants populated urban areas as is also common when migrants seek areas where employment is more accessible. Historically, Brazilian migrants were engaged heavily in mining activities in Peru, however with artisanal mining restrictions enforced by military police, and diminishing resources of gold, few if any, Brazilian migrants continued to be involved in mining. On the other hand, we found that internal migration in Peru is quite extensive and warrants further investigation. Additionally, we found that high incidences of ACL in Rio Branco, Acre were the result of referrals from forested rural areas, with few locally transmitted cases.

### **D. Practical Application of Results**

Our results show that migration is associated with American Cutaneous Leishmaniasis in Madre de Dios, Peru and Assis Brasil, Brazil as a border crossing point is a high risk area for ACL transmission. Additionally, while migration could increase the risk of the distribution of Bartonellosis from endemic areas due to migration, we found few migrants from the high risk areas of Cajamarca, Ancash and Piura and no active cases of Bartonellosis diagnosed in Madre de Dios or Acre during the study period. With confirmation through the ongoing PCR testing, we suspect that we can conclude with 95% certainty that Madre de Dios, Peru and the border region of Brazil are free from Bartonellosis disease.

However, it became evident that as ACL is an ongoing public health problem in Madre de Dios, Peru and Acre, Brazil and is associated with migration, clear steps must be taken for environmental control and increased preventive and diagnostic outreach among migrants, residents and travelers to the region. Thus, with dissemination of results to Ministries of Health, a collaborative response mechanism that extends environmental vector control, outreach for prevention (such as insecticide treated bednets and repellent use), early diagnosis and treatment particularly in rural and forested areas of occupational risk such as mining and harvesting areas. Additionally, prevention education can be extended through border points, particularly targeted to those from non-endemic areas that may be unfamiliar with ACL and at higher risk for transmission.

Lastly, dissemination and roundtable discussions with Departments of Immigration and Brazilian Consular services regarding findings gleaned from inaccessibility to *MERCOSUR* facilitated residency would seek to reduce precarious living, stabilize employment, and reduce barriers to public health access.

### **E. Questions for Further Exploration**

1. Does the use of deltamethrin-impregnated Insecticide Treated Bednets (ITNs) reduce ACL in areas of high occupational risk in forested areas?
2. Is a community-based approach (training farmers and employers of forest-based activities) an effective response in increasing ACL/Bartonellosis prevention, disease identification, early diagnosis and access to treatment and which are other non-traditional actors in information distribution such as taxi drivers?
3. Do harvesters and miners disrupt vector habitats at times other than normal biting hours, placing them at increased risk for disease?
4. What types of environmental control can be utilized in outdoor and peri-domestic areas to reduce vector density in forested and deforested areas?
5. Is ACL transmission anthropophilic (human to human) in the New World as has been documented in Old World transmission, thus increasing risk for disease when infected humans come in contact with uninfected vectors
6. What are the mammalian reservoirs at highest risk for transmission in the Southwestern Amazon, and what types of environmental controls could facilitate mammal host transmission reduction?

### **F. Policy Recommendations**

As policy issues are primary barriers to residency, healthcare access, and disease prevention, we recommend the following:

1. Increase preventive education for vector-borne diseases (malaria, dengue, ACL, Bartonellosis, etc.) through pamphlets and placards placed strategically in sight of travelers and migrants at border points between Brazil, Peru and neighboring Bolivia
2. Increase and provide sustainable allocation of funding for MoH outreach efforts into rural zones, including high occupational risk areas for ACL, and transport for suspected cases to and from rural zones of operation.
3. Remove all prescription treatments (pentavalent antimony injections) from pharmacies, requiring procurement at public health facilities. Consider extending clinic hours to Saturday and Sunday in areas with high occupational risk
4. Increase access to low-cost ITNs, effective repellents, and environmental vector control
5. Place satellite Brazilian consular services in Madre de Dios, Peru to facilitate access to residency

### **G. Publications, Conferences and Workshops**

Our multidisciplinary team has conducted one workshop on the Brazil-Peru border for MoH staff in both Madre de Dios, Peru and Acre, Brazil. In addition one manuscript has been published, one submitted and 4 are currently in preparation. A Doctoral and Masters theses were completed and two Doctoral theses are currently in progress with subsequent future publications. Three conference presentations have been given. The team is currently working on the working paper to be published by SNIS entitled Migration and Vector Borne Diseases in the Southwest Amazon. A list of publications, conferences and workshops is available in the **Annex 2**.



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7. Peru M (2014) Boletín Epidemiológico (Lima)
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Annex 1

**Figure 1** Series of satellite images of a part of the highway South of Inapari, Madre de Dios, Peru. The paved highway was opened in 2010 and already in 2013 new side roads away from the highway are visible. The opening of the highway increased utilization of the Peruvian Amazon.



Figure 2 PCR diagnosis of Leishmaniasis in Peru



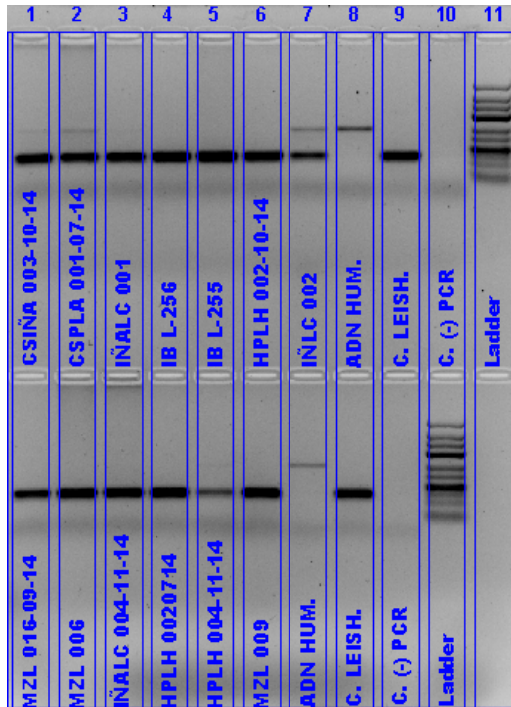
UNIVERSIDAD PERUANA CAYETANO HEREDIA  
Instituto de Medicina Tropical "Alexander von Humboldt" Laboratorio de  
Biología Molecular de Tripanosomátidos

Unidad de Epidemiología Molecular

Responsable: Milagros Suárez

Protocolo: PCR kDNA

Fecha: 28-04-2015



**Annex 1**

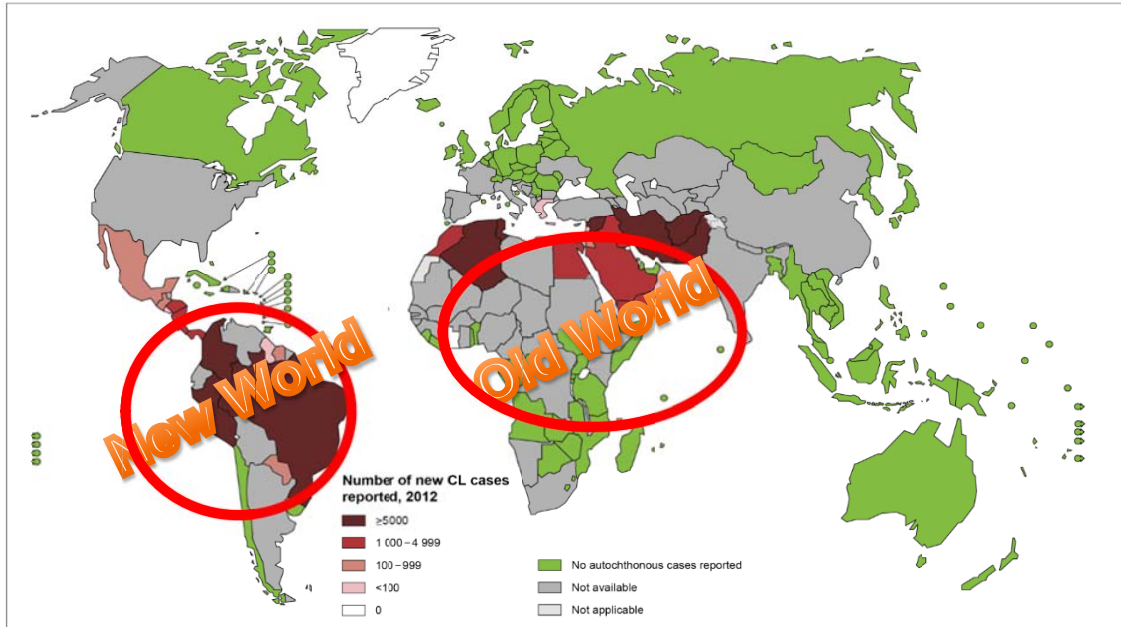
**Table 3** Results of PCR diagnosis of Leishmaniasis in Peru

| Carril No. | Código           | Establecimiento              | LEISHMANIA | Carril No. | Código          | Establecimiento | LEISHMANIA |
|------------|------------------|------------------------------|------------|------------|-----------------|-----------------|------------|
| 1          | CSÑALC 003-10-14 | C.S. Iñapari                 | Positivo   | 1          | MZL 016-09-14   | C.S. Mazuko     | Positivo   |
| 2          | CSPLA 001-07-14  | C.S. Planchon                | Positivo   | 2          | MZL 006-11-13   | C.S. Mazuko     | Positivo   |
| 3          | INALC 001-07-14  | C.S. Iñapari                 | Positivo   | 3          | INALC 004-11-14 | C.S. Iñapari    | Positivo   |
| 4          | IB L-256         | Hospital San Martín (Iberia) | Positivo   | 4          | HPLH 0020714    | C.S. Huepetuhe  | Positivo   |
| 5          | IB L-255         | Hospital San Martín (Iberia) | Positivo   | 5          | HPLH 004-11-14  | C.S. Huepetuhe  | Positivo   |
| 6          | HPLH 002-10-14   | C.S. Huepetuhe               | Positivo   | 6          | MZL 009-09-14   | C.S. Mazuko     | Positivo   |
| 7          | INLC 002         | C.S. Iñapari                 | Positivo   | 7          | ADN HUM.        | -               | Negativo   |
| 8          | ADN HUM.         | -                            | Negativo   | 8          | C(+) LEISH.     | -               | Positivo   |
| 9          | C(+) LEISH.      | -                            | Positivo   | 9          | C. (-) PCR      | -               | Negativo   |
| 10         | C. (-) PCR       | -                            | Negativo   | 10         | Ladder          | -               | -----      |
| 11         | Ladder           | -                            | -----      | 11         |                 |                 |            |

Annex 1

Map 1 Cutaneous leishmaniasis (CL) globally. New World American Cutaneous leishmaniasis counts for a third of all cases

Status of endemicity of cutaneous leishmaniasis, worldwide, 2012



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2013. All rights reserved

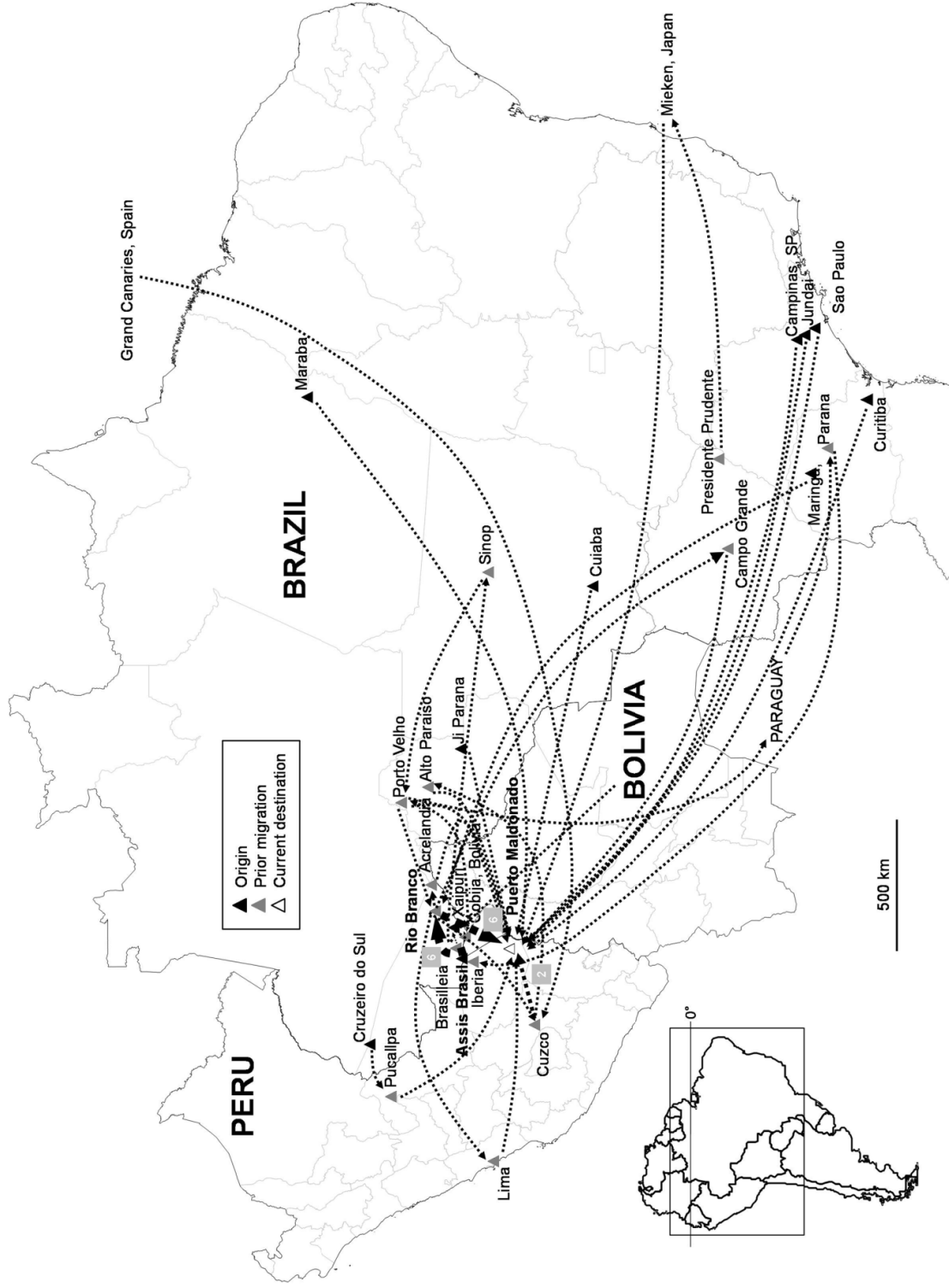
Data Source: World Health Organization  
Map Production: Control of Neglected Tropical Diseases (NTD)  
World Health Organization



Map 2 Internal migration flows in Peru



Map 3 Migration flows of Brazilians in Peru



Map 4 Migration flows of Peruvians in Brazil





## List of Attachments

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1. Abstract Murto et al. presented at the Inaugural International Conference on Migration, Melbourne, Australia, 2014
2. Conference proceedings Cesario et al. presented at VIII Encontro Nacional sobre Migracoes, Belo Horizonte, Brazil, 2013
3. Cesario, R.R. *The Influence of International Legislation on The Access to Health by Migrants*. Submitted to Caderno CRH, Faculdade de Filosofia e Ciências Humanas da Universidade Federal da Bahia.
4. Cesario, R.R., Fabriani, C.B. & Cesario, M. *Peruvian migration in Acre, Amazonia: determinants, vulnerabilities and opportunities for Health Promotion*. Submitted to Revista Latinoamericana de Población.
5. Presentation of Murto et al. at the Inaugural International Conference on Migration, Melbourne, Australia, 2014