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Chagas disease knowledge within the Latin American community in Hamburg

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Abstract

Background

Chagas disease, a neglected tropical disease, used to be confined to the Latin American region. Migration has expanded its geographical boundaries and made it a global disease. Since Chagas disease poses a public health challenge in areas that were formerly free of Chagas disease, the World Health Organization recommends prevention and control measures. If these measures such as targeted screening are to be applied, it would be essential to know what the target group knows about Chagas disease. This thesis aims to evaluate the knowledge about Chagas disease in a sample of Latin American migrants living in Hamburg and to identify socio-demographic characteristics associated with the knowledge.

Methodology

To investigate knowledge about Chagas' disease, a survey questionnaire developed by the German Chagas network ELCiD was used among adult Latin American migrants living in Hamburg. The knowledge assessment of the survey covered knowledge of transmission mechanisms and clinical aspects of the disease. Descriptive statistics were used to characterise knowledge about Chagas disease. In order to identify associations with socio-demographic characteristics of the sample, multiple linear regression analysis with knowledge about transmission pathways as a dependent variable was performed.

Principal findings

A total of 102 participants (mean age: 36.9; 71.6% female) were recruited. Only one-third of the sample had ever heard of Chagas disease. There was a considerable lack of knowledge regarding the non-vectorial transmission mechanisms and the symptoms of the disease. In the linear regression analysis, having heard of Chagas disease was the only characteristic that was associated with knowledge of transmission pathways.

Conclusion

More quantitative and qualitative insights into the knowledge about Chagas' disease from representative samples of other German regions are needed. Awareness campaigns about Chagas disease should specifically address the manifestations and transmission routes of the disease.

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List of abbreviations

CI	Confidence interval
ELCiD	Detection and Guidance of Patients with Chagas Disease in Germany (Erkennung und Lenkung von Chagas Patienten in Deutschland)
EU	European Union
NTD	Neglected tropical disease
PAHO	Pan American Health Organization
PP-Plot	Probability-Probability Plot
SD	Standard deviation
USA	United States of America
VIF	Variance inflation factor
WHO	World Health Organization
ZPred	Standardised predicted value
ZRes	Standardised residual

1. Introduction

Chagas disease, also known as American trypanosomiasis, is a parasite infection. Primarily, it transmits to humans via an insect vector. It is recognised as a neglected tropical disease (NTD) by the World Health Organization (WHO) and is disproportionately represented among people living in poverty[1,2]. The disease is tightly linked to marginalisation and social disadvantage and faces a low public health priority as well as difficulties in attracting research investments.

The two current treatment options that are available for Chagas disease are a good example of this. They are poorly effective in the chronic phase and can have toxic side effects. These drugs were developed more than 40 years ago, and since then, no other drug therapy has been approved[3].

Chagas disease is endemic in 21 Latin American countries and affects around six to seven million people worldwide[2]. An additional 70 million people in Latin America are at risk of acquiring a *T. cruzi* infection[4]. According to estimates, the global annual burden of Chagas disease is $627.46 million in health-care costs and 806,170 DALYs. The disease thereby exceeds burden estimates other infectious diseases such as Cholera and Rota virus[5].

Chagas disease takes place in two phases: the initial acute phase lasts for about four to eight weeks and is followed by a lifelong chronic phase, if not treated successfully. Acute Chagas disease is usually asymptomatic or might present mild and unspecific symptoms such as fever[6,7]. Chronic Chagas infection is initially asymptomatic, and around 60-70% of patients will remain without any symptoms for life. The remaining 30 to 40% will over decades develop a determinate form of chronic Chagas disease that is characterised by irreversible and potentially life-threatening cardiomyopathy and/ or gastrointestinal involvement[6].

Due to global migration streams, Chagas disease has become increasingly relevant in non-endemic countries. About 70,000 to 120,000 migrants from Chagas disease-endemic countries infected with *T. cruzi* are estimated to live in Europe[8]. Based on estimations combining the number of migrants from endemic countries with the prevalence rates of their respective home country, it is expected that about 2000 Chagas disease patients live in Germany[8,9]. To date, only two seroprevalence studies have been carried out in Germany reporting a Chagas disease prevalence

rate in their tested samples of 2% and 9%, respectively, with the latter tested in a sample consisting of Bolivians only[10,11].

Even though the disease is present in many European countries, including Germany, it is not recognised well by authorities. As many as 94% to 96% of cases is estimated to be undiagnosed in Europe. In Germany, the figures are as high as 99%-100% of cases[8]. Moreover, as other non-vectorial mechanisms of transmission exist, for example, the transmission through contaminated blood transfusions, or vertical transmission, Chagas disease can spread outside endemic areas.

The WHO strongly recommends measures to prevent and control Chagas disease in the European context[12]. Among others, they highlight the screening of potential blood and organ donators as well as women of childbearing age at risk of being infected with *T. cruzi*. Control measures include early detection of congenital infections and subsequent treatment. However, these measures are far from being implemented uniformly throughout Europe[13].

In Germany, the European Commission's directives related to the quality and safety of blood, tissue, and cell donation in blood banks apply. These documents specify that individuals known to be infected with *T. cruzi* should be excluded from blood donation. However, they do not clarify how blood donors at risk of being *T. cruzi* infected, who have not been tested, should be handled[13]. Besides, no European or German legislative for monitoring and controlling congenital transmission of Chagas disease is applied in Germany[10,13].

Should WHO recommendations for prevention and control of Chagas disease be carried out in Germany, it is vital to know what the target group, i.e., the population at risk of being *T. cruzi* infected, knows about Chagas disease. An individual should be adequately informed about a disease and its consequences in order to perform an informed decision about getting tested. Information campaigns alongside the provision of diagnostic testing could be a useful instrument to raise awareness and promote reflection and action.

With insight on the level of knowledge related to Chagas disease, campaigns could be specifically tailored for priority target groups, e.g., groups with little knowledge and awareness about Chagas disease that have the potential to transmit the disease. Thereby, the prevention and control of Chagas disease could be strengthened.

To date, only one study has been performed in Germany that describes the knowledge related to Chagas disease in a population at risk of being infected. Conducted in a sample only consisting of people of Bolivian origin living in Munich, the study stated a severe lack of knowledge. While 70% of the sample had heard about the disease, about half of it did not know the symptoms that it causes and had none or inadequate knowledge about its transmission pathways. Qualitative results of the study showed that participants considered it very important to be informed about Chagas disease at relevant meeting points[10].

The main aim of this thesis is to investigate the knowledge about Chagas disease among the Latin American community living in Hamburg. Specifically, the knowledge about clinical aspects of the disease, as well as its transmission routes, will be in focus.

The following chapter, chapter 2, will provide the reader with background information about the parasite and the disease that it causes whereby a focus on the non-endemic context is taken. The rationale of the thesis and its objectives are described in detail in chapter 3. Next, the methodology of the thesis that includes three main components: a literature review about Chagas disease knowledge, a cross-sectional survey investigating Chagas disease knowledge among the Latin American community in Hamburg, and a multiple linear regression analysis to identify associations between socio-demographic characteristics and knowledge on Chagas disease is described in detail in chapter 4. Subsequently, the results of the literature review, knowledge assessment, and multiple linear regression analysis will be presented (chapter 5). This section is followed by a discussion of the results related to previous studies, possible explanations for findings, their implications, and the inherent limitations to the thesis (chapter 6). The last chapter, chapter 7, is the conclusion which seeks to provide clear answers to the raised research questions and to summarise essential implications and recommendations, limitations as well as the overall contribution of the work. Chapter 8 and chapter 9 contain all the references used and appendices, respectively.

2. Background

2.1. Trypanosoma cruzi

Trypanosoma cruzi is a flagellated protozoan of the order Kinetoplastida. *T. cruzi* can survive in, reproduce and transmit between two very different environments: the midgut of a bug and the cytoplasm of a mammalian host cell, including domestic, farm, and wild animals, as well as human beings[14]. *T. cruzi* presents a high degree of genetic diversity with different lineages, strains, and isolates. Although not fully understood, this heterogeneity of *T. cruzi* is believed to partly explain the variation in clinical manifestations and differences in the spatial distribution of morbidity and mortality[15,16].

The parasite was discovered in 1909 by Carlos Chagas, the name giver to Chagas disease, who named *T. cruzi* after his teacher Oswaldo Cruz[17]. Although documented for the first time 110 years ago, there is evidence that *T. cruzi* already infected human beings 9000 years ago and began millions of years ago as an enzootic disease in wild animals[18,19].

2.1.1. Vectorial transmission of Chagas disease

T. cruzi can be transmitted to humans by various routes. Vector-borne transmission, to date exclusively occurring in the Americas, is the primary mechanism of transmission in endemic areas and occurs through contact with faeces of triatomine bugs[20]. The *T. cruzi* life cycle is complex and involves both an insect vector and a mammalian host.

The starting point of the *T. cruzi* life cycle is when the triatomine bug belonging to the *Triatominae* subfamily takes a blood meal from an infected human host and thereby ingests the parasite[21]. These large, blood-sucking triatomine bugs, commonly also known as kissing bugs, are subdivided into different species, of which *Triatoma infestans, Rhodnius prolixus,* and *Triatoma dimidiata* are most important concerning *T. cruzi* transmission to humans[6]. In the midgut of the triatomine, the parasites actively divide and then migrate to the hindgut where they as an infective stage exit when the triatomine defecates while taking a blood meal[6]. Either through mucous membranes or through the bite wound, caused by the triatomine, into which the infectious faeces can be rubbed, the parasites enter the

human body. Here they multiply within its cells, infect other cells of the body, and are released to the blood flow from where the triatomines can ingest the parasite with a blood meal and the cycle recurs[22].

2.1.2. Other transmission routes

Infection with *T. cruzi* does not necessarily require an insect vector. Other non-vectorial pathways can be responsible for the transmission. In Europe, where the insect vector is not a native resident, contaminated blood transfusions and mother to child transmission are the main routes of transmission[23].

The reported risk of mother to child, or congenital, transmission varies between studies. In countries where the disease is endemic, congenital infection, referring to the transmission in utero as well as at the time of delivery, is occurring in 5% of infants born to infected mothers on average. In the non-endemic context, lower transmission risk has been reported with approximately 2.7%[24]. The clinical outcomes associated with congenital infections are related to socio-economic conditions. For instance, in Bolivia, the neonatal mortality related to congenital Chagas disease decreased from 13% to 2% from 1992 to 2001, when the socio-economic situation and maternal care improved[25].

The asymptomatic nature of Chagas disease poses a challenge because infected individuals, who are frequently unaware of their status, can transmit the disease through blood and organ donations[22]. About 10% of recipients of one unit of contaminated blood are expected to become infected with *T. cruzi* after transfusion[26]. The level of parasitemia in the blood donor, the recipient immune status, the type of component transfused (the transmission potential seems to be higher for platelets than for other components), and the strain of the parasite appear to influence the Chagas disease transmission risk[27,28].

Infection with *T. cruzi* can also be acquired orally through the ingestion of *T. cruzi* contaminated food and drinks. Particularly fruit juices, such as açai berry and sugar cane juice, have been associated with outbreaks of varying size[29]. Another source of infection is the consumption of blood or undercooked meat of infected animals that carry the parasite[30].

2.1.3. Chagas disease risk factors

Risk factors for non-vectorial transmission of Chagas disease concern the exposure to contaminated food and drinks, blood derivates and organs, and maternal seropositivity, respectively[31,32].

As the vectorial transmission of Chagas disease represents the main route of transmission in endemic settings, many of the well-established Chagas disease risk factors relate to the presence of triatomines in the domestic or peri-domestic setting. The triatomine bugs live in the cracks of adobe houses and thatched roofs[22,33]. Houses with mood floors and ceilings constructed from cardboard lamina tiles seem to be preferred by triatomine bugs as well[34]. Peri domestic constructions such as henhouses or other animal enclosures are places where triatomines are often found, too[35]. These housing conditions reflect a rather rural and poor setting. Thus, vectorial Chagas disease transmission is directly associated with the household socio-economic position, and it is why the disease is more prevalent in poor, rural populations of Latin America[36,37].

Although Chagas disease is also prevalent in other settings, e.g., large cities, the association between poor and rural living conditions and the disease often leads to stigmatisation of Chagas disease patients and their families. This stigmatisation can develop into discrimination and can have severe social consequences for infected individuals, such as the exclusion from labour and health care access restrictions[38]. While stigmatisation and discrimination further deteriorate the living conditions of affected persons, it also prevents individuals from getting tested due to fear of becoming discriminated against[38].

2.2. Chagas disease and migration

The globalisation of Chagas disease can only be understood in conjunction with migration patterns, which have been influenced by historical, economic, and political developments. Different push- and pull factors encouraged the migration within and from Latin America to other countries and continents.

Associated with the social process of looking for better opportunities in life elsewhere, different migration flows, usually departing from rural situations, take place[39]. In the context of Chagas disease, the rural-urban migration and the migration from endemic to non-endemic countries are particularly relevant[40]. In the

following, these two migration flows will be outlined, the latter with a focus on European non-endemic countries.

The rural-urban migration is highly influenced by the changes that have taken place in the productive system of Latin American countries. Industrialisation and the weakening of the rural familial economy that is mostly dependent on small-scale agriculture are among others responsible for the rural exodus[39]. Through moving away from a provisional standard of life and unstable working situations, migration gives the prospect for a better life.

Resulting from this, Chagas disease has, in recent decades, become an urban disease. A study from the province of Buenos Aires in Argentina exemplifies this change of the epidemiological landscape. The province of Buenos Aires is considered vector free. However, the prevalence of Chagas disease is 4.3% among its citizens. Being infected is among others associated with being born in the endemic province Santiago del Estero. Moreover, the study showed that a considerable proportion of Argentinian (infected) mothers to infected children have never been in an endemic region and have never received blood transfusions. Hence, they must have become infected through mother to child transmission, and their infected children were, thus, the second generation of congenital Chagas disease patients[41].

It should be pointed out that the rural population living in poverty continues to live in conditions that favour vectorial transmission of the disease. What has changed is that above and beyond the presence of the disease in rural areas, it has now also become manifested in poor urban areas[42].

The transcontinental migration from Latin American countries to European countries is not only influenced by the economic situation but is also rooted in colonial history and political developments. Migration from Latin America to Europe can be categorised into three different stages that are colonial and post-colonial migration, political-exile migration, and contemporary waves of economic migration[43].

Post-colonial migration concerns returning emigrants who have once left Spain, Portugal, Italy, or other countries in search of a better life. Even until today, the former colonisation of Latin American countries affects today's migration flows as policies permitting dual citizenship or citizenship based on ancestry allow the descendants of emigrants to come to Europe[43].

Between the 1960s until the 1980s, European countries became the new home to many political refugees from Argentina, Brazil, Chile, and Uruguay, among others, that were in search of safety from dictatorships[43].

After joining the European Union (EU) in 1986, Spain and Portugal became increasingly attractive destinations for Latin Americans as labour was warranted due to economic growth. This migration further accelerated after the millennium shift[44]. Furthermore, in recent years educationally motivated migration to Europe has increased substantially[45].

After the United States of America (USA), Spain is the second most popular destination with more than 2.5 million Latin American and Caribbean migrants who resided in the country in 2018[45,46].

The Spanish legislation facilitates an obtainment of the Spanish citizenship for Latin Americans[47]. Other countries, like the United Kingdom and Germany, have also granted citizenships to a considerable amount of people from Latin America. From 1998 to 2009, more than half a million European citizenships have been granted to people from Latin American and Caribbean countries, of which Spain granted 350,000, the United Kingdom 60,000, and Germany 28,000 citizenships, respectively[48].

Once the citizenship is acquired, a migrant is no longer identified as one in statistics, unless the country of birth is in focus. The right of free movement of persons manifested in the Schengen agreements and the adoption of Directive 2004/38/EC gives EU citizens and their family members the right to move and reside freely within the EU[49]. A person who originally migrated from Latin America to Spain and obtained Spanish citizenship will, in case of migration to other European Union member states, be identified as Spaniard and not as a citizen of a Latin American country. The obtainment of European citizenship is a critical issue for the identification of the population at risk of being Chagas disease infected residing in European countries.

2.3. Epidemiology of Chagas disease

2.3.1. Endemic countries

Chagas disease is the most common of all NTDs in Latin America[50]. About 6 to 7 million people in Latin America are infected with Chagas disease, as reported by the

Pan American Health Organization (PAHO), and each year 30.000 new cases accrue[50]. It is most prevalent in poor, rural regions where the transmission mainly occurs through the vector[50]. This insect vector is only seen in the Americas and is found between 40°N and 45°S latitude, and at altitudes up to 1,500 m above sea level[51]. Countries are classified as endemic when vectorial transmission takes place. According to the WHO, Argentina, Belize, Bolivia, Brazil, Chile, Columbia, Costa Rica, Ecuador, El Salvador, French Guyana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Surinam, Venezuela and, Uruguay are classified Chagas disease endemic countries[2].

The prevalence of Chagas disease not only varies between countries but also within them. Thus, it is challenging to determine country-specific prevalence rates. On the one hand, results from seroprevalence studies likely offer an overestimate due to being preferably conducted in regions known to be hyperendemic[52]. On the other hand, limited resources and limited access to health care services might impede the effectiveness of surveillance systems in place.

Despite limited data, the WHO compiles available national data to provide an overview of the epidemiological situation. The most recent available data are from 2010. Despite the uncertainty of estimates, it becomes apparent that the prevalence of Chagas disease is highest in Bolivia, with around 6.1% of the population being infected[4]. However, in Bolivian community-based samples, prevalence rates as high as 51.2% have been reported[53]. The countries with the highest estimated absolute number of Chagas disease cases are Argentina, Brazil, and Mexico, with 1,505,235, 1,156,821, and 876,458 cases, respectively[4].

A peculiarity of Chagas disease is the local outbreaks of orally acquired infections in endemic regions. About 1000 cases of Chagas disease acquired through the ingestion of contaminated food and drinks have been reported in Latin American countries. The majority of cases have been reported in Brazil, with almost 600 cases. Oral outbreaks of Chagas disease have also taken place in Argentina, Bolivia, Colombia, French Guiana, Ecuador, and Venezuela[30]. The largest outbreak of oral Chagas disease, with 103 confirmed cases, has been reported in Caracas in Venezuela[32].

During the last decades, the incidence and prevalence of Chagas disease have decreased considerably in Latin American countries, from 18 million infected people during the 1980s to about 6 million, reported in the most recent estimates from

2010[4,54]. According to the WHO, this reduction is strongly associated with the control and prevention activities implemented by the regional initiatives[4].

2.3.2. European (non-endemic) countries

The reported prevalence of Chagas disease in Latin American populations living non-endemic countries varies considerably by the country of origin of the population studied. A systematic review of European prevalence studies from the year 2015 estimated a pooled prevalence of 4.2% for people of Latin American origin. However, the pooled prevalence for Bolivians was as high as 18.1%[55].

In absolute numbers, estimations go up to 123,000 *T. cruzi* infected individuals residing in Europe, with 75,000 cases in Spain and about 2,000 in Germany[8,9]. These estimations are based on the combination of the number of migrants from endemic countries with the prevalence rates of their respective home countries.

Chagas disease is not a notifiable disease in Germany. Hence, the German national Public Health authority, the Robert-Koch-Institute, does not monitor Chagas disease and its transmission systematically[12]. To date, only two seroprevalence studies have been carried out in Germany, that provide information about the prevalence of Chagas disease. One study, conducted in 1997, found a seroprevalence of 2% (2/100) in the study sample, diagnosed according to WHO criteria[11]. The second and more recent study from 2017 found a prevalence of 9.3% (4/43). However, in this study, only people of Bolivian origin were tested, which limited the representativeness of results for other Latin American migrants.

As described earlier in chapter 2.1.2., Chagas disease can spread outside endemic regions through non-vectorial routes. It is estimated that up to three cases of congenital transmission per 1000 pregnancies in Latin American women occur[8]. Less is known about the incidence of blood- and organ donation related transmission. However, a study from Switzerland has shown that 16.9% of identified Bolivian Chagas disease patients living in Switzerland have priorly donated blood[56]. The results of a blood donor screening in France showed that 0.3% of Latin American blood donors were infected with *T. cruzi*[57], while in Spain, transmission through blood transfusion has been officially reported[58].

A particular challenge of Chagas disease in the non-endemic context is insufficient knowledge about the disease among health professionals[59,60]. With the absence of

knowledge, physicians cannot consider Chagas disease in their diagnoses. Furthermore, the asymptomatic nature of Chagas disease as well as limited access to the health care systems and, thus, diagnosis and treatment further complicates the situation[8]. Resulting from a calculation that compares the observed number of cases with the expected number of cases in nine European countries, including Germany, it is assumed that about 94%-96% of Chagas disease cases are not diagnosed[8].

2.4. Clinical manifestation of Chagas disease

Chagas disease is a heterogeneous condition and shows a wide variation in clinical course and prognosis. It takes a silent course and develops over decades, often without being noticed or diagnosed. It takes place in two phases: the initial acute phase, which is followed by a lifelong chronic phase, if not treated successfully. As a rule of thumb, about 30-40% of chronic cases will develop a determinate form of Chagas disease, characterised by grave and potentially life-threatening symptoms, whereas the remaining 60-70% of chronically infected will stay asymptomatic, while still infectious, and will most likely not take notice of the infection unless it is diagnosed[6].

2.4.1. Acute Chagas disease

The acute phase of the infection is asymptomatic in most cases and lasts for about four to eight weeks[6]. If symptoms appear at all, they are usually mild and might present as a febrile illness. The course of acute Chagas disease is usually harmless. Symptoms occur after an incubation period of one to two weeks, in case of vectorial transmission, and up to a few months if the infection is acquired through an infected blood transfusion[6]. Alongside symptoms of systemic manifestations (fever, headaches, arthralgia, myalgia, malaise) common to many other infectious diseases, some symptoms, specific to Chagas disease, might appear. One of these is the so-called Chagoma, which is an oedema caused by the parasite entry. It often appears on the face and limbs[33]. Likewise, a sign of the parasite entry is the so-called Romaña's sign, which involves a characteristic swelling of the upper and lower eyelids[33]. Acute Chagas disease might also present with cardiac involvement, which is usually expressed as tachycardia and low blood pressure[61].

As a result of the increased parasite load, oral acute infection has a more severe and faster course than vectorial Chagas disease. The symptoms of systemic infection are similar but more severe. Fever, headache, myalgia, vomiting, abdominal pain, diarrhoea, and gastrointestinal bleeding may be seen[6]. Also, cardiac involvement is more pronounced and more frequent. Cardiological manifestations may result in chest pain, palpitations, and breathlessness. Inflammation of the heart and heart failure due to severe arrhythmia or accumulation of fluid in the pericardium are potentially fatal[29,61].

2.4.2. Chronic Chagas disease

After the acute phase, most patients will progress into the indeterminate (asymptomatic) form of chronic Chagas disease. Over time, around 30% to 40% of these patients will progress into the determinate form of chronic Chagas disease, which takes a severe course and can lead to fatal outcomes. Generally, a distinction between the cardiac manifestation and the manifestation of the digestive tract can be made. In a proportion of patients, both forms of chronic Chagas disease will manifest simultaneously.

Typically, the oesophagus or colon are affected when the digestive tract is involved. The damage to the innervations caused by parasites impedes the motility of organs, which leads to the typical enlargement, the megaoesophagus, and megacolon[62]. Common symptoms of a megaoesophagus are impaired and painful swallowing, hiccups, aspiration, coughs, and weight loss[63]. The most common complaint of the megacolon is chronic severe constipation. Patients might also present with abdominal cramps and flatulence. Severe complications of the megacolon that can appear are volvulus (loop of the intestine twisted around itself) and perforation of the colon wall[63].

Chagas disease related cardiomyopathy leads to the highest morbidity and mortality of all Chagas disease manifestations[54]. It is a very heterogeneous condition with a variety of clinical courses and prognoses.

The pathogenesis of Chagas cardiomyopathy is to date not fully understood. It is assumed that the parasite persistence and parasite-driven immune response are responsible for the myocardial damage that is characterised by inflammation, cell death, and fibrosis (scarring events)[64].

The dilation (the enlargement) of the heart in combination with fibrosis to the left ventricle and electric conduction system of the heart is very characteristic for Chagas cardiomyopathy [61]. Progressive dilation can often lead to heart failure, the impaired ability of the heart to pump enough blood. Presenting signs of heart failure include shortness of breath, peripheral oedemas, and fatigue.

Conduction system abnormalities and arrhythmias, irregular heartbeats such as bradyarrhythmia, a heartbeat that is too slow, and tachyarrhythmia, a heartbeat that is too fast, are common findings in symptomatic Chagas disease patients[61]. Left ventricular aneurysms, the swelling of tissue and filling with blood, is also seen in patients. Due to the poor ventricular function and the arrhythmias, Chagas cardiomyopathy patients may suffer from thromboembolic events[65]. The most common causes of deaths in Chagas cardiomyopathy are sudden cardiac death, heart failure, and thromboembolic events[61].

2.5. Treatment

To date, there are only two drugs available for the aetiological treatment of Chagas disease: nifurtimox and benznidazole, which is used more commonly. Both drugs were developed more than 40 years ago[66]. A major obstacle for the evaluation of trypanocidal drugs is the lack of suitable tests to assess treatment success. Currently, the only way to assess drug treatment efficacy is to use serological tests showing the disappearance of *T. cruzi* antibodies (seroconversion). For treated adults, seroconversion can take decades to occur, if at all[67].

The two available pharmacological treatment options have demonstrated effectiveness in the acute stage and during the chronic stage in children. However, the efficacy is inversely related to the age of the patients[68,69]. Adverse events are common, and are, too, associated with increasing age[70]. Discontinuation of treatment due to adverse events occurs in about 20% of treatments[66].

A large multi-centred randomised controlled trial has been conducted to study the treatment with benznidazole compared to placebo treatment in adult chronic patients with cardiac damage. The trypanocidal treatment did not significantly reduce the primary outcomes (death, resuscitated cardiac arrest, sustained ventricular tachycardia, insertion of a pacemaker or implantable cardioverter-defibrillator, cardiac transplantation, among others). Nearly a fourth of the

benznidazole treatment group had to interrupt the treatment because of adverse events. Cutaneous rash, gastrointestinal symptoms, and nervous system symptoms were the most frequent adverse events[71].

Currently, the WHO strongly recommends trypanocidal treatment with benznidazole or nifurtimox for patients with acute or congenital *T. cruzi* infection, for female patients in childbearing age and chronic pediatric patients. While drug therapy is suggested for adult chronic patients without organ damage, treatment for adult patients with specific organ damage is advised against[72]. However, the organization refers to the low level of evidence that the latter suggestions are based upon.

The efficacy of other therapeutic options for Chagas disease, such as posaconazole, have been studied but yielded even less promising results than the established treatment options[73].

Management strategies for Chagas disease differ depending on the clinical stage of the disease. In the absence of symptoms, trypanocidal therapy is in focus, aiming at the reduction or elimination of parasitic load. With a symptomatic course of disease, prevention of progression, complications, and death, together with the maintenance of the quality of life, are in focus[74]. For patients with Chagas cardiomyopathy, different medical treatments for heart failure are used, including β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, among others[61]. In severe cases, cardiac transplantation may be needed. Other treatment measures of patients with advanced Chagas cardiomyopathy include antiarrhythmic drugs, implantable cardiac defibrillators, ablation therapy, and implantation of a pacemaker[61]. Patients with a severe form of gastrointestinal Chagas disease might need to undergo surgical organ resection[6].

It goes without saying that Chagas disease patients need to be monitored thoroughly. For severe cases of Chagas cardiomyopathy, a follow up of patients is needed every three to six months[74].

2.6. Prevention and control in the non-endemic context

There is no available vaccine to prevent infection with *T. cruzi.* Thus, primary prevention activities focus on the prevention of transmission through the different routes. In the endemic context, prevention of vectorial transmission, through health education, improved housing conditions, and vector elimination, plays a key role[75].

As a result of intense prevention activities, Uruguay, Chile, and some states in Brazil, have declared the interruption of vectorial and transfusional transmission of Chagas disease[75]. However, due to the different reservoirs of the disease in wildlife, Chagas disease cannot be eradicated[76].

Because the vectorial transmission is confined to endemic countries, prevention activities in the non-endemic context focus on the prevention of spread through non-vectorial mechanisms, i.e., transmission through contaminated blood transfusion and organ transplants. Congenital transmission can be prevented by treating infected women of childbearing age before they become pregnant[77,78]. For all these strategies, systematic screening procedures need to be in place to prevent the transmission from one person to another effectively.

2.6.1. Programs and recommendations for prevention and control in Europe

The WHO strongly recommends measures to prevent Chagas disease transmission in the European context. Among others, the screening of potential blood, tissue, cell, and organ donators, as well as women of childbearing age at risk of being infected with T. cruzi, is highlighted[12]. Recommended control measures include early detection of congenital infections and subsequent treatment[12].

However, these measures are far from being implemented uniformly throughout Europe[13]. Except for three regions in Spain and the Tuscany region in Italy, no official protocols or standards are requiring systematic Chagas disease screening of pregnant women at-risk and their newborns, let alone women of childbearing age at risk of being infected[79,80]. Congenital transmission of *T. cruzi* infection is virtually unknown to obstetricians in Germany and, thus, pregnant women and newborns at risk do not receive for Chagas disease testing routinely[12].

Concerning the screening of blood donations, the UK, Spain, France, and Switzerland have implemented a systematic screening of blood donations from individuals born in endemic areas, born to mothers native of endemic areas, or from individuals who have received a blood transfusion in endemic areas[13]. In other countries, including Germany, the European Commission's directives 2004/33/CE and 2006/17/CE related to quality and safety of blood, tissue, and cell donation in blood banks apply[81,82]. These documents define individuals known to be infected with *T. cruzi* to be excluded from blood donation. However, they do not clarify how

blood donors at risk of being *T. cruzi* infected, who have not been tested, should be handled[13].

3. Rationale and study objectives

3.1. Rationale

If WHO recommendations for prevention and control of Chagas disease will apply in Germany, it is important to know what the target group, i.e., the population at risk of being *T. cruzi* infected, knows about Chagas disease. A study on Latin American migrants has shown that lack of knowledge is a critical barrier to seek medical attention and get tested for Chagas disease in the non-endemic context[83]. Furthermore, in order to perform an informed decision about whether to get tested, it is crucial that an individual is adequately informed about the disease and its consequences[84]. Therefore, it is important to assess the knowledge on Chagas disease within the population at risk of being infected.

Information campaigns alongside the provision of diagnostic testing could not only be a useful instrument to inform about the disease but also to raise awareness and promote reflection and action nationwide. Insights on the state of knowledge related to Chagas disease in the population at risk could, on the one hand, serve as a starting point for assessing the need for educational interventions. On the other hand, results could be useful for developing control and prevention campaigns and could be used to specifically tailor programs for priority target groups, e.g., groups with little knowledge and awareness about Chagas disease that have the potential to transmit the disease.

3.2. Objectives and research questions of the thesis

This thesis seeks to meet the following three objectives:

1. To identify and compile literature about Chagas disease knowledge among populations at risk of being, or being *T. cruzi* infected, in order to summarise existing studies.
2. To assess and describe the familiarity with and knowledge about Chagas disease among the Latin American community living in Hamburg.
3. To identify socio-demographic characteristics that are associated with knowledge about Chagas disease.

Thus, this thesis seeks to provide answers to the following three research questions:

1. What insights does literature provide about the knowledge on Chagas disease in populations at risk of being, or being T. cruzi infected?
2. What do citizens of Latin American origin living in Hamburg know and not know about Chagas disease?
3. Are there socio-demographic characteristics that are associated with knowledge about Chagas disease among citizens of Latin American origin living in Hamburg?

4. Methods

4.1. Literature search

To answer the first research question and to get an overview of the existing literature on Chagas disease knowledge, a literature search of two bibliographic databases, namely Pubmed and SciELO, was conducted on the 11.12.2019. The search strategy combined two sets of terms with an “AND” Boolean operator: (chagas OR “trypanosoma cruzi” OR “T. cruzi” OR “american trypanosomiasis”) AND (knowledge OR attitude OR perception OR awareness OR familiar*).
The search strategy was also used in Spanish and Portuguese language in the database SciELO. Appendix 1 shows the full search string.
Following eligibility criteria had to be met for inclusion:

1. Observational study (cross-sectional or longitudinal), interventional study with control-arm (pre-intervention, control group),
2. Reported descriptives of any Chagas disease knowledge measure,
3. Study population: Latin Americans, or people of Latin American origin,
4. Study population: adults aged 18 or older, or adult-child mix,
5. Study population: Not health care workers/ health professionals only,
6. Articles published in German, English, Spanish, or Portuguese.

No time restrictions were applied. After conducting database searches and exporting results, duplicate references were removed. Titles and abstracts were screened. Complete texts of articles that met eligibility criteria, or articles where it was not possible to judge eligibility from the title or abstract, were retrieved for further assessment. All full-text articles were compared against eligibility criteria.

An assessment of the content of all eligible articles was undertaken by using a data extraction form. Following information was summarised: author, year, study design, study population and setting, number of participants, participant characteristics, the instruments used to measure Chagas disease knowledge (familiarity, transmission knowledge, vector knowledge, symptom knowledge, sum score), main results for each knowledge category, and overall evaluation of knowledge by authors.

For the quality assessment of studies, the Appraisal Tool for Cross-Sectional Studies (AXIS) and the CASP tool for qualitative studies were used[85,86]. Mixed methods studies were evaluated with the AXIS tool, as descriptions of their results were quantitative. One pre-post interventional study was included. However, only the baseline pre-intervention knowledge assessment was of interest. Thus, the AXIS tool was used to appraise the quality of the baseline survey. A scoring system was not employed; instead, each domain of interest was considered and described narratively.

4.2. Cross-sectional survey

4.2.1. Study design

To answer the second and third research questions, a cross-sectional survey was carried out with the Bernhard-Nocht-Insitute in Hamburg from May to September 2019. The location Hamburg was part of a multicentred study in Germany led by the national Chagas disease network named “Detection and Guidance of Patients with Chagas Disease in Germany” (Erkennung und Lenkung von Chagas Patienten in Deutschland (ELCiD)) who was responsible for the survey content and questionnaire preparation[87].

The survey, together with the offer to get tested for Chagas disease free of charge, was advertised in Hamburg through various channels such as printed flyers and posters, radio announcements, and social media. Flyers and posters were distributed to focal points for both regular and irregular migrants in Hamburg. General practitioners, paediatricians, and gynaecologists, reporting to be able to speak Spanish or Portuguese, received informative materials, too. These physicians were asked to inform their Latin American patients about the study and, if possible, to provide their patients with the survey questionnaire within their practice, or to forward contact details of the survey investigators to them.

Furthermore, on three different Latin American cultural events, and during a visit to a hairdresser in Hamburg, participants were actively recruited and asked to fill out the survey questionnaire.
All study documents were written in Spanish, Portuguese, and German. In order to avoid biased survey results, participants were verbally informed about Chagas disease and were handed an information flyer after completion of the questionnaire. However, before completion, the purpose of the study was explained to participants. In order to participate, participants had to sign a written informed consent sheet. The ethics committee of Hamburg's Medical Council approved the survey.

4.2.2. Sample

The target population of the survey was individuals with an epidemiological risk of infection, i.e., Latin American migrants living in Hamburg, whose origin or background is related to Chagas disease-endemic regions. Participants were eligible for inclusion:

1. If they were born in a Chagas disease endemic country,
2. If they had spent at least ten years in a Chagas disease endemic country before age 25,
3. If their mother was born in a Chagas disease endemic country.

In line with the WHO classifications, the countries Argentina, Belize, Bolivia, Brazil, Chile, Columbia, Costa Rica, Ecuador, El Salvador, French Guyana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Surinam, Venezuela, and Uruguay were defined as Chagas disease endemic countries[2]. Further, participants could only be included in the survey if they were at least 16 years of age, agreed to participate, and they or their legal guardians signed a written informed consent sheet.
For determining the sample size, required for estimating population parameters, the following formula was used:

$$n = \frac{z^{2}_{\alpha/2} * p(1-p)}{d^2},$$

where n is the necessary sample size, $z^2_{\alpha/2}$ is the standard normal variate, p is the anticipated proportion in the population, and d is the precision. In line with conventions, a standard normal variate of $z^2_{\alpha/2}$ = 1.96 was used, reflecting a type I error of 5%. Several different categorical variables of unknown proportions were looked at in the survey. Hence, the anticipated proportion was set at p = 0.5, which is the most conservative value. The purpose of the study was to provide a general overview. Therefore, the estimate precision was given somewhat more allowance with d = 0.1. These values resulted in a sample size of n = 96.

4.2.3. Measures

The conducted survey covered different topics of interest beyond knowledge about Chagas disease. Only the measures that were analysed will be presented and described in this chapter. The full survey questionnaire is displayed in Appendix 2.

4.2.3.1. Socio-demographic measures

Socio-demographic measures included sex, year of birth, country of birth, nationality (multiple were possible), and size of the place (>10,000 inhabitants (urban)/ <10,000 inhabitants (rural)) in which participants had spent the longest part of their childhood. Information about the last place of residence before emigrating to Europe was also available. However, only the information on the place of residence during childhood was included, as a rural dwelling is a Chagas disease risk factor, and most transmissions take place during childhood[88].

Also, the number of children, participants' and participants' parents' highest educational level (no school degree/ primary education/ secondary education/ apprenticeship/ university), arrival year to Europe, reasons for migrating to Europe for which multiple answers were possible (work/ studies/ marriage or partner/ family lives in Europe/ other reasons), and current insurance status of participants (statutory or private German health insurance/ health insurance for students/ foreign health insurance/ no health insurance) was inquired.

Furthermore, the survey included participants blood donation history (yes/ no), and in case of prior blood donation, the country where blood was donated, as well as the willingness to donate blood and organs (yes/ no).

The estimates of participants' age and the years they have spent in Europe were derived by subtracting the birth and arrival year, respectively, from the year of inquiry: 2019.

4.2.3.2. Chagas disease risk factors

Potential Chagas disease risk factors were also assessed. The participants were asked to describe the material of the dwelling in which they spent most of their childhood (stone, cement, concrete/clay, clay/wood/other materials). This information was also available for the last dwelling in Latin America. However, as fewer values were missing and a higher proportion of transmission take place in childhood, the variable on housing materials of the childhood dwelling was used.
By showing a picture of the triatomine bug, participants were asked whether they had seen the insect in one of their Latin American residences (yes/ no). Furthermore, the questionnaire inquired whether participants knew of Chagas disease infected family members (yes/ no/ don't know). Lastly, it was inquired whether participants had received a blood transfusion (yes/ no), and if so, where they had.

4.2.3.3. Chagas disease knowledge and familiarity

In the survey, both familiarity with Chagas disease, and knowledge about Chagas disease were inquired.
To assess the familiarity with Chagas disease, the following questions were asked:

- *Have you ever heard about Chagas disease in your country?* (yes/ no)
- *Do you know anyone in your former Latin American place of residence who is infected with Chagas disease?* (yes/ no/ don't know)
- *Have you ever been tested for Chagas disease?* (yes/ no)
- *Result of the test* (positive/ negative)

The knowledge about Chagas disease was explored by asking the following three questions:

- *Which health complaints can Chagas disease cause? Please mention the three most frequent complaints.* (Open question)

Beforehand, a list of possible Chagas disease symptoms and outcomes with their related lay explanations was created in English based on clinical literature (please see Appendix 3).

The symptoms reported by the participants were translated from Spanish and German into English and compared against symptoms and lay terms from the list. The answers were subsequently categorised into:

- Chronic, affecting the heart
- Chronic, affecting the digestive tract
- Asymptomatic
- Acute
- General
- Untypical
- Don’t know
- Unable to read

Some answers could both be indicative of an acute symptom as well as a chronic symptom. In this case, a decision in favour of the chronic symptoms was made. Abdominal pain, a possible symptom in acute orally transmitted Chagas disease but also in the chronic phase if the digestive tract is affected, is an example of this. Other examples are fatigue and palpitations.

Some answers were too unspecific, so they could not be classified as a specific Chagas disease category. They were instead categorised as “general” symptoms. Pain or infection are both examples of this. One answer, “muscular dystrophy”, was not typical for Chagas disease and was categorised as “untypical”.

Answers within the three symptom categories “chronic, affecting the heart”, “chronic, affecting the digestive tract”, and “acute” were subcategorised further to enable more insight. The category “chronic, affecting the heart” was divided into “heart problems”, “affects the heart”, “chest pain”, “arrhythmia”, “fatigue”, “death”, and “fainting”. "Death" in itself cannot be seen as a symptom of Chagas disease, but rather as an outcome of it. However, since sudden cardiac death is characteristic of the disease and a common cause of death in Chagas disease patients, it was included in the category “chronic, affecting the heart”.

“Chronic, affecting the digestive tract” was divided into “problems with the digestive system”, “abdominal pain”, “difficulties with swallowing”, and “constipation”. The

category “acute” was classified as follows: “fever”, “skin irritations”, “headaches”, “muscular pain”, “general discomfort”, “diarrhoea”; “seropositivity”, “enlarged spleen”, “chagoma”, and “Romaña’s sign”. “Skin irritations” was used as an umbrella term for various skin-related symptoms. These were: flushing, rash, itchiness, and spots on the skin. Appendix 4 shows all responses, their translation and categorisation.

- *How is Chagas disease transmitted? Please check all the modes of transmissions that you know:*
  (by a chinche (triatomine bug) [correct]*/ by sexual intercourse [incorrect]/ by blood transfusion* [correct]*/ by mosquito bites[incorrect]/ by organ transplantation* [correct]*/ by drinking sugar cane juice* [correct]*/ during birth from mother to child* [correct]*/ by physical contact[incorrect]/ I don’t know the modes of transmission)*

For this question, it was possible to give multiple answers. An individual sum score of correct and incorrect answer options was calculated. The number of reported routes in total were also calculated. In a subsequent multiple linear regression analysis, the sum of correct transmission pathways was the dependent variable.

The third knowledge question assessed was:

- *Are there people who feel well even though they are infected with Chagas disease? (Yes* [correct]*/ No/ Don’t know)*

4.2.4. Statistical analysis

Survey data were entered into the online database REDCap and were analysed using IBM SPSS Statistics version 24. The full syntax is shown in Appendix 5.
All measures were categorised as missing when no box was ticked, or no answer was written, and when participants did not indicate that he or she did not know the answer. Missing values were kept in the data set and included in calculations of proportions. The number of missing values for each variable was reported alongside the results.

Sample characteristics were described with means and standard deviations (SD), absolute frequencies, and proportions, where appropriate.
To answer the second research question, descriptive statistics, absolute frequencies, and proportions were used to analyse the three knowledge variables and the Chagas disease familiarity variables quantitatively.

To answer the third research question, a multiple linear regression analysis was performed with the formula:

$$Y_i = (b_0 + b_1 X_{i1} + b_2 X_{i2} + \cdots + b_n X_n) + \epsilon_i ,$$

where Y is the outcome variable, b_0 the constant, i.e., the point where thy Y-axis and the regression line intersect, b_1 is the coefficient of the first predictor (X_1), b_2 is the coefficient of the second predictor (X_2), b_n is the coefficient of the nth predictor (X_n), and ϵ is the individual error term.
The dependent variable was the sum of correct transmission pathways cited by the participants. It had a possible range of 0 to 5.
Bivariate analysis of socio-demographic characteristics identified the independent variables for the multiple linear regression analysis. Point-biserial correlations (Pearson's correlation) were calculated for the dependent variable and the independent variables of interest. Potential independent variables were selected based on the results of included studies of the literature review (Please see chapter 5.1.6). These were sex (Reference: Male)[89,90], age[89,91], having heard about Chagas disease (Reference: Not having heard about Chagas disease)[89], having seen triatomine bugs in the Latin American residence (Reference: Not having seen triatomine bugs)[89,92], and rural childhood residency (Reference: Urban childhood residency)[92,93].
In order to reduce the number of redundant predictors, variables were only included in the regression model when bivariate analysis yielded correlations with p-values smaller than 0.2. The selected dependent variables were entered simultaneously (enter method).
In the final model, rural childhood residency, having heard about Chagas disease, and having seen triatomine bugs were included as independent variables.

Based on results from the literature review (chapter 5.1.6), it was hypothesised that rural childhood residency, having seen the triatomine bug, and having heard about Chagas disease are positively associated with the number of correctly identified transmission pathways.

Listwise exclusion of cases, i.e., exclusion of cases with any missing model variable, was applied. The minimum sample size was calculated according to Green's rule of thumb, which is:

$$N > 50 + 8 * m\,,$$

where m is the number of predictors[94]. The minimum sample size was thus 75 (N > 74) as three predictors were included in the final model.

In addition to standardised and unstandardised regression coefficients, confidence intervals (CI) and significance level, model fit statistics (F-ratio, R^2), and casewise diagnostics (identification of outliers outside with more than 3 SD, Cook's distance, DFBeta values, Mahalanobis' distance) were retrieved. Cases were deemed problematical if Cook's distance > 1, dfBeta > 1, or Mahalanobis distance > 15[95]. Furthermore, model assumptions were checked in order to assess the generalisability of the model. Linear relationships between the independent variable and the continuous dependent variable a*ge* was checked visually with a scatter plot. The absence of multicollinearity was checked using the variance inflation factor (VIF) and tolerance statistic. The absence of multicollinearity was indicated with VIF values of 1 and tolerance statistic > 0.2[95]. Homoscedasticity, the equality of variances, was assessed visually with a scatter plot depicting the standardised residuals (ZRes) and standardised predicted values (ZPred) of the model. Moreover, for the two dichotomous predictors *heard about Chagas disease* and *seen triatomine bugs,* Levene's test statistic was retrieved to test the null hypothesis of equal variances between groups. The absence of autocorrelation, i.e., independent errors, was assessed with the Durbin-Watson statistic for which values between 1 and 3 are acceptable to fulfil the assumption[95]. The normal distribution of residuals was checked visually on a Probability-Probability Plot (P-P Plot) of the observed and predicted cumulative probability.

5. Results

5.1. Literature review

5.1.1. Study selection

Database searches resulted in 675 references, of which 106 duplicates were removed. Title and abstract screening yielded 33 potentially eligible articles which were all subsequently assessed based on their full text. In total, 21 studies met the eligibility criteria and were included. Seven of the 12 excluded studies were excluded because knowledge about Chagas disease was either not assessed or not presented in the manuscript. An additional four studies were excluded because of their study population: three studies only included children; one consisted of health professionals only. One study turned out to be a duplicate, in a different language, of a study that was already included. Figure 1 depicts the flow of information of the literature review.

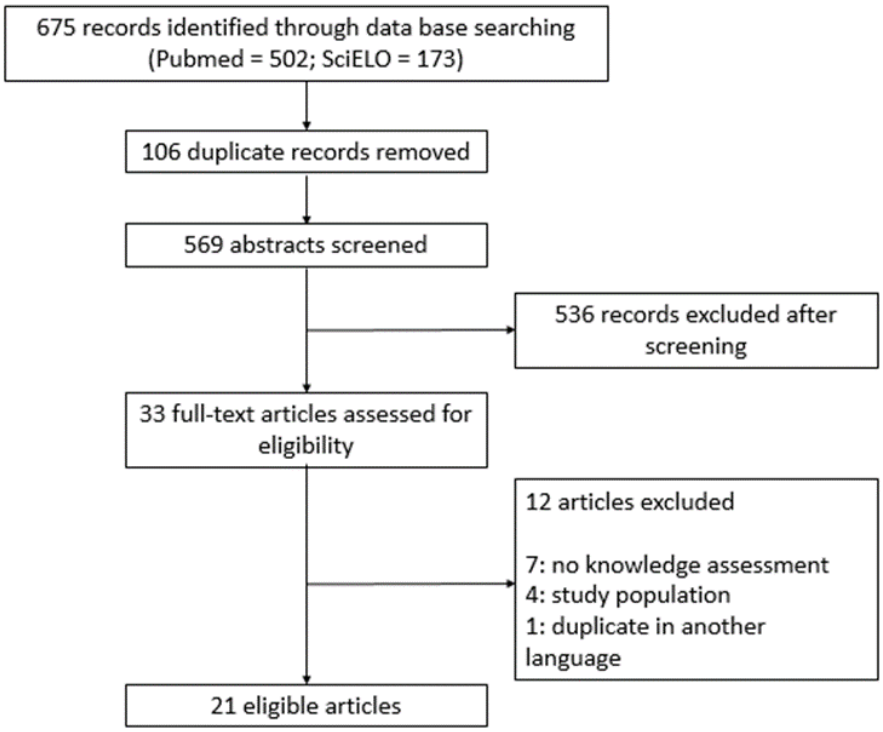

Figure 1. Flow of information through different phases of the literature review

5.1.2. Study characteristics

The included studies were published between 1998 and 2019. Most studies were conducted in Argentina (n = 4)[93,96-98], followed by Brazil (n = 3)[91,92,99]. Other

countries were Bolivia, Colombia, Germany, Honduras, Mexico, Panama, Spain, USA, and Venezuela. A majority of 13 studies were of quantitative nature of which 12 were survey-based cross-sectional studies[90-93,96,99-105], and one study a pre-post interventional study[97]. Five studies had a qualitative study design[98,106-109], and three studies had a mixed-methods approach with both quantitative and qualitative components[10,89,110].

In quantitative studies, different approaches were used to assess the knowledge about Chagas disease. Some studies had used a sum score instrument to quantify the level of knowledge[93,96,97,102,104,105]. Other studies assessed specific aspects of knowledge with single questions[90,92,99-101,103,110]. In four studies, answer options were provided for respondents in the form of multiple-choice questions[10,103-105], whereas others aimed to receive spontaneous answers without the influence of given answer options[91,93,99]. In most cases, it was not possible to tell whether open-ended or closed questions have been applied[90,93,96,100,102,104].

Among qualitative and mixed-methods studies, data collection strategies were diverse, too. Observations and in-depth interviews were used[98,106,107], as well as free recall techniques[109] and field notes and triangular groups[108].

Study populations were very heterogeneous. Some studies included Chagas disease patients only[101,108], whereas others assessed Chagas disease knowledge in communities[91,92,96,97,99,100,102,106,110]. Some studies restricted their study populations to rural indigenous communities[90,98], and other studies looked at Latin American migrants living abroad[10,103,108]. Sample sizes ranged from 14 to 2677 participants[103,108].

Because of the heterogeneity of studies regarding data generation techniques and the samples in which the knowledge assessments took place, it is difficult to compare results among these studies directly. As a result, the overall evaluation of authors, rather than specific quantitative estimates, such as percentages of respondents providing a particular answer, was in focus in the following narrative review of the literature. For completeness of results, however, an overview of study characteristics and knowledge instruments in quantitative studies (Appendix 6, Table A6a), results of quantitative studies (Appendix 6, Table A6b), and characteristics and results of qualitative studies (Appendix 6, Table A6c) is provided.

5.1.3. Chagas disease knowledge in migrant populations

Although the few studies that assessed the knowledge about Chagas disease in Latin Americans living outside Latin America were very different in their design, there was one similarity in all of them: a statement of lack of knowledge.

It was found in a qualitative study with a grounded theory approach that Bolivian women infected with Chagas disease living in Spain were well aware of the vectorial transmission route. However, a poor understanding of other transmission routes and the clinical progress of the disease was also stated[108]. A study on Bolivians living in Munich in Germany reflects these findings. In the cross-sectional survey, more than half of the sample had little or no knowledge about transmission mechanisms. In further evaluation through qualitative interviews, considerable confusion about transmission pathways, other than the vectorial and congenital, was observed.

Similarly, a lack of knowledge and confusion about the clinical manifestations were found both within the survey and qualitative interviews[10]. In a large cross-sectional survey on Latin Americans, predominantly Mexicans, living in Los Angeles, California, 86% of respondents had never heard about Chagas disease, and 81% believed that it is not a severe disease[103]. The authors of all three studies strongly advocated health education campaigns addressing Chagas disease.

5.1.4. Chagas disease knowledge in urban Latin American populations

A study from Argentina assessing Chagas disease knowledge among rural and urban primary school teachers concluded that among both groups of schoolteachers Chagas disease was limited to the idea of a rural disease present in farmhouses and ranches. While 42% of the urban teachers cited transmission through blood transfusion as an important transmission route in urban areas, only 5% of the urban teachers were aware of congenital transmission[93]. A pre-post intervention study, also conducted in an urban area of Argentina, reported similar findings for the pre-intervention knowledge assessment. Although the interviewees had a good level of knowledge (more than half of them were categorised with the highest level of knowledge), there was a knowledge gap regarding non-vectorial transmission pathways. Only 14% were aware of congenital transmission. The high knowledge scores seemed to have arisen from the generally good knowledge about the disease vector. For instance, 86% of respondents were able to recognise the triatomines

and 71% knew that they feed on blood[97]. Similar findings were seen in a study from Caracas in Venezuela. Respondents were generally knowledgeable about the disease vector and the process of vectorial transmission but demonstrated a lack of understanding regarding non-vectorial transmission routes, the disease progress and epidemiological dynamics[109].

5.1.5. Chagas disease knowledge in rural Latin American populations

A similar pattern is seen in the rural populations that were studied. Although the studies were conducted in different settings with different populations, there was a consensus among studies that there was a general awareness about the vector as a potential route of transmission. While participants exhibited basic vector knowledge, non-vectorial transmission routes and Chagas disease manifestations were less well-understood [90,91,100-102]. As an example, a study from Mexico found that the studied sample was very knowledgeable about the disease vector, including its natural habitat. However, the clinical knowledge that the samples presented was incomplete. While 93% of this partly indigenous sample was able to identify the vector and 73% knew that it feeds on blood, only 38% of respondents cited that Chagas disease can affect the heart. Instead, most participants (61%) mentioned swelling of the bite wound when asked about the health consequences of a triatomine bite[110].

Only a few studies contrast these findings. For example, two articles reported that their samples studied did not consider the triatomine bug a health risk. The participants did not associate it with a disease and normalised the bite event. Both samples were either entirely or partly indigenous[98,106].

Another contrasting study emphasised that participants, who lived in a rural endemic area of Brazil, had a high level of knowledge and awareness of Chagas disease and the triatomine bug. Participants were able to differentiate spontaneously between seropositivity and chronic symptomatic Chagas with its different manifestations without induction by answer options. It should be mentioned, though, that these participants had priorly been exposed to a Chagas disease control program[99].

5.1.6. Factors related to Chagas disease knowledge

Nine studies formally tested whether relationships between knowledge about Chagas disease and other characteristics exist. Only one study performed a multivariate analysis to investigate relationships[89]. The remaining performed some form of bivariate analysis (t-test, Chi²-test, correlation coefficients)[90,92,93,96,97,100,103,105]. Three studies generated hypotheses without formally testing them[91,99,107].

In rural residents, Chagas disease knowledge and sex were associated. Male respondents tended to be aware of the association between triatomine bugs and Chagas disease more frequently. Among urban Bolivian residents, age and education were positively associated with better knowledge on the triatomine-Chagas-disease association[89]. Age also seemed to play a role in a Brazilian study, where older participants performed better in the knowledge assessment than younger ones[91]. The better knowledge was partly explained by the fact that the vector had been eliminated in the study area, and younger participants were no longer exposed to its presence.

An association with sex was also seen in another study from Bolivia. In a sample of indigenous community members living in a rural, endemic and vector infested area, men tended to relate the triatomine bug with Chagas disease more often than women did[90].

Rural and urban residency might likewise be associated with knowledge about Chagas disease. In a Brazilian study of rural and urban communities, a higher proportion of rural residents gave correct responses to a battery of Chagas disease questions, e.g., identifying the triatomine bug, whether the triatomine bug transmits a disease, and the name of the disease that it transmits[92]. An ethnographic study conducted in Columbia showed a similar association. The place of residence (rural, semi-urban, urban) tended to influence the local understanding of the disease[107]. In a study on Argentinian teachers, rural teachers were more knowledgeable about the vectorial transmission route of Chagas disease and the triatomine insect habitat than were teachers from urban areas[93]. The same tendency was also seen in a cross-sectional field study conducted in Bolivia where inhabitants of urban, vector-free areas were compared to those of rural, vector infested areas[89].

Furthermore, exposure to Chagas disease control programs seems to affect the knowledge about Chagas disease positively. In the pre-post interventional study conducted in Argentina, an increase in basic Chagas disease knowledge (vector, transmission, and clinical knowledge) was observed. Post-intervention, a higher proportion of participants were categorised with the highest knowledge level than before the intervention[97]. Likewise, in a study comparing members of rural communities with no prior and prior control activities, respectively, members of the community with prior control activities were more knowledgeable about the risk of vectorial transmission and Chagas disease consequences[100]. An additional two studies hypothesised that the level of knowledge that they observed could be explained by the exposure to prior prevention and education activities[96,99].

5.1.7. Quality appraisal of studies

A summary table of the quality appraisals can be found in Appendix 7. In all quantitative cross-sectional studies, a study objective or research question was provided, and in all studies, except one, the study design was appropriate to meet the objective. The study for which this criterion did not apply aimed to define the basic notions that constitute the optimal level of knowledge about Chagas disease that every inhabitant of endemic areas should have. However, the study did not reveal the process of this identification. Rather, the level of knowledge assessed with this tool was described[96]. While all studies defined their target population, only three studies provided the reader with a sample size calculation that justified their sample sizes[91,97,102]. The selection process of the sampling was rated problematical in seven studies[10,92,93,96,97,101,105]. For instance, to represent the local community households that were most easily accessible[96], or attendees of a Chagas disease awareness day were sampled[105]. However, the population base from which the samples were drawn was rated appropriate in all studies for which this information was available.

No study with the available information undertook measures to address non-response. The majority of studies did not mention the response rate, and of those who did, two studies exhibited response rates that raised concerns about non-response bias[92,97]. In no study information of non-responders was described.

In all but one study, the outcome measure was rated appropriate to meet the aim of the study[103]. Eight studies mentioned that their outcome measure had been validated, pilot-tested or used in a previous study[91-93,97,100,102,104,110]. Regarding statistical significance, only one study did not describe how significance was determined[99]. In six studies, the methods were described sufficiently to enable reproduction of results[91,92,97,101,105,110]. In the remaining studies, the coding of open-ended questions was deemed problematical as they did not provide information on this process. In five studies, no basic socio-demographic information of study participants was described[91-93,96,101]. In all studies, the results were presented for the analyses described in the methodology section and were internally consistent. Although only six studies discussed their limitations[10,97,101,103,105,110], author's discussion and conclusions were justified in all studies. While little information was given about funding sources and conflicts of interest (only six studies declared absence thereof[10,89,100,102,103,110]), most studies stated to have had an ethical approval or that informed consent from participants was obtained[10,89,91,92,97,101-105,110].

All five qualitative studies stated a precise research aim. The qualitative approach and the research design chosen were appropriate to meet the study aim in all of them. In four studies, the sample recruitment was appropriate, while too little information about the sampling process was given in the fifth study to appraise this domain[98]. The same study provided insufficient information about the data collection, so that it was not clear whether an appropriate strategy had been applied. Only one study critically considered the relationship between researchers and participants and how this relationship could have influenced the study[106]. The remaining studies did not comment on this issue. However, four of the studies discussed ethical issues[98,106-108]. One study discussed findings that it did not describe in the results section. Also, these findings were not reflected in the presented exemplary quotes[107]. For the other four studies, the data analysis was appropriate. All studies provided the reader with a clear statement of findings. Their conclusions were valuable as they gave out recommendations for action, e.g., contents for health education programs, and future research.

5.2. Cross-sectional survey

5.2.1. Survey sample description

In the survey conducted in Hamburg, a total of 102 participants were recruited. The majority of participants was recruited on four different outreach activities. In total, 96 participants were recruited this way. Five participants participated in the survey while being tested for Chagas disease. They had initiated the contact themselves and had heard about the service either through other people or through distributed flyers. One participant who agreed to participate in the survey was referred to the study for diagnostic testing by a collaborating medical praxis for undocumented migrants.

The sample was predominantly female, with 71.60% (n = 73). The mean age of the sample was 36.86 years with an SD of 10.13. The age ranged between 18 and 64 years. Figure 2 shows the age distribution in groups of five years in a histogram. The two peeks at 30-35 year and 40-45 years represent a bi-modal distribution of age.

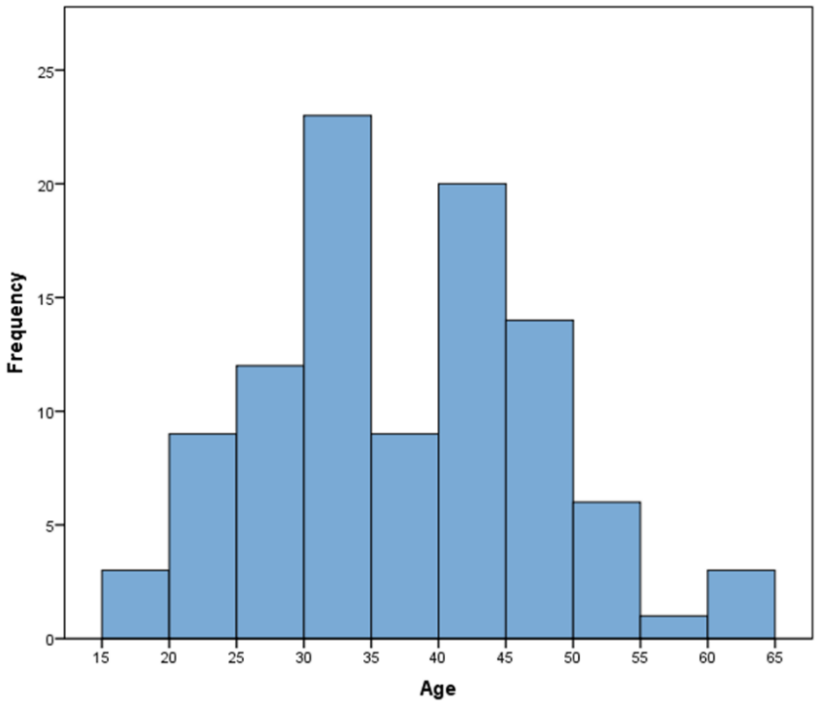

Figure 2. Age histogram (n=100)

Five participants were born in Europe. The remaining 97 were born in different countries throughout the Americas (Figure 3). Most participants were born Ecuador (n = 20), followed by Mexico (n = 17), and Peru (n = 16).

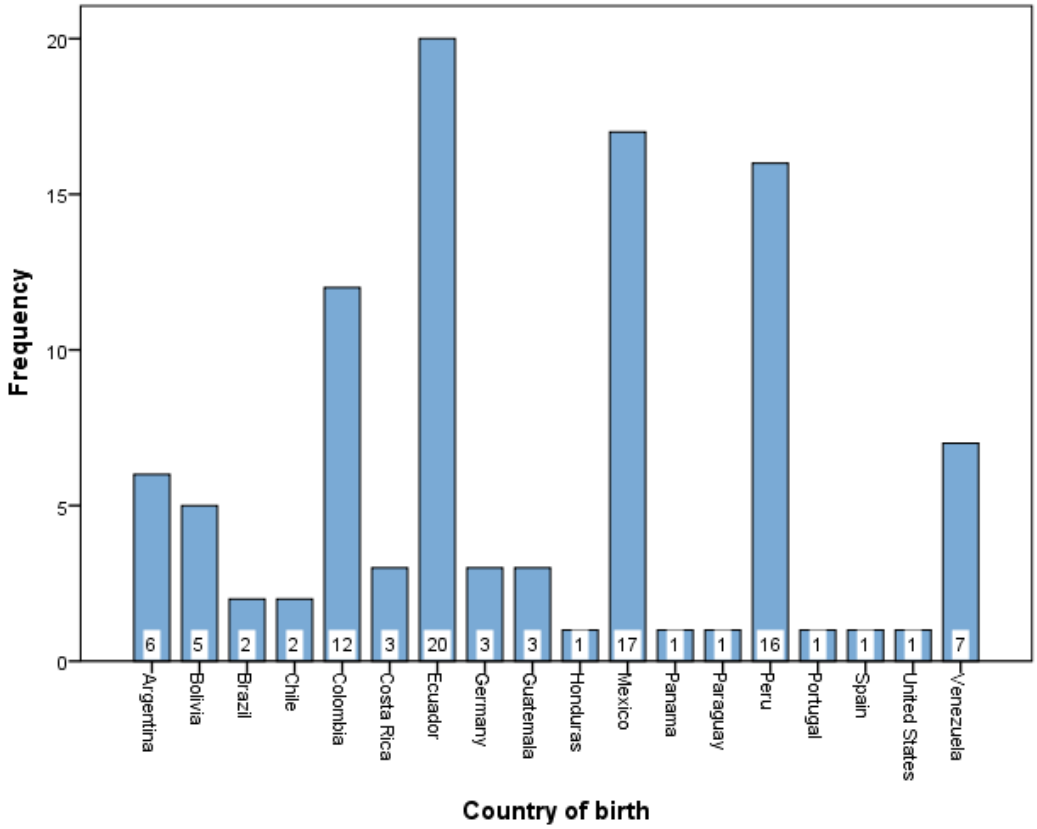

Figure 3. Country of birth by frequency (n=102)

The distribution of the sample's nationalities was different, however. Around a third of the sample had a European nationality. Twentytwo participants identified as Germans, nine as Spaniards, and each one as Italian and Portuguese. The largest group of non-Europeans were Mexicans (n = 16), followed by Ecuadorians (n = 11). On average, the sample had lived for 13.7 (SD 10.29) years in Germany or other European countries and the time span ranged from no completed year to 43 completed years. The median time lived in Europe was 14.50 years.

The most frequently mentioned reason for moving to Europe was marriage or partnership, followed by education, and work (Table 1). In total, 43 participants reported having at least one child, of which 33 were female. About 60% of the sample (n = 58) had obtained a university education. The distribution of the sample's highest educational attainment, as well as their parents' highest educational attainment, is shown in Table 1. Generally, the sample was well educated and tended to have higher educational attainments than the parents.

Variable	Number of participants (%) / Mean (SD)	Number of missing values (%)
Sex		0 (0)
Male	29 (28.4)	
Female	73 (71.6)	
Mean Age	36.9 (10.1)	2 (2.0)
Highest educational level		5 (4.9)
No school completed	0 (0.0)	
Primary school	1 (1.0)	
Secondary school	17 (16.7)	
Apprenticeship	21 (20.6)	
University	58 (56.9)	
Parents' highest level of education		6 (5.9)
No school completed	1 (1.0)	
Primary school	11 (10.8)	
Secondary school	19 (18.6)	
Apprenticeship	21 (20.6)	
University	44 (43.1)	
Area of residence in Latinamerica		13 (12.7)
Rural (<10.000 inhabitants)	13 (12.7)	
Urban (>10.000 inhabitants)	76 (74.5)	
Reason for migrating to Europe		4 (3.9)
Work	19 (19.4)	
Studies	30 (30.6)	
Marriage / Partner	36 (36.7)	
Family	14 (14.3)	
Other reasons	15 (15.3)	
Mean number of years spent in Europe	13.7 (10.3)	6 (5.9)
Health insurance status		3 (2.9)
Statutory or private German health insurance	85 (83.3)	
Health insurance for students	6 (5.9)	
Foreign health insurance	4 (3.9)	
No health insurance	4 (3.9)	
History of blood donation	27 (26.5)	10 (9.8)
In Europe	11 (10.8)	
In Latin America	14 (13.7)	
Willingness to donate blood	72 (70.6)	7 (6.9)
Willingness to donate organs	57 (55.9)	5 (4.9)

Note: SD = Standard deviation

Table 1. Socio-demographic characteristics of the sample and missing values

A majority of 83.3% (n = 85) stated to have a German statutory or private health insurance. Only four participants indicated that they did not have a health insurance scheme (Table 1).

There was a high willingness to donate blood and organs in the sample with 70.6% and 55.9%, respectively. Around a quarter of the sample had already donated blood in European or Latin American countries (Table 1).

5.2.2. Results on Chagas disease risk factors

While 76 participants (74.5%) had lived in a city with more than 10.000 inhabitants during their childhood, considered an urban area, 13 participants (12.7%) had lived in areas with less than 10.000 inhabitants, considered rural (Table 1).

Eighty-eight participants reported that the house, in which they had lived the longest time during their childhood, had been constructed from concrete, stone, or cement. Four participants reported to have lived in a house made from adobe or clay, and five in a house made from wood, respectively (Table 2). Despite these former living conditions, as many as 46 participants reported that they had seen the triatomine bug in their Latin American dwelling (Table 2).

Variable	Number of participants (%)	Number of missing values (%)
Material of dwelling during childhood		4 (3.9)
Stone/ cement/ concrete	88 (86.3)	
Adobe /Clay	4 (3.9)	
Wood	5 (4.9)	
Other materials	1 (1.0)	
Seen triatomine bugs in LA dwelling		5 (4.9)
Yes	46 (45.1)	
No	51 (50.0)	
Blood transfusion receipt		5 (4.9)
In CD endemic country	2 (2.0)	
In CD non-endemic country	3 (2.9)	
No	92 (90.2)	
Family member with CD		9 (8.8)
Yes	2 (2.0)	
No	59 (57.8)	
Don't know	32 (31.4)	
Note: CD = Chagas disease; LA = Latin American		

Table 2. Frequency of Chagas disease risk factors

In total, five participants had previously received a blood transfusion, of which two of them had received them in their country of origin, which were Ecuador and Costa Rica, respectively. The others had received their blood transfusion in Germany.
Two participants reported knowing of Chagas disease infected family members. In one case, the mother was infected, in the other case, it was the grandmother. Whether it was the maternal or paternal grandmother was not indicated by the respondent.

5.2.3. Descriptive results of Chagas disease familiarity and knowledge

Around a third of the sample reported having heard about Chagas disease (n = 36; 35.3%). Answers from five participants (4.9%) were missing. Furthermore, nine participants (8.8%) reported knowing a Chagas disease infected person in their prior Latin American town of residence (six answers (5.9%) were missing). In total, nine participants (8.8%) had taken a test for Chagas disease (six answers (5.9%) were missing), of which one person was tested positive.
Regarding Chagas disease knowledge, participants were asked whether there are people, infected with Chagas disease, who feel well despite their infection.

Variable	Number of participants (%)	Number of missing answers (%)
Chagas disease patient can feel well		10 (9.8)
Yes	27 (26.5)	
No	3 (2.9)	
Don't know	62 (60.8)	
Number of reported CD symptoms		72 (70.6)
1	7 (6.9)	
2	10 (9.8)	
3	13 (12.7)	
Number of correct transmission pathways		15 (14.7)
0	39 (38.2)	
1	28 (27.5)	
2	11 (10.8)	
3	3 (2.9)	
4	6 (5.9)	
5	0 (0)	
Number of wrong transmission pathways		15 (14.7)
0	79 (77.5)	
1	7 (6.9)	
2	1 (1.0)	

Note: CD = Chagas disease

Table 3. Frequencies of Chagas disease knowledge responses and missing answers

Most participants (n = 62; 60.8%) reported not knowing the answer to this question. While 27 participants answered “Yes”, three participants answered with “No”.

When participants were asked to list three common symptoms of Chagas disease, only 35 participants provided at least one answer to this question. In total, 75 answers were provided. However, five of those were spontaneous “don’t know” answers and four answers were not readable, leaving 66 answers from 30 respondents for subsequent analysis.

Of those who provided an answer, most (n = 13) named three symptoms (Table 3). An overview of the answers can be seen in Figure 4, where acute symptoms are most frequent with 31 mentions. Symptoms of the chronic phase affecting the heart were mentioned less often, namely 24 times. Symptoms of the category chronic affecting the digestive tract were even less frequent, with six mentions. That Chagas disease can be asymptomatic was only mentioned once.

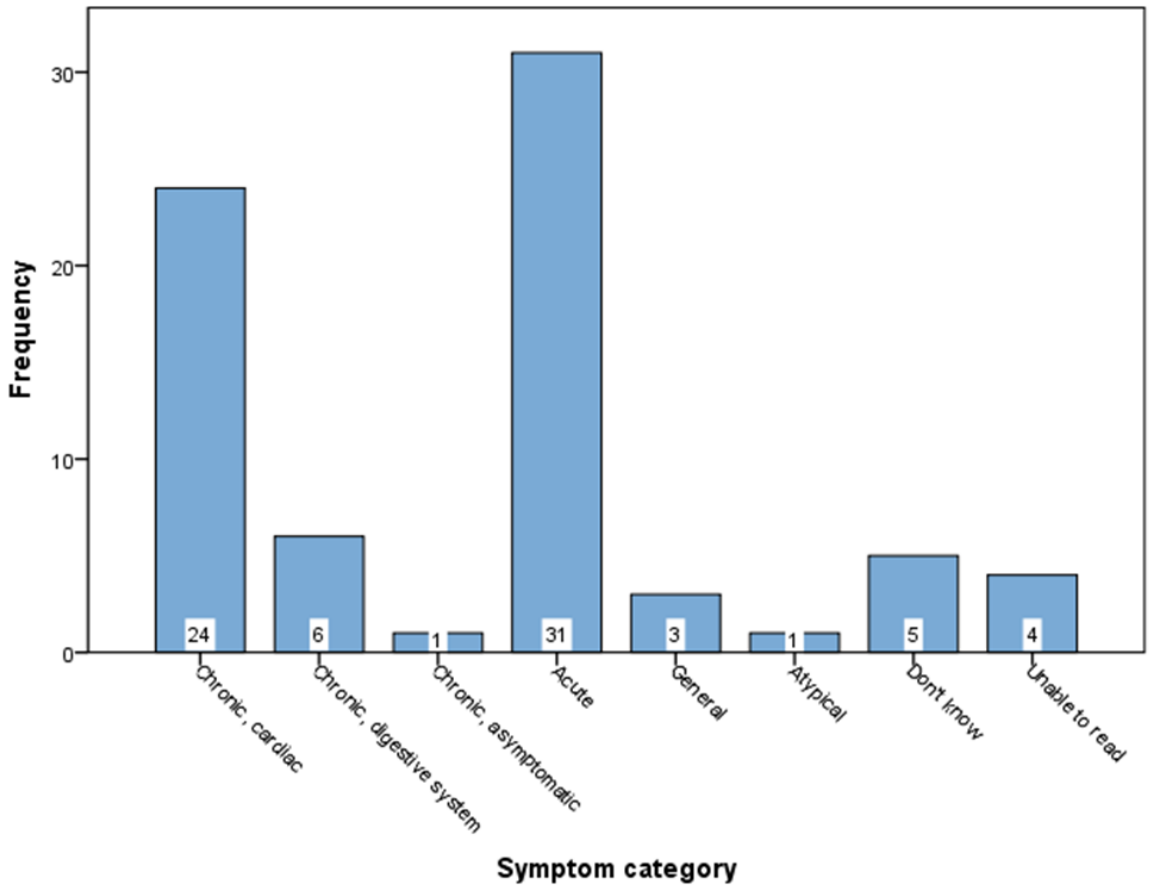

Figure 4. Frequency of reported Chagas disease symptoms among provided answers (n = 35).

Figure 5 to 7 show the further subcategorisation of three categories “chronic, affecting the heart”, “chronic, affecting the digestive tract”, and “acute”. Within the category “chronic related to the heart”, heart problems were mentioned most often (six times). More specific symptoms like arrhythmia and chest pain were both mentioned four times. Within the few symptoms reported in the category “chronic, affecting the digestive tract”, problems with the digestive system and abdominal pain were both mentioned two times. Fever was mentioned 12 times as an acute symptom, and thereby most often. Romaña‘s sign, a particular Chagas disease symptom, was only mentioned once.

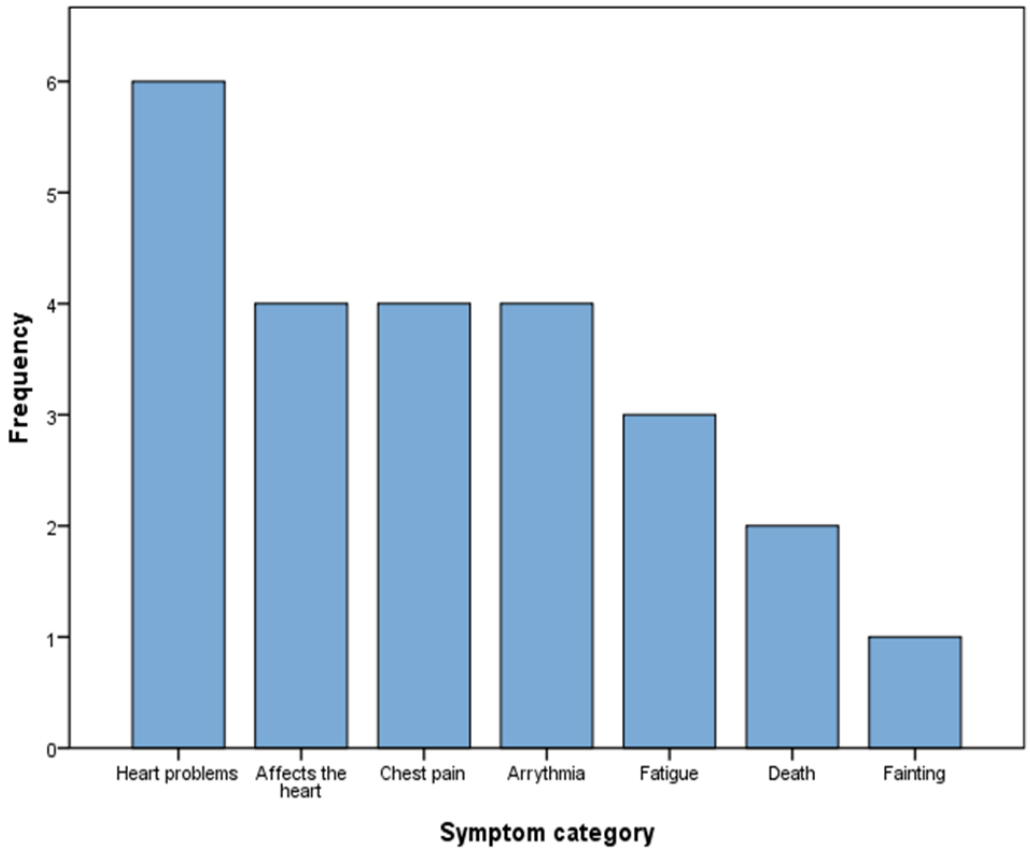

Figure 5. Symptoms reported in the category “chronic, affecting the heart” (n=18)

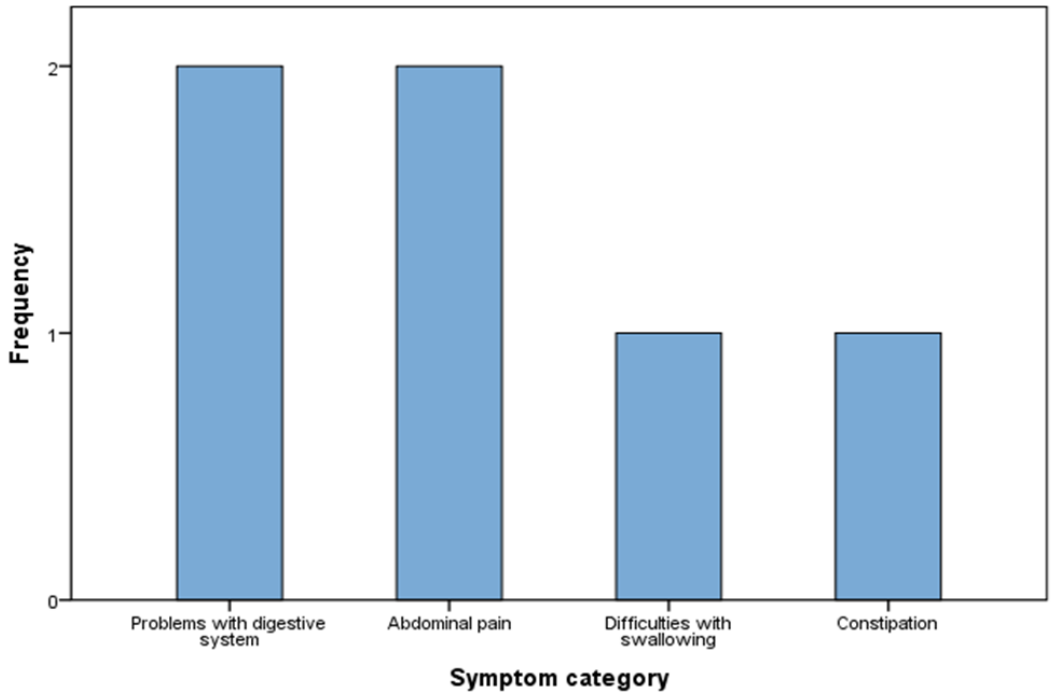

Figure 6. Symptoms reported in the category "chronic, affecting the digestive tract" (n = 5)

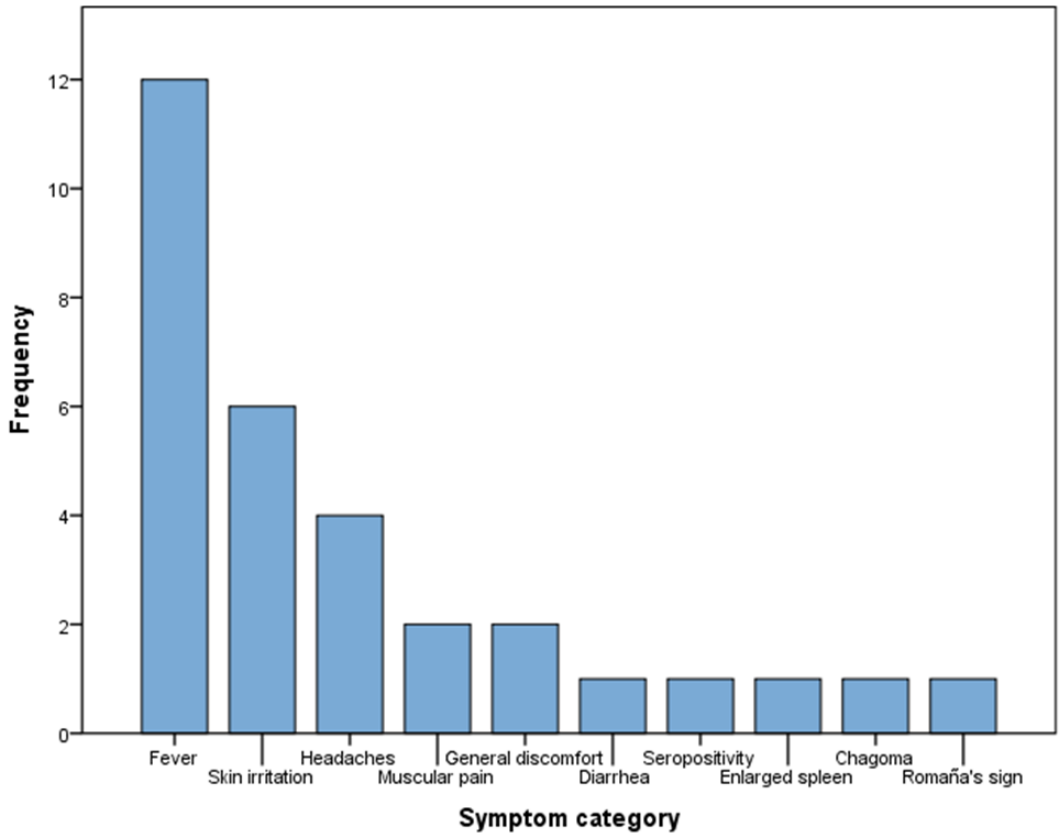

Figure 7. Symptoms reported in the category "acute" (n = 15)

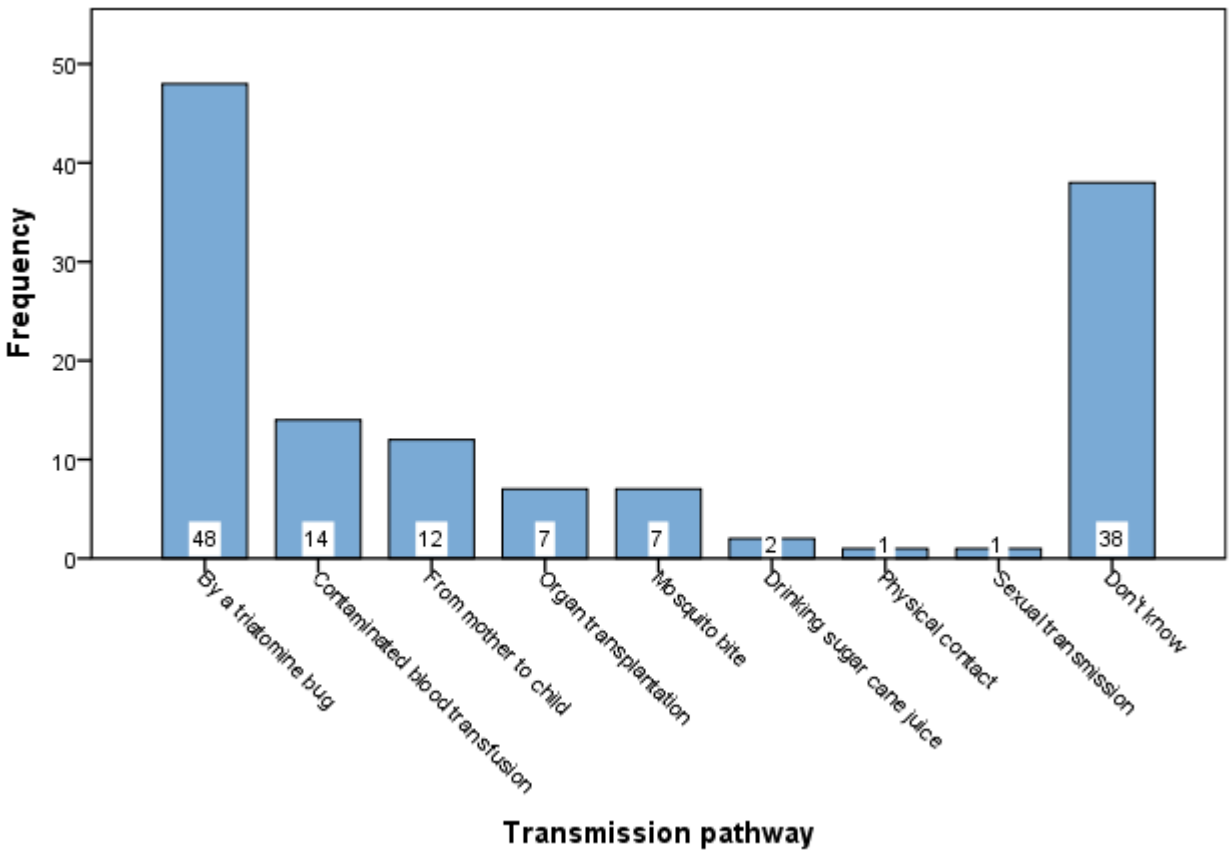

Figure 8. Frequency of transmission pathways with multiple answers (n =85)

Concerning the transmission pathways, 38 participants indicated that they did not know any transmission pathway of Chagas disease. Fifteen participants had missed answering to this question. No participant cited all five correct transmission pathways. The highest number of correct pathways was four, which was attained by six participants. Wrong answer options were not frequent; eight participants selected at least one wrong transmission pathway (Table 3).

The responses to transmission pathways are shown in figure 8. Multiple answer options were possible. Forty-eight participants (47.06%) stated that Chagas disease can be transmitted via triatomine bugs. While 14 participants (13.73%) cited blood transfusion as a possible route of transmission, 12 participants (11.76%) indicated that the disease can be transmitted from mother to child. The transmission through organ transplants (n = 7; 6.86%) and drinking sugar cane juice (n = 2; 1.96%) were mentioned even less frequently. Incorrect answer options were not frequent. Transmission through mosquitos was mentioned seven times, and sexual transmission and physical contacts each one time, respectively.

5.2.4. Regression analysis results

The bivariate analysis of potential predictors and the outcome variable (number of correct transmission pathways reported) yielded three correlations with p-values below or equal to or 0.2. These were included in the linear regression model and were *age*, having *heard about Chagas disease*, and having *seen triatomine bugs* in a former Latin American residence. Table 4 shows the correlation matrix of these variables.

The analytical sample of the regression model included data from 83 respondents. Model fit statistics were as follows: $F(3,82) = 10.75$, $p<0.001$. The p-value for the F-statistic was below the chosen level of significance of $p<0.05$. Therefore, the alternative hypothesis was accepted: the fit of the intercept-only model, i.e., a model with no predictors, can be seen as significantly reduced compared to the present model with the three predictors. The R^2 was 0.29, which means that the model accounts for 29% of the variation in the correctly stated transmission pathways.

Table 5 shows the model parameters. The intersection of the regression line with the Y-axis (the constant), was close to zero and had a large confidence interval and a large standard error. All unstandardised regression coefficients yielded positive relationships; having *heard about Chagas disease* (compared to not having heard about it) increased the number of correct transmission pathways reported by participants by 1.12 points.

Variables	Nr. of correct pathways	Age	Sex	Heard about CD (Ref.: not)	Seen triatomine bugs (Ref.: not)	Rural (Ref.: Urban)
Nr. of correct pathways	1	0.23 (**p= 0.03)**	0.07 (p=0.52)	0.52 **(p<0.001)**	0.19 **(p=0.08)**	-0.13 (p=0.26)
Age		1	0.13 (p=0.19)	0.35 (p<0.001)	0.07 (p=0.51)	0.04 (p=0.70)
Sex			1	0.19 (p=0.07)	-0.19 (p=0.06)	-0.08 (p=0.43)
Heard about CD (Ref.: not)				1	0.17 (p=0.11)	-0.02 (p=0.86)
Seen triatomine bugs (Ref.: not)					1	0.10 (p=0.37)
Rural (Ref.: Urban)						1

Note: CD = Chagas disease; Nr. = Number

Table 4. Pearson correlation coefficients of the dependent and potential independent variables

Having *seen triatomine bugs* (compared to not having seen them), increased the number of correctly reported transmission pathways by 0.31 points. For every increase of *age* in years, the number of correct transmission pathways increased by 0.01 points. However, the 95% confidence interval for the unstandardised regression coefficients b of the predictor *seen triatomine bugs* was quite large, and the confidence intervals for this variable and the variable *age* included negative values. Confidence intervals that include negative and positive values impede a statement on the directionality of associations. Furthermore, the T-statistics were not significant for both predictors.

The variable *heard about Chagas disease* was the only significant predictor, with a relatively wide, but algebraic consistent confidence interval.

Regarding outliers in the model, two cases had standardised residuals above 3 SD. The casewise diagnostic showed that for all cases in the analysis, Cook's distance was smaller than one and all DfBeta values were smaller than one. Furthermore, the largest Mahalanobi's distance was 7.33, which is smaller than 15. Hence, the two cases were kept in the model as they had little influence on the overall model.

	B [95%CI]	SE B	β	T	p-value
Constant	0.01 [-0.86; 0.87]	0.43		0.02	0.99
Age	0.01 [-0.01; 0.03]	0.01	0.08	0.82	0.42
Seen triatomine bugs (Ref.: not)	0.31 [-0.14; 0.75]	0.23	0.13	1.36	0.18
Heard about CD (Ref.: not)	1.12 [0.64; 1.60]	0.24	0.47	4.67	0.00

Note: CD = Chagas disease

Table 5. Linear regression parameters

5.2.4.1. Assumptions

A linear tendency between *age* and the sum of correct transmission pathways could be seen when assessed visually. For the two other dichotomous independent variables, linearity was given by definition. The VIFs for each predictor were about 1 (VIF range: 1.02 – 1.14) and the tolerance statistics between 0.88 to 0.98, indicating no problem with multicollinearity. Absence of multicollinearity was further supported by the lack of high correlations between independent variables (Table 4).

The Durbin-Watson statistic was 1.41, which is rather low, and indicates a positive relationship between adjacent residuals. For assuming independent residuals, this value was still within the acceptable range. Levene's test statistic for the variables s*een triatomine bugs* and *heard about Chagas disease* was non-significant (Levene statistic = 2.056, p=0.155; Levene statistic = 1.218, p = 0.273). Therefore, the null hypothesis of equal variances between groups was accepted. Visual assessment of ZPred plotted against ZRes showed an approximal equal distribution of variance (Figure A8a, Appendix 8). However, the P-P Plot showed a non-normal distribution of residuals which is a violation of the assumption of normally distributed residuals (Figure A8b, Appendix 8).

6. Discussion

6.1. Main findings

6.1.1. Literature review

It was one of three objectives of this thesis to provide an overview of the literature about Chagas disease knowledge in populations at risk of being infected or infected populations. Several valuable insights emerged from the literature review on Chagas disease knowledge. In the endemic context, a strong focus on the vectorial transmission routes and vector knowledge was taken in studies. There was a tendency that interviewed participants were better informed about the vector and vectorial transmission than about other aspects of Chagas disease. Indigenous population were less aware of the health risks posed by triatomines.

Other transmission routes (congenital, blood transfusion) tended to be neglected by participants who associated the disease with a rural farm-like context. The same holds for the few studies conducted in non-endemic countries. Even though vectorial transmission does not take place in this context participants were better informed about the vectorial transmission and demonstrated a lack of knowledge related to other transmission pathways and the health consequences of Chagas disease. Through mostly bivariate analyses, some studies showed associations between Chagas disease knowledge and different factors such as sex, education, exposure to the vector, rural living circumstances, and exposure to prior control or educational activities.

A majority of studies showed deficits in their quality, specifically raising concerns about the methodological quality. Very few quantitative studies justified their sample size with a calculation. Likewise, studies barely addressed non-response. Incomplete reporting impeded the reconstruction of applied methods and limited the transparency of studies.

6.1.2. Cross-sectional survey

This thesis also aimed to assess the knowledge about and familiarity with Chagas disease among the Latin American community in Hamburg and to identify socio-demographic variables that are associated with knowledge about Chagas disease.
The survey was conducted in a well-educated, middle-aged and predominantly female sample. The sample was mostly unfamiliar with Chagas disease and exhibited relatively little exposure to the risk factors housing materials, rurality, and prior blood transfusions. While only a third of the sample had mentioned any Chagas disease symptom, almost half of the reported symptoms could be assigned to the acute manifestation of Chagas disease. The vectorial transmission pathway was the pathway cited most frequently while blood transfusion and congenital transmission were rarely considered. Multiple linear regression analysis revealed that having heard about Chagas disease previously was positively associated with reporting correct transmission pathways of the disease.

6.2. Interpretations of results

In the following chapter, the characteristics of the sample, the results of the knowledge assessment, and the results of the linear regression analysis are discussed and related to the study hypotheses, previous research and data. This chapter aims to discuss similarities and explain unexpected results. Since the characteristics of the sample are necessary to put the results into perspective, they will be discussed first, followed by the knowledge assessment and regression analysis results.
When compared to Hamburg's residence register, female and Mexican participants were overly represented in the sample. According to Hamburg's residence register, the proportion of Mexican residents in Hamburg, in comparison to all Latin American nationalities included in the study, was 9.7% in 2017 (compared to 17% in the study

sample)[111]. The same data revealed that about 57% of the registered Latin American residents in 2017 were female (compared to 70% in the sample). Brazilians who represent the largest nationality of Latin Americans in Hamburg, according to the register, were underrepresented in the sample (2% vs 25%). The figures are not fully comparable as the register only presents the characteristics of the population with foreign citizenship. However, since there are no official statistics on the population born in Latin America, regardless of the nationality, the present register was used for comparison.

It is striking that nearly 60% of the sample had obtained a university degree. No official data of the educational level of Latin American citizens in Hamburg is available. However, in comparison, only 18% of the German population holds a university degree[112]. This observation could be partly explained by the increase in educationally motivated migration from Latin America to Europe[45]. However, a selection effect introduced through the sampling seems more likely to explain the large discrepancy.

One participant was referred to the study by a medical praxis for irregular migrants, while only four participants reported not to have a health insurance scheme. Using the lack of a health insurance scheme as an indicator for the absence of legal residency status, this would lead to an estimated 3.9% of participants without a legal residence status. A report on undocumented migrants in Hamburg from 2009 estimated the number of irregular migrants (migrants without legal residency status) and assumed that about 1.300 irregular migrants from Latin America and the Caribbean lived in Hamburg during that time[113]. According to this estimate and data from Hamburg's residence register from 2007, irregular migrants represented almost 20% of the population with Latin American and Caribbean nationality living in Hamburg. Although more than a decade has passed since this report was published, it can be assumed that irregular migrants were underrepresented in the present study sample. In the only other German study that assessed Chagas disease knowledge, the same problem of not being able to reach irregular migrants was noted[10].

The report on irregular migrants in Hamburg might explain this observation: the fear of being identified as an undocumented migrant by official authorities discourages many from seeking medical help[113]. Since the survey was conducted with the

Bernhard Nocht Institute in Hamburg, the official impression of this institute may have had a deterrent effect on contacting them.

That some sample characteristics dissent from registry data and estimations could be due to normal variation of data. However, the estimate-precision of 10% hampers comparison of data that deviates within this range. With a larger sample size, a higher estimate precision could have been achieved. Another explanation for the deviation from official data could be the sampling strategy. Outreach activities at Latin American cultural events could have introduced a selection effect. Certain events such as the “Taco Festival” a Mexican street food event attended in Altona might have attracted certain people, such as Mexicans, more than others. Moreover, an entrance fee of 2.00 € that was required in addition to relatively pricy street food starting at 5.00 € for small snacks could have prevented people from attending the event who could not afford these expenses.

Another aspect of the sample that needs to be discussed and put into perspective is the exposure to Chagas disease risk factors and points of contact with the disease. A vast majority of participants had lived in an urban setting during their childhood, in houses made from cement or stone. It is therefore surprising that a good 45% of the respondents reported having seen the triatomine bug in their home in Latin America. A similar observation was found in a study from Brazil, which was conducted in different epidemiological contexts. In an area declared free of vector infestation, 75% of the respondents reported that they had seen the triatomine bug in their homes[92]. In the study from Munich conducted among migrants of Bolivian origin, only 25% reported having seen the insect[10].

Familiarity with Chagas disease was generally low in the present sample of this study. It seems plausible that some may have confused the appearance of the depicted insect with other insects. Another explanation could be that other samples that were more aware of Chagas disease such as the one in Munich (where 70% had heard about Chagas disease) were also more aware of the stigmatisation that patients and families of patients face[10,114]. Denying the presence of triatomines in the former Latin American residence could have been a result of a social desirability bias. Due to a lower familiarity with Chagas disease, this effect could have been less prominent in the present sample.

Despite the former, primarily urban, living conditions, there were several points of contact with Chagas' disease in the sample. One participant self-identified as having

been tested positive while two participants stated to know a family member infected with Chagas disease. In one case it was the own mother. Approximately one out of ten respondents stated that they knew of a person with Chagas' disease or had been tested themselves, respectively. This finding is in line with the results seen in other studies conducted in Europe[10,56,115].
The frequent history of blood donations and high willingness to donate blood and organs among the sample is also noteworthy. Compared to Germans in general and other Latin American samples in Europe, the willingness of the sample to donate blood and organs was higher[10,56,115,116].

Only about a quarter of the respondents knew that Chagas patients could also feel well, about a third stated at least one symptom of the disease (although the relevance of the symptoms can be discussed), and slightly less than half of the sample could name at least one correct transmission route. No respondent was able to report all correct transmission routes. The results are generally consistent with the results seen in other studies. In particular, the confusion about symptoms and non-vectorial transmission pathways observed in this thesis is a typical result of many knowledge assessments from different contexts. As the knowledge about the vector, e.g. habitat and feeding habits, has not been evaluated, no comparison with previous studies can be made on this aspect.
Compared to the results of the literature search, knowledge on Chagas disease of this sample seemed to be particularly low. Only one third had ever heard of the disease before. For comparison, the results of other studies on the same question were around 60% to 90%[10,89,101,104]. Only the study from the USA showed a lower figure of around 14%[103]. One explanation for this finding could be the characteristics of the sample. Many participants had grown up in urban areas and were thus more unlikely to have had contact with the vector and the disease. A study from Argentina supports this explanation as it showed that residents from local endemic areas were generally better informed about Chagas disease than residents from local non-endemic areas[96].
Most of the symptoms reported by the respondents were acute. The participants mentioned fever and various skin reactions most frequently. More specific acute symptoms, such as the Romaña’s sign were rarely considered. This focus on acute symptoms was already noted in other studies. For example, a study from Mexico

found that far more respondents associated the bite of the triatomine bug with swelling of the skin than with other more prominent symptoms of Chagas disease[110]. This observation is probably due to the silent, asymptomatic course of the disease. However, these silent and slowly emerging manifestations such as Chagas cardiomyopathy, and not the mild unspecific symptoms like fever or skin alterations, are the ones responsible for the high global burden of Chagas disease. In addition, it cannot be ruled out that some participants have guessed the symptoms and just wrote down what came to their mind.

The focus on the vectorial transmission pathway has also been reported in other studies. This observation could be attributed to the fact that many of the control initiatives carried out in Latin America aimed at vector elimination[75]. Thus, the population had been sensitised to this one aspect of the disease, while other transmission routes faded into the background.

What is also interesting about the results is that only about a third of the respondents stated that they had heard of Chagas disease previously. However, considerably more participants answered the questions about Chagas disease knowledge and did not indicate that they did not know answers. As an example, concerning the transmission routes, about half of all respondents ticked at least one transmission pathway option. It can, therefore, be assumed that some of the participants have guessed their answers.

Using linear regression analysis, the hypothesised positive association between knowledge about the transmission pathways and age or having seen triatomine bugs in Latin America could not be confirmed. Other variables, such as rural background or sex, were not included in the final model due to lack of correlation with the dependent variable and a restriction to include more variables because of the small sample size. Only having heard about Chagas disease was positively associated with the number of correct transmission routes. However, this is not particularly surprising, since those who have never heard of Chagas disease would not know anything about the disease.

The findings contrast with the results of other studies that have found an association between the above-mentioned variables[89-92]. There may be various explanations for this: On the one hand, the sample had specific characteristics that were not seen in other studies. The survey was conducted in a well-educated, formerly urban sample

that migrated to Europe for professional or academic reasons or because of a spouse. Emigration to another country or continent is initially associated with costs. While everyone in this sample somehow had the financial resources to settle in Europe, it would probably not have been possible for all participants of the studies presented in the literature review.

It could have been more meaningful to not only differentiate between rural and urban childhood dwellings but to divide them into locally endemic and non-endemic. A rural place can be protected, for example by its altitude, from vector infestation, while urban places too can be infested[117]. However, the information on local endemicity was not available, and that is why having seen the triatomine bug was used as an indicator for vector infestation. Yet, as mentioned earlier, it is questionable that 45% of the respondents have seen the triatomine bug. It is possible that this result does not represent the true proportion, so that the use of the variable as an independent variable was problematic.

Similarly, using the dependent variable could have been problematic when assumed that some of the respondents have guessed their answers. Post hoc calculations showed that 15 participants who stated that they had never heard of Chagas' disease named at least one transmission route.

6.3. Limitations of the thesis

The results of this thesis are tied to a list of limitations that will be presented in the following. First, the limitations of the literature review will be discussed, followed by the cross-sectional survey and the data analyses.

Regarding the limitations of the literature review, one should keep in mind that the search was likely not exhaustive. More studies probably exist that could not be considered with the search of the two databases Pubmed and SciELO and the search strings used. Furthermore, only published literature was considered, excluding conference abstracts, theses, and reports, among others. Thus, the review could not present the full scope of literature which limited the generalisability of results.

Since the literature review served the purpose of providing an overview of published literature rather than synthesising evidence, and studies were too heterogeneous to quantify their results in a meaningful way, a meta-analysis was not performed.

Therefore, useful analysis techniques used in meta-analyses such as assessing statistical heterogeneity of studies or assessing publication bias with a funnel plot were not applied.

It was difficult to compare results of the different studies as various techniques of data generation were applied, and the samples in which knowledge assessments took place were very diverse. Therefore, a narrative approach was chosen, in which the overall evaluation of authors, rather than specific quantitative estimates, was focused on in the review of the literature.

Regarding the reliability of results, this thesis resulted from individual work and duplicate information retrieval and quality appraisal of studies were therefore not performed. Discussing and resolving differences or uncertainties with a second or even third reviewer, however, reduces the risk of making mistakes and the possibility of influenced assessments by a single person's biases. By expanding eligibility criteria to studies published in Spanish and Portuguese, results from endemic countries were included that otherwise would not have been. While this procedure expanded the scope of literature and enabled the inclusion of more studies from the endemic context, language barriers could have introduced errors to the content and quality assessment of studies.

As described in the sample size calculation (chapter 4.2.), the estimate-precision in the cross-sectional survey was 10%. On the one hand, this allowed for a smaller sample size to represent the population. On the other hand, comparison with results from other studies was only possible with restrictions due to this generous allowance.

Also, the representativeness of the sample needs to be addressed. As discussed before, the characteristics of the sample were not representative of the Latin American community in Hamburg. A high proportion of highly educated individuals was observed along with an overrepresentation of female and Mexican participants, as well as an underrepresentation of irregular migrants and Brazilians. The results of the knowledge assessment should, therefore, not be seen as representative for the whole Latin American community in Hamburg, nor Germany.

Another point that needs to be addressed is the questionnaire used. The application of the questionnaire revealed some weaknesses that were not considered by the German Chagas network. For example, for some questions, there was no possibility

to indicate that one did not know the answer. This was the case with the question about the symptoms of Chagas disease. A total of 72 participants did not provide any information. It can be assumed that these participants did not know what to answer, rather than refusing to answer. Firstly, this was the only open-ended question about knowledge, which made guessing difficult. Secondly, the response rates on all other questions, including those on sensitive topics such as the insurance status, were considerably higher.

This flaw, however, resulted in the loss of valuable information. It was initially planned to calculate a knowledge sum score and use it as a dependent variable in the linear regression model. For this purpose, all three Chagas disease knowledge questions were to be brought together to form a score. However, due to the many missing values, this was not done. Therefore, the focus was only on the routes of transmission. It should be mentioned, though, that the questionnaire was not specifically designed to calculate knowledge sum scores.

Some aspects of Chagas disease knowledge were not included in the questionnaire, such as knowledge about the vector. Although this information is less critical in a non-endemic context, no comparison with other studies could be made under this aspect. Knowledge about Chagas disease treatment options and where to seek help and medical attention concerning Chagas disease would have been helpful to assess. These insights could have been used to inform educational campaigns. In the case of knowledge gaps, this aspect would be important to include in the dissemination of information. However, this information could, unfortunately, not be retrieved with the present investigation.

The questionnaire also failed to distinguish between participants born in endemic and non-endemic countries. The inclusion criteria explicitly mentioned the participation of second-generation migrants. However, there was some confusion among these participants when filling in the questionnaire. As they had not lived in Latin America, they could not answer questions that addressed former living conditions in Latin America. Answer options like “Not applicable” were not given. As a result, some participants answered questions that were not addressed to them.

A further limitation of the analysis could be the revision and classification of symptoms. There was some overlap of responses with chronic and acute symptoms, as was the case with abdominal pain. In this case, it was decided in

favour of chronic symptoms even though it was not clear what the participant specifically had in mind when providing his or her answer.

Furthermore, the list of possible Chagas symptoms was based on clinical literature and thus represented expert knowledge. It was not possible to decide what a lay would know and what not. Therefore, all manifestations and possible complications identified in the literature, such as sinus node dysfunction, ventricular aneurysms, or intestinal wall perforation, were included, even if their mention was considered unlikely. Also, the language skills of the investigator may have been insufficient to interpret the subtleties of the Spanish language correctly. The potential language barrier could have restricted the reliability of the results. Furthermore, as the thesis resulted from individual work, a duplicate classification of Chagas disease symptoms could not be carried out.

Two comments on the transmission pathways must also be made. First, sexual transmission was not considered a correct route of transmission. Indications exist that this form of transmission may indeed be possible[118]. It was decided against the inclusion of this route to the list of correct transmission pathways, as it was considered unlikely that a lay would be familiar with recent scientific insights to Chagas disease.

Second, as described before, some participants responded to this question by choosing transmission pathways even though they indicated that they had never heard about Chagas disease before. It raises questions about the validity of using this variable as an indicator of Chagas disease knowledge. Indeed, the aim of the survey, namely to understand what people of Latin American origin know about Chagas disease and its consequences, was described in the information brochures for the participants. Nevertheless, a few introductory sentences in the corresponding section of the questionnaire could have reduced the number of guessed answers.

In connection with the assessment of Chagas disease knowledge, it could be that some participants had already come into contact with information flyers or announcements of the study before taking part. Particularly those participants who contacted the research group themselves for a diagnostic test have already engaged themselves with the topic. However, this would lead to an overestimation of knowledge rather than underestimation thereof.

As for the regression analysis, the violation of model assumptions needs to be addressed. Most assumptions were met, although some statistical indicators were

only rated acceptable, such as the Durbin-Watson statistic for indicating independent residuals. Due to the apparent deviation from normality that the distribution of the residuals exhibited, a violation of the normally-distributed-residuals assumption had to be noted. Findings of the regression analysis should, therefore, only be generalised beyond the sample with caution.

Another aspect is the dependent variable used in the regression analysis. The questionnaire was not specifically developed for constructing knowledge sum scores or assessing associations between the level of knowledge and socio-demographic characteristics. Due to missing data, it was decided not to create a sum score of multiple knowledge questions. Therefore, only the number of correctly cited transmission pathways was used as the dependent variable, representing only one aspect of Chagas disease knowledge. The use of this variable as an indicator of knowledge has not yet been psychometrically evaluated. Therefore, no precise statement can be made about the validity and reliability of its use.

6.4. Implications of results

Despite the many limitations of the investigation, this thesis contributes to the understanding of Chagas disease knowledge in the German context, where only very little insight on this topic exists. To date, only one study addressing Chagas disease knowledge in Latin American migrants living in Germany has been published. In addition, the description of results in that study were less rich in details and resulted from a sample confined to people of Bolivian origin only.

Besides describing the implications resulting from the Chagas disease knowledge assessment, results can also be used to describe and understand the context in which the knowledge assessment took place. Important implications for future research may arise from this aspect. In this chapter, the implications of the present investigation will be discussed concerning public health and future research.

6.4.1. Public health

Despite the limited representativeness of the sample and rather low precision of estimates, a lack of knowledge on Chagas disease can be noted. Particularly, non-vectorial transmission routes, chronic manifestations and the asymptomatic nature

of the disease were unknown to the sample. The results of knowledge assessments from varying contexts support this finding.

The lack of knowledge regarding all three aspects mentioned above has significant health implications for the individual and the public. Should someone be infected with *T. cruzi*, this person would not be able to contextualise symptoms and to link them with Chagas disease, should they occur. Furthermore, the person would not be able to assess his or her own risk of being infected, as he or she would not know how the disease is transmitted. Nor would this person seek medical attention to get tested. A qualitative study among Latin American migrants in Georgia, USA, showed that the lack of Chagas disease awareness was a critical barrier to seek medical attention and to get tested for the disease[83]. Given the lack of knowledge of the disease among many physicians, it cannot be assumed that they will offer diagnostic testing for at-risk patients.

The lack of knowledge about transmission pathways poses a risk to the health of other people, too. The pathogen could be transmitted unintentionally via blood or organ donation, or from mother to child. Considering the high proportion of undiagnosed cases, the lack of knowledge facilitates a spread of the disease through these mechanisms. The incidence of Chagas disease through non-vectorial transmission is unknown in Germany. Based on findings from other non-endemic countries it can be assumed, however, that the transmission takes place to some extent. Therefore, efforts should be made to prevent it.

To date, no screening procedures for women of childbearing age at risk of being infected nor for at-risk blood- and organ donators are carried out in Germany to prevent transmission of *T. cruzi.* The lack of knowledge combined with the absence of control and prevention measures highlights the need for educational campaigns. If screening procedures were to be implemented, as recommended by the WHO, there would be a great need for information about the disease. In this context, individuals should first be informed about the existence of the disease. Then, the consequences and ways of transmission, aspects for which the knowledge is particularly lacking, should be in focus so that individuals at-risk could then make an informed decision on whether to undergo testing. Results from Germany and Italy have shown that a vast majority of Latin American migrants would favour public information campaigns about Chagas disease[10,115].

In this thesis, it was only partially possible to identify a target population for which educational campaigns would be most beneficial. It turned out that participants who had never heard about Chagas disease reported correct transmission pathways less frequently as compared to those who had heard about the disease before. This information could be used as a filter to identify those who know the least about Chagas disease. It gives room for hope that educational campaigns could positively influence the level of knowledge in those who have never heard about the disease. Given the generally low level of knowledge, specifically concerning non-vectorial transmission pathways, it would be sensible to provide information for the whole population at risk in settings where transmissions are more like to occur.

Highlighted by the blood donation history of the sample and the high willingness to donate blood, the blood donation context would be an essential starting point. Family planning should be considered, too. Early treatment of acute and congenital Chagas disease increases the chances of a cure, which is why pregnant women should be informed about the disease and be offered testing for themselves and their newborns[72]. Moreover, diagnosing and treating Chagas disease in girls and women of childbearing age before pregnancy can prevent congenital transmission[72].

Further, those who are most vulnerable and have a higher risk of being infected would especially benefit from educational campaigns in combination with the offer to get tested. Risk factors for Chagas disease were not addressed in this study. However, other studies conducted in Europe have investigated which socio-demographic characteristics are associated with a higher chance of being infected[56,119,120]. Among others, age, Bolivian origin, former rural residence, the material of the former Latin American dwelling, familial history of Chagas disease and history of blood transfusion in endemic countries have been identified as risk factors. Also, the residence status has been identified as a dimension that must be taken into consideration[56]. Results of these studies could be used to define priority groups for screening and informational campaigns that, based on findings from this thesis, are urgently needed.

As described in chapter 2.2., and observed in this thesis as well, a considerable proportion of migrants have obtained a European nationality. Future engagements with migrants of Latin American origin living in Germany should consider the obtainment of European citizenships. It would not be sufficient to focus on the

nationality only in order to address all persons with an epidemiological risk of being *T. cruzi* infected. The country of birth and the maternal country of birth would be more useful clues.

The importance of addressing Chagas disease is emphasised with the sample's points of contact with the disease despite its rather privileged characteristics. One participant self-identified as being Chagas disease infected while some participants reported about Chagas disease infected family members and acquaintances. Around one out of 10 participants had been tested before, indicating that a physician or other health professional had previously assumed a reasonable risk of infection. A large proportion of respondents reported that they had seen the triatomine bug in their own home in Latin America. Although it is unclear how many have actually seen the vector, it must be assumed that they were exposed to a major risk factor of the disease.

It can only be assumed that in a sample with less privileged characteristics (lower education, a higher proportion of undocumented migrants), the points of contact and direct experiences with Chagas disease would be even more frequent and measures to prevent and control the disease would be needed more urgently.

6.4.2. Future research

Several recommendations for future research evolve from this thesis. To verify the findings of this study, more data is needed. In order to do this, optimised knowledge assessments should be carried out among representative samples of Latin American migrants, also living in other parts of Germany. Validated knowledge assessment instruments should be used to ensure the validity and reliability of the measurement.

Other recruitment strategies should be explored that increase the representativeness of samples. It should specifically be aimed for the inclusion and representation of irregular migrants. Irregular migrants play a vital role in the context of Chagas disease due to their marginalisation and limited access to health care services[56,113,121]. To date, this population group has not been included in investigations related to Chagas disease in Germany. Neither prevalence estimates, nor data about access to health care or Chagas disease knowledge are available for Latin American irregular migrants living in Germany. As it was not possible to

provide insights on this aspect with this thesis, it should be a priority to address this knowledge gap in future research.

It has been pointed out in previous studies, that Chagas disease poses a specific challenge to public health. A disease-centred public health approach such as a relying on screening strategies might be insufficient when dealing with uncertain situations such as the incomplete statistical data and the lacking awareness of the disease among health professionals on the one side, and migrants on the other[122]. Moreover, limited access to health care services among migrants limits the usefulness of screening procedures only. This thesis was one of the first steps towards elucidating other aspects of Chagas disease beyond its distribution and proliferation in Germany. While it was possible with this thesis to make statements about the knowledge characteristics of the respondents, it was not possible to investigate how this knowledge, or the lack of it, affected health behaviour and prevention practices. Multidisciplinary approaches with both qualitative and quantitative components, bringing together expertise from social sciences, epidemiology and other disciplines are needed to do this.

To further understand the distribution of Chagas disease and the circumstances in which it exists, and to control Chagas disease in the non-endemic context, more insights on the social representation and stigmatisation of the disease, barriers to seeking medical attention and perceived needs and priorities of Latin American migrants are needed.

A group that is important to consider, but was not addressed in this thesis, are physicians and health professionals who treat and engage with people of Latin American origin. General practitioners, for instance, are often an important contact person for patients regarding their health. Their knowledge about Chagas disease would likewise have been interesting and important to evaluate. However, since the focus of this thesis was directed towards the Latin American community, conclusions can only be drawn for this group. Therefore, future research should also consider assessing the knowledge about Chagas disease among health professionals treating patients at epidemiological risk of being *T. cruzi* infected.

7. Conclusion

This thesis pursued three objectives. These were to provide an overview of the literature on Chagas disease knowledge in populations at risk of being infected or infected populations, to assess the knowledge on Chagas disease among the Latin American community in Hamburg, and to identify socio-demographic characteristics associated with the knowledge about Chagas disease.

In brief, the literature review performed showed that a majority of studies reported a lack of Chagas disease knowledge. Mainly, non-vectorial transmission pathways and the manifestations of the disease were not understood well.

Similar results arose from the survey conducted within the Latin American community in Hamburg. Only half of the respondents were able to name a correct transmission pathway. Moreover, the majority of them focused on vectorial transmission. Also, a focus on acute Chagas disease symptoms, rather than the severe chronic symptoms, or absence of symptoms, was observed. Linear regression analysis revealed that having heard about Chagas disease previously was positively associated with reporting correct Chagas disease transmission pathways. An association with other characteristics such as age could not be confirmed.

Despite its many limitations, including the limited representativeness of the sample and the resulting limited generalisability of results, this thesis generated valuable insights on Chagas disease knowledge that have not been presented in same depth in Germany before. Although these initial results would need to be repeated and confirmed in other studies, the observed lack of knowledge about non-vectorial transmission pathways points to an important issue. Because of the possibility of non-vectorial transmission, this knowledge gap should be addressed. Also, the limited understanding of Chagas disease symptomology should be considered in information campaigns. Knowing the course and consequences of a disease helps to understand its severity and to take preventive action. Information campaigns alongside the provision of diagnostic testing could not only be a useful instrument to inform about the disease but also to raise awareness and promote reflection and action and to help control Chagas disease.

These campaigns could either focus on the whole population with an epidemiological risk or concentrate on settings where the transmission can occur, e.g., family planning or blood donation settings. More representative and

multidisciplinary studies are needed to understand the socio-cultural context of Chagas disease in Germany better.

8. References

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Statutory Declaration

I hereby declare that I wrote this thesis without any assistance and used only the aids listed. Any material taken from other works, either as a quote or idea have been indicated under ‘References‘.

_____ _____

Place, Date Signature

9. Appendices

Appendix 1

Search string of the literature review

Pubmed

((knowledge[Title/Abstract] OR attitude[Title/Abstract] OR perception[Title/Abstract] OR awareness[Title/Abstract] OR familiar*[Title/Abstract]) AND (chagas[Title] OR “trypanosoma cruzi” [Title] OR “T. cruzi” [Title] OR “american trypanosomiasis” [Title]))

SciELO

((knowledge) OR (conocimiento) OR (conhecimento) OR (attitude) OR (actitud) OR (atitude) OR (perception) OR (percepción) OR (percepção) OR (awareness) OR (conciencia) OR (consciência) OR (familiarity) OR (familiaridad) OR (familiaridade)) AND ((ti:(chagas)) OR (ti:(trypanosoma cruzi)) OR (ti:(t. cruzi)) OR (ti:(american trypanosomiasis)) OR (ti:(tripanosomosis americana)) OR (ti:(tripanossomíase americana)))

Appendix 2

Survey questionnaire developed by ELCiD

Número de participante (llenado por el

ELCiD (Erkennung und Lenkung von Chagas-Patienten in Deutschland (ELCiD)/ Querschnittstudie)

Proyecto alemán de Chagas
Cuestionario sobre la enfermedad de Chagas en Alemania

Estimado(a) Participante,
Uno de los objetivos del estudio de Chagas, es mejorar la atención médica en Alemania para inmigrantes o personas con riesgo para la enfermedad de Chagas. Para esto requerimos información acerca de su persona y de los conocimientos que Usted tiene sobre el Chagas. En el contexto de nuestra oferta de asesoramiento y de la prueba de Chagas, le solicitamos contestar algunas preguntas.
Su información se mantendrá estrictamente confidencial y estrictamente por separado de su información personal (por ejemplo, nombre, fecha de nacimiento). La evaluación se realiza exclusivamente de manera estadística. De esta manera ninguna conclusión sobre datos y personas individuales será posible.
¡Le agradecemos su ayuda!

1. Su sexo es ☐ **masculino** ☐ **femenino**

2. Año de nacimiento _____

3. País de nacimiento: _____ **4. Cuidad de nacimiento:** _____

5. Nacionalidad: _____ **6. Idioma materno:**_____

7. ¿En qué año llegó a Europa? _____

8. ¿Cual fue la razón por su traslado/ mudanza a Europa?

☐ trabajo ☐ estudios ☐ matrimonio/pareja ☐ familia vive en Europa
☐ otras razones, que son (9) _____

10. ¿En qué país pasó la mayor parte de su infancia? _____

11. ¿En qué ciudad pasó la mayor parte de su infancia? _____

12. ¿En qué país/ ciudad fue su último domicilio antes de trasladarse a Europa?

país: _____ ciudad/región (13) :_____

14. ¿En qué lugar de Latinoamérica pasó la mayor parte de su infancia?

☐ En la ciudad (más de 10.000 habitantes)
☐ En el campo (menos de 10.000 habitantes)

15. Su último domicilio en Latinoamérica fue....

☐ En la ciudad (más de 10.000 habitantes)
☐ En el campo (menos de 10.000 habitantes)

16. ¿De qué material fue construida la casa en que pasó su infancia?

☐ piedra/concreto/ cemento ☐ adobe/ barro ☐ madera
☐ otros materiales de construcción

17. ¿De qué material fue construida la casa de su último domicilio en Latinoamérica?

☐ piedra/concreto/ cemento ☐ adobe/ barro ☐ madera
☐ otros materiales de construcción

18. ¿Ha visto alguna vez en su domicilio un insecto llamado chinche (o vinchuca, barbeiro, chirimacha, pito, chichâ...)?

☐ sí ☐ no

19. ¿Cuántos hijos tiene? _____

20. ¿Cuál es su máximo nivel de educación?

☐ Ningún título escolar ☐ primaria ☐ secundaria ☐ formación técnica
☐ formación universitaria

21. ¿Cuál es el máximo nivel de educación de sus padres?

☐ Ningún título escolar ☐ primaria ☐ secundaria ☐ formación técnica

☐ formación universitaria

22. ¿Ha escuchado de la enfermedad de Chagas en su país?

☐ Sí ☐ no

23. ¿Cuáles son las molestias que la enfermedad de Chagas puede causar?
Por favor mencione las tres más frecuentes

1._____

2._____

3._____

24. ¿Cómo se transmite la enfermedad de Chagas?
(por favor marque todas las maneras de transmisión que conoce)

☐ Por un chinche (vinchuca)
☐ Por relaciones sexuales
☐ Por una transfusión de sangre
☐ Por una picadura de zancudo
☐ Por un transplante de órganos
☐ Por beber jugo de caña
☐ Durante el nacimiento de la madre al bebé
☐ Por contacto físico con personas infectadas
☐ No conozco las maneras de transmisión

25. ¿Hay personas que se sienten bien aunque están infectadas con la enfermedad de Chagas?

☐ sí ☐ no ☐ no sé

26. ¿Alguien de su familia cercana padece/padeció de la enfermedad de Chagas? (padres, abuelos, hermanos, niños)

☐ Sí, es mi (27) _____ ☐ no ☐ no sé

28. ¿Conoce a personas de su lugar de residencia en Latinoamérica con la enfermedad de Chagas?

☐ sí ☐ no

29. ¿Podría imaginarse donar sangre en el futuro?

☐ sí ☐ no ☐ no sé

30. ¿Ha donado sangre alguna vez?

☐ sí, en el siguiente país (31) _____ en el año (32) _____

☐ no

33. ¿Ha recibido una transfusión de sangre alguna vez?

☐ sí, en el siguiente país (34) _____en el año (35) _____

☐ no

36. ¿Podría imaginarse donar sus órganos después de su muerte?

☐ sí ☐ no ☐ no sé

37. ¿Le han hecho una prueba de Chagas alguna vez?

☐ Sí, en el año (38) _____

(39) el resultado dio ☐ positivo ☐ negativo

☐ no

40. Si el resultado fue positivo, ¿recibió algún tratamiento para la enfermedad de Chagas?

☐ sí, en el siguiente país (41): _____ en el año (42) _____

con el siguiente medicamento (43) _____

☐ no

44. Si ha padecido de la enfermedad de Chagas alguna vez, ¿cuáles molestias ha tenido/tiene?

1. _____

2._____

3._____

45. ¿Padece de una enfermedad al corazón?

☐ sí ☐ no

46. Si padece de una enfermedad al corazón, ¿cuáles molestias tiene?

1._____

2._____

3._____

47. Si padece de una enfermedad al corazón, ¿cuál es el nombre de su enfermedad?

1._____

2._____

3._____

48. ¿Padece de una enfermedad al tracto digestivo (estómago, esófago, intestino)**?**

☐ sí ☐ no

49. Si padece de una enfermedad al tracto digestivo, ¿cuáles molestias tiene?

1._____

2._____

3._____

50. Si padece de una enfermedad al tracto digestivo, ¿cuál es el nombre de su enfermedad?

1._____

2._____

3._____

51. ¿Usted personalmente siente que su atención médica en Alemania es suficiente?

☐ sí, ya que no tengo problemas con el acceso a la atención médica

☐ sí, pero tengo algunos problemas para acudir a servicios médicos

☐ no, porque tengo grandes dificultades para obtener servicios médicos

52. ¿Qué seguro médico tiene usted en Alemania?

☐ seguro alemán obligatorio o privado

☐ seguro para estudiantes

☐ seguro extranjero

☐ no tengo seguro médico

Appendix 3

List of Chagas disease symptoms and outcomes and related references

Chronic Chagas disease, Asymptomatic[1]

Asymptomatic (not having/causing symptoms)

Chronic Chagas disease, affecting the heart[1]

General lay terms

Heart problems

Large/ big heart

Heart failure (heart cannot pump enough blood)

Dilated cardiomyopathy (enlargement of left/right/both ventricles, big/large heart)

Abnormalities of systolic function (impaired emptying of the left ventricle/ heart)

Abnormalities of diastolic function (impaired filling of the left ventricle/ heart)

Ventricular aneurysm (outward bulging and deformation of the heart muscle)

Dyspnea (shortness of breath)

Peripheral oedema (accumulation of fluid, swelling, usually of the lower limbs)

Fatigue (tiredness, lack of energy)

Chest pain (pain in the heart)

Arrhythmia (problem with the heart rate, problem with the heart rhythm)

Sinus node dysfunction (unnormal impulses/signals impaired heart rhythm control)

Bradyarrhythmia (slow heart rate)

Tachyarrhythmia (fast heart rate)

Palpitations (sensation that the heart is racing)

Presyncope (sensation of being about to pass out)

Syncope (loss of consciousness)

Aborted sudden death (unexpected/ sudden death due to cardiac causes/ heart problems, the heart stops beating)

Thromboembolic events (blockage-causing piece of material, inside a blood vessel)

Stroke

Pulmonary or systemic emboli

Chronic Chagas disease, affecting the digestive tract[2]

General lay terms

Problems with the digestive tract/ digestive system

Digestion problems

Megaoesophagus (enlargement of the oesophagus)

Dysphagia (difficulties with swallowing)

Odynophagia (painful swallowing)

Regurgitation (bringing swallowed food up to the mouth again)

Weight loss

Aspiration (sucking/ breathing in food/foreign object into the airways)

Heartburns

Hiccups

Cough

Ptyalism (excessive saliva)

Constipation

Megacolon (enlargement of the colon)

(Chronic) constipation

Abdominal cramps (stomach ache, stomach pain, stomach cramps)

Abdominal distention (accumulation of gas/ fluids)

Scybalous-type faeces (hardened stool)

Volvulus (loop of intestine twisted around itself)

Faecaloma or faecal impaction (mass of hardened, impacted faeces)

Colonic perforation (puncture/ tear/ hole in the wall of the colon/intestine)

Bowel ischaemia (impaired blood flow to bowel/intestines)

Other enlarged viscera (enlarged internal organs)

Megagastria (enlarged stomach)

Megaduodenum (enlarged duodenum, the first part of the intestine)

Megajejunum (enlarged jejunum, the middle section of the small intestine)

Dilated gallbladder (widened gallbladder)

Urinary tract dilations (widened urinary tract)

Acute Chagas disease (vectorial)[3,4]

Parasite entry/ skin reactions to bite

Romañas sign (painful oedema/swelling on eyelids)

Chagoma (oedema/swelling at the bite site)

Skin redness

Itching

Hives

Systemic infection

Facial and limb oedema (swelling of face, arms and legs)

Fever

Restlessness

Hyporexia (decreased appetite)

Somnolence (drowsiness, sleepiness)

Asthenia (physical weakness, lack of energy)

Malaise (general discomfort)

Vomiting

Diarrhoea (loose stool)

Signs of bronchitis

Headache

Ocular pain (eye pain)

Myalgia (muscle pain)

Arthralgia (joint pain)

Hepatosplenomegaly (enlargement of liver and spleen)

Cardiac involvement

Tachycardia (fast heart rate)

Hypotension (low blood pressure)

Acute Chagas disease (oral)[5]

Fever

Headache

Facial and limb oedema

Abdominal pain (stomach ache, stomach pain)

Myalgia (muscle pain)
Arthralgia (joint pain)
Myocarditis (inflammation of the heart/ heart muscle)
Chest pain
Cardiac tamponade (accumulation of fluid in the pericardium (sac around the heart))
Arrhythmia
Palpitations (sensation that the heart is racing)
Dyspnea (shortness of breath)
Cardiomegaly (enlarged heart)
Heart failure (heart cannot pump enough blood)

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Appendix 4

Categorisation of participant responses concerning Chagas disease symptoms

Participant response	English translation	Category	Subcategory
Arritmia del Corazón cuando la enfermedad esta avanzanda	Heart arrhythmia when the disease is advancing	Chronic, affecting the heart	Arrhythmia
Arritmias cardiacas	Cardiac arrythmia	Chronic, affecting the heart	Arrhythmia
Arritmia	Arrhythmia	Chronic, affecting the heart	Arrhythmia
Arritmias	Arrhythmia	Chronic, affecting the heart	Arrhythmia
Dolor de pecho	Chest pain	Chronic, affecting the heart	Chest pain
Dolor de corazon	Pain in the heart	Chronic, affecting the heart	Chest pain
Dolor en el pecho	Chest pain	Chronic, affecting the heart	Chest pain
Dolor en el pecho, Palipitaciones	Chest pain, heart palpitations	Chronic, affecting the heart	Chest pain
Tot	Death	Chronic, affecting the heart	Death
Muerte	Death	Chronic, affecting the heart	Death
Fatiga	Fatigue	Chronic, affecting the heart	Fatigue
Languidez	Langour	Chronic, affecting the heart	Fatigue
Fatiga (al Caminar)	Fatigue, while walking	Chronic, affecting the heart	Fatigue
Fase crónica: Desmayos	Chronic phase: fainting	Chronic, affecting the heart	Fainting
Al corazón	Affects the heart	Chronic, affecting the heart	Affects the heart
Ataca al corazón	Attacks the heart	Chronic, affecting the heart	Affects the heart
Ataca al corazón	Affects the heart	Chronic, affecting the heart	Affects the heart
Afecta al corazón	Affects the heart	Chronic, affecting the heart	Affects the heart
Problemas en el corazon	Heart problems	Chronic, affecting the heart	Heart problems
Problemas de corazón	Heart problems	Chronic, affecting the heart	Heart problems
Problemas cardiacos	Heart problems	Chronic, affecting the heart	Heart problems
Herzprobleme	Heart problems	Chronic, affecting the heart	Heart problems
Sintomas/ Problemas del Corazon	Heart problems/ Heart symptoms	Chronic, affecting the heart	Heart problems
Herzproblem	Heart problems	Chronic, affecting the heart	Heart problems
Dolor abdominal	Abdominal pain	Chronic, affecting the digestive tract	Abdominal pain

Dolor de estomago	Stomach aches	Chronic, affecting the digestive tract	Abdominal pain
Estreñimiento	Constipation	Chronic, affecting the digestive tract	Constipation
Dificultades para tragar, comer	Difficulties with swallowing/ with eating	Chronic, affecting the digestive tract	Difficulties with swallowing
Problemas del aparato digestivo	Digestive system problems	Chronic, affecting the digestive tract	Problems with digestive system
Problemas del tracto digestivo	Problems with the digestive tract	Chronic, affecting the digestive tract	Problems with digestive system
No tiene sintomas	Not having symptoms	Chronic, asymptomatic	
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
fiebres	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre (momento agudo)	Fever (acute phase)	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Fiebre	Fever	Acute	Fever
Sarpullido	Rash	Acute	Skin irritation
Picazón	Itchiness	Acute	Skin irritation
Ronchas?	Hives	Acute	Skin irritation
Picadura	Bite	Acute	Skin irritation
Enrojecimiento	Flushing	Acute	Skin irritation
Manchas en la piel	Spots on the skin	Acute	Skin irritation
Augen Anschwellen(Anfang)	Eyes swell (Beginning)	Acute	Romaña's sign
Hinchazon	Swelling	Acute	Chagoma
Dolor de Cabeza	Headaches	Acute	Headaches
Dolor cabeza	Headaches	Acute	Headaches
Dolor de cabeza	Headaches	Acute	Headaches
Dolor de cabeza	Headaches	Acute	Headaches
Malestar	Discomfort	Acute	General discomfort
Malestar general	General discomfort	Acute	General discomfort
Bazo agrandado	Enlarged spleen	Acute	Enlarged spleen
Dolor muscular	Muscular pain	Acute	Muscular pain
Dolor muscular	Muscular pain	Acute	Muscular pain
Infecta la Sangre	Infects the blood	Acute	Seropositivity
Diarrhia - Durchfall	Diarrhea	Acute	Diarrhea
Inflamación	Inflammation	Unspecific	
Dolores	Pain	Unspecific	

Infección	Infection	Unspecific	
Distrofia muscular	Muscular dystrophy	Untypical	
no se	Don't know	"Don't know"	
ni idea	No idea	"Don't know"	
No sé	Don't know	"Don't know"	
ni idea	No idea	"Don't know"	
no sé	Don't know	"Don't know"	
...	...	Unreadable	
.... en la picadura	... in the bite	Unreadable	
Dolor de ...	... pain	Unreadable	
....		Unreadable	

Table A4. Categorisation of participant responses concerning Chagas disease symptoms

Appendix 5

SPSS syntax of statistical analysis

```
*****CREATING NEW VARIABLES.
*create new variable, age.
COMPUTE Age=2019-birth_year.
EXECUTE.

*create new variable, years lived in Europe.
COMPUTE years_europe=2019-arr_year.
EXECUTE.

*create new variable, having or not having children.
RECODE num_children (1 thru 10 =1) (SYSMIS=SYSMIS) (ELSE=0) INTO children_di.
VARIABLE LABELS children_di "Having children".
EXECUTE.

*create new variable, counting missing data for the question about transmission pathways.
DO IF  (transmission_9 = 0).
COUNT missing_trans=transmission_1 transmission_2 transmission_3 transmission_4
transmission_5 transmission_6 transmission_7 transmission_8(0).
VARIABLE LABELS  missing_trans 'Missing information on transmission pathways (no boxes
ticked)'.
END IF.
EXECUTE.

FREQUENCIES VARIABLES=missing_trans
/BARCHART FREQ
/ORDER ANALYSIS.

RECODE missing_trans (8=1) (SYSMIS=0) (1 thru 7=0).
EXECUTE.

*create new variable, sum score variable of correct answers related to transmission pathways.
COMPUTE
trans_num_correct=SUM(transmission_1,transmission_3,transmission_5,transmission_6,transmiss
ion_7).
VARIABLE LABELS trans_num_correct 'Sum of correct answers given to question about
transmission pathways'.
EXECUTE.
```

```
DO IF (missing_trans = 1).
RECODE trans_num_correct (0=SYSMIS).
END IF.
EXECUTE.

*create new variable, sum score variable of wrong answers related to transmission pathways.
COMPUTE trans_num_wrong=SUM(transmission_2,transmission_4,transmission_8).
VARIABLE LABELS trans_num_wrong 'Sum of incorrect answers given to question about
transmission pathways'.
EXECUTE.
DO IF (missing_trans = 1).
RECODE trans_num_wrong (0=SYSMIS).
END IF.
EXECUTE.

*create new variable, sum of any transmission pathway reported.
COMPUTE
trans_num=SUM(transmission_1,transmission_3,transmission_5,transmission_6,transmission_7,tr
ansmission_2,transmission_4,transmission_8).
VARIABLE LABELS trans_num 'Sum of all answers given to question about transmission
pathways'.
EXECUTE.

*create new variables, symptoms_1_cat, symptoms_2_cat and  symptoms_3_cat were created
manually, by assessing the content of the string variables symptoms_1, symptoms_2 and
symptoms_3 ({1, Chronic, affecting the heart, 2, Chronic, affecting the digestive system, 3, Chronic
asymptomatic, 4, Acute, 5, General, 6, Atypical, 7, Don’t know, 8, Unable to read}.

*create new variable, counting missing data for reported Chagas disease symptoms.
COUNT missing_symptoms=symptoms_1_cat symptoms_2_cat symptoms_3_cat(SYSMIS).
VARIABLE LABELS  missing_symptoms 'Number of missing answers to Chagas disease
symptoms'.
EXECUTE.
RECODE missing_symptoms (3=1) (1 thru 2=0).
EXECUTE.

*create new variable, counting number of Chagas disease symptoms reported.
COUNT num_symptoms=symptoms_1_cat symptoms_2_cat symptoms_3_cat(1 2 3 4 5 6).
VARIABLE LABELS  num_symptoms 'Number of Chagas disease symptoms reported'.
EXECUTE.
```

```
COUNT num_answer=symptoms_1_cat symptoms_2_cat symptoms_3_cat(1 2 3 4 5 6 7 8).
VARIABLE LABELS  num_answer 'Number of reported answer to Chagas disease symptoms'.
EXECUTE.

*create new variable, chronic Chagas disease symptom reported.
COMPUTE symptoms_chronic=0.
VARIABLE LABELS symptoms_chronic 'Chronic symptom of Chagas disease reported'.
EXECUTE.
If symptoms_1_cat < 4 OR symptoms_2_cat < 4 OR symptoms_3_cat < 4 symptoms_chronic = 1.
EXECUTE.

*create new variable, acute chagas disease symptom reported.
COMPUTE symptoms_acute=0.
VARIABLE LABELS symptoms_acute 'Acute symptom of Chagas disease reported'.
EXECUTE.
If symptoms_1_cat = 4  OR symptoms_2_cat = 4 OR symptoms_3_cat = 4 symptoms_acute = 1.
EXECUTE.

*create new variable, question about Chagas disease asymptomacy, dichotomised (correct=1, not
correct=0).
RECODE feel_well (1=1) (SYSMIS=SYSMIS) (2 thru 3=0) INTO feel_well_dicho.
VARIABLE LABELS  feel_well_dicho 'Are there people who feel well even though they are infected
with Chagas disease? (Dichotomised)'.
EXECUTE.

*create new variable, missing data for question about Chagas disease asymptomacy.
RECODE feel_well (SYSMIS=1) (ELSE=0) INTO missing_feel_well.
EXECUTE.
VARIABLE LABELS  missing_feel_well 'Missing data for question about Chagas disease
asymptomacy'.

*****DESCRIPTIVES.
*descriptives of sex, country of birth, participants' education, participants' parents' education, health
insurance status.
FREQUENCIES VARIABLES=sex birth_country edu edu_par insurance
  /BARCHART FREQ
  /ORDER=ANALYSIS.

*desciptives of female participants having at least one child.
```

```
CROSSTABS
  /TABLES=sex BY children_di
  /FORMAT=AVALUE TABLES
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

*descriptives of intention to donate blood and organs.
FREQUENCIES VARIABLES= don_organ don_future don_blood don_country
  /ORDER=ANALYSIS.

*descriptives of risk factors: dwelling during childhood, material of housing during childhood, last residence, material of last residence, blood transfusion received, blood transfusion received in endemic country, knows infected familiy member in LA residence.
FREQUENCIES VARIABLES=child_place child_mat last_res last_res_mat transf_endem trans chagas_fam chagas_mem1
  /BARCHART FREQ
  /ORDER=ANALYSIS.

*descriptives and histogram of Age and years living in Europe.
FREQUENCIES VARIABLES=Age years_europe
  /STATISTICS=STDDEV RANGE MINIMUM MAXIMUM MEAN MEDIAN
  /HISTOGRAM NORMAL
  /ORDER=ANALYSIS.

*descriptives of Chagas disease familiarity (seen a chinche, heard about Chagas, knows about infected people in former Latin American residence, being tested for CD, test result).
FREQUENCIES VARIABLES= chinche heard_chagas chagas_res test test_result
  /BARCHART FREQ
  /ORDER=ANALYSIS.

*frequencies related to question whether Chagas disease patients can feel well.
FREQUENCIES VARIABLES= feel_well
  /BARCHART FREQ
  /ORDER=ANALYSIS.

*frequency of correct and incorrect answers to transmission pathways, and symptoms.
FREQUENCIES VARIABLES= num_symptoms num_anwer trans_num_wrong trans_num_correct
/STATISTICS=STDDEV MINIMUM MAXIMUM MEAN MEDIAN MODE
/BARCHART FREQ
/ORDER=ANALYSIS.
```

```
CROSSTABS
  /TABLES=trans_num BY heard_chagas
  /FORMAT=AVALUE TABLES
  /CELLS=COUNT ROW COLUMN TOTAL
  /COUNT ROUND CELL.

*frequency of answers by symptom category, chronic, affecting the heart & chronic, affecting the digestive system.
TEMPORARY.
SELECT IF symptoms_1_cat=1.
Frequencies Variables = symptoms_1.

TEMPORARY.
SELECT IF symptoms_2_cat=1.
Frequencies Variables = symptoms_2.

TEMPORARY.
SELECT IF symptoms_3_cat=1.
Frequencies Variables = symptoms_3.

TEMPORARY.
SELECT IF symptoms_1_cat=2.
Frequencies Variables = symptoms_1.

TEMPORARY.
SELECT IF symptoms_2_cat=2.
Frequencies Variables = symptoms_2.

TEMPORARY.
SELECT IF symptoms_3_cat=2.
Frequencies Variables = symptoms_3.

*frequency of answers by symptom category, acute.
TEMPORARY.
SELECT IF symptoms_1_cat=4.
Frequencies Variables = symptoms_1.

TEMPORARY.
SELECT IF symptoms_2_cat=4.
```

```
Frequencies Variables = symptoms_2.

TEMPORARY.
SELECT IF symptoms_3_cat=4.
Frequencies Variables = symptoms_3.

*****GRAPHS.
*Barchart for Nationality, chart builder.
GGRAPH
  /GRAPHDATASET NAME="graphdataset" VARIABLES=nationality COUNT()[name="COUNT"]
MISSING=LISTWISE
    REPORTMISSING=NO
  /GRAPHSPEC SOURCE=INLINE.
BEGIN GPL
  SOURCE: s=userSource(id("graphdataset"))
  DATA: nationality=col(source(s), name("nationality"), unit.category())
  DATA: COUNT=col(source(s), name("COUNT"))
  GUIDE: axis(dim(1), label("Nationality"))
  GUIDE: axis(dim(2), label("Frequency"))
  SCALE: linear(dim(2), include(0))
  ELEMENT: interval(position(nationality*COUNT), shape.interior(shape.square))
END GPL.

*Barchart for reasons moving to Europe, creating graph from table.
MULT RESPONSE GROUPS=$europe_move 'Reasons for moving to Europe' (move___1
move___2 move___3
    move___4 move___5 (1))
  /FREQUENCIES=$europe_move.

*Level of education participants and parents, creating a graph from table.
CTABLES
  /VLABELS VARIABLES=edu edu_par DISPLAY=LABEL
  /TABLE edu [COUNT F40.0] + edu_par [COUNT F40.0]
  /CLABELS ROWLABELS=OPPOSITE
  /CATEGORIES VARIABLES=edu edu_par ORDER=A KEY=VALUE EMPTY=INCLUDE
  /CRITERIA CILEVEL=95.

*Table for frequency of symptoms, creating graph from table.
MULT RESPONSE GROUPS=$freq_symptoms 'Frequency of reported symptoms'
(symptoms_1_cat symptoms_2_cat symptoms_3_cat (1,8))
```

```
  /FREQUENCIES=$freq_symptoms.

MULT RESPONSE GROUPS=$freq_heart 'Frequency of reported symptoms related to chronic
cardiac Chagas disease' (heart_cat_1 heart_cat_2  heart_cat_3 (1,7))
  /FREQUENCIES=$freq_heart.

MULT RESPONSE GROUPS=$freq_digest 'Frequency of reported symptoms related to chronic
digestive Chagas disease' (digest_cat_1 digest_cat_2  digest_cat_3 (1,4))
  /FREQUENCIES=$freq_digest.

MULT RESPONSE GROUPS=$freq_acute 'Frequency of reported symptoms related to acute
Chagas disease' (acute_cat_1 acute_cat_2  acute_cat_3 (1,10))
  /FREQUENCIES=$freq_acute.

**Barchart for frequency of transmission pathways reported.
CTABLES
  /VLABELS VARIABLES=transmission_1 transmission_2 transmission_3 transmission_4
transmission_5 transmission_6 transmission_7 transmission_8 transmission_9
    DISPLAY=LABEL
  /TABLE transmission_1 [COUNT F40.0] + transmission_2 [COUNT F40.0] + transmission_3
[COUNT F40.0] + transmission_4 [COUNT F40.0] + transmission_5 [COUNT F40.0] +
transmission_6 [COUNT F40.0] + transmission_7 [COUNT F40.0] + transmission_8 [COUNT
F40.0] + transmission_9 [COUNT F40.0]
  /CLABELS ROWLABELS=OPPOSITE
  /CATEGORIES VARIABLES=transmission_1 transmission_2 transmission_3 transmission_4
transmission_5 transmission_6 transmission_7 transmission_8 transmission_9
ORDER=A KEY=VALUE EMPTY=INCLUDE
  /CRITERIA CILEVEL=95.

***** MULTIPLE LINEAR REGRESSION.
*linear regression with number of correct transmission pathways as dependent variable.

CORRELATIONS
  /VARIABLES=Age sex chinche child_place heard_chagas trans_num_correct
  /PRINT=TWOTAIL NOSIG
  /MISSING=PAIRWISE.

GRAPH
  /SCATTERPLOT(BIVAR)=Age WITH trans_num_correct
  /MISSING=LISTWISE.
```

```
ONEWAY trans_num_correct BY chinche
  /STATISTICS HOMOGENEITY
  /MISSING ANALYSIS.

ONEWAY trans_num_correct BY heard_chagas
  /STATISTICS HOMOGENEITY
  /MISSING ANALYSIS.

REGRESSION
  /DESCRIPTIVES MEAN STDDEV CORR SIG N
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS CI(95) R ANOVA COLLIN TOL CHANGE ZPP
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT trans_num_correct
  /METHOD=ENTER Age chinche heard_chagas
  /PARTIALPLOT ALL
  /SCATTERPLOT=(*ZRESID ,*ZPRED) (*SRESID ,*ZPRED)
  /RESIDUALS DURBIN HISTOGRAM(ZRESID) NORMPROB(ZRESID)
  /CASEWISE PLOT(ZRESID) OUTLIERS(2)
  /SAVE PRED ZPRED ADJPRED MAHAL COOK LEVER ZRESID DRESID SDRESID SDBETA
SDFIT COVRATIO.

SUMMARIZE
  /TABLES=MAH_1 COO_1 LEV_1 COV_1 SDB0_1 SDB1_1 SDB2_1 SDB3_1
  /FORMAT=VALIDLIST NOCASENUM TOTAL
  /TITLE='Case Summaries'
  /MISSING=VARIABLE
  /CELLS=COUNT MIN MAX MEAN.

GRAPH
  /SCATTERPLOT(BIVAR)=Age WITH ZRE_1
  /MISSING=LISTWISE.

GRAPH
  /SCATTERPLOT(BIVAR)=chinche WITH ZRE_1
  /MISSING=LISTWISE.

GRAPH
```

```
/SCATTERPLOT(BIVAR)=heard_chagas WITH ZRE_1
/MISSING=LISTWISE.
```

Appendix 6

Characteristics and results of studies of the literature review

Author, Year	Country	Study design	Study setting	Sample size	Participants	CD familiarity	Transmission knowledge instrument	Vector knowledge instrument	Clinical knowledge instrument	Knowledge sum score instrument
Ávila Montes et al, 1998[100]	Honduras	CS	1: Rural + endemic + prior control activities; 2: Rural + endemic + no control activities	1: n = 682 2: n = 167	Community members	Heard about CD	Any transmission pathway	Recognition; Habitat; Feeding habit	Any CD symptom	NA
Crocco et al., 2013[93]	Argentina	CS	1: Rural + endemic 2: Urban + endemic	1: n = 29 2: n = 70	Teachers	Personal definition of CD	Any transmission pathway	Habitat; Feeding habits	CD affects the heart; Parasites cause CD	OLK with 25 notions; range 0 - 100 points; Vector + transmission + clinical knowledge
Dias et al., 2016[92]	Brazil	CS	Urban + rural + endemic + No, low, medium, and high infestation	n = 583	Community members	Heard about CD; Seen vector; Knowing someone with CD	Vectorial	Recognition; Measures to avoid infestation	Organs affected by CD	NA
Donovan et al., 2014[101]	Honduras	CS	Rural + endemic	n = 177	Clinic attendees	Heard about CD; Family member with CD	Vectorial; Blood; Congenital; Organ transplant	NA	Possibility to have CD and not know it; Perceived severity	NA
Genero et al., 2018[97]	Argentina	PPS	Urban + endemic + pre-intervention	n = 621	Heads of household	NA	Vectorial; Congenital	Recognition; Habitat; Feeding habits	CD affects the heart	OLK with 15 notions; Vector + transmission + clinical knowledge; 0-4 low; 5-9 medium; 10-15 high
Hurtado et al., 2014[102]	Panama	CS	Rural + endemic	n = 201	Community members	Heard about CD	Vectorial; Faeces; Ingestion	Recognition; Habitat; Feeding habits	Any CD symptom; CD affects the heart	OLK with 9 notions; Transmission + clinical + vector biology knowledge ≤ 60% very poor; 61-70% poor; 71-80% medium; 81-90% good; 91-100% optimal
Manrique et al., 2011[104]	Colombia	CS	Rural + urban endemic	n =154	Pregnant women + CD seronegative	Name of CD	Vectorial; Blood; Congenital; Ingestion	Recognition; Habitat; Feeding habits	CD affects the heart; CD affects the digestive system	OLK with 15 notions; Vector + transmission + clinical knowledge; 0-3 insufficient; 4-7 low; 8-11 medium; 12-15 optimal
Mundaray et al., 2013[105]	Venezuela	CS	Rural + urban + endemic	n = 90	CD screening participants	Definition of CD	Vectorial; Congenital; Ingestion; Blood	Habitat	CD causes fever; CD causes cardiomyopathy	OLK with 10 notions; Vector + transmission + clinical knowledge; 0-3 low; 4-8 medium; 9-10 high

Navarro et al., 2017[10]	Germany	CS + QC	Urban + non-endemic (Germany)	n = 43	Bolivian migrants in Germany	Heard about CD; Family member with CD	Vectorial; Blood; Organ transplant; Congenital; Ingestion	NA	Any CD symptom; CD patients can feel well	NA
Rosecrans et al., 2014[110]	Mexico	CS + QC	Rural + endemic + seasonal infestation	n = 239	Community members, partly indigenous	NA	Vectorial	Recognition; Feeding habit	Any CD symptom	NA
Salm & Gertsch, 2019[89]	Bolivia	CS +QC	Urban + non-endemic; Urban + endemic; Rural + endemic	n = 480 5 groups; individual size: n = 50 to 120	Indigenous community members; Non-indigenous community members	Heard about CD	Vectorial	Recognition	NA	NA
Sanchez et al., 2014[103]	USA	CS	Urban + non-endemic (Los Angeles, California)	n = 2677	Migrants from endemic countries living in the USA	Heard about CD	NA	NA	Perceived seriousness of CD	NA
Sanmartino & Crocco, 2000[96]	Argentina	CS	1: Rural + high endemic + high infestation; 2: Rural + low endemic + low infestation	1: n = 121 2: n = 161	Community members	Name of CD	Vectorial; Blood; Organ transplant; Congenital; Ingestion	Recognition; Habitat; Feeding habit	CD affects the heart; Parasites cause CD	OLK with 25 notions, range 0 - 100 points; Vector + transmission + clinical knowledge
Verdu & Ruiz, 2002[90]	Bolivia	CS	Rural + endemic + infestation	n = 98	Indigenous community	Name of CD	Vectorial	Recognition	Any CD symptom	NA
Villela et al. 2009[91]	Brazil	CS	Rural + infestation + prior control activities	n = 312	Community members	NA	Vectorial	Recognition; Measures to avoid infestation	Organs affected by CD	NA
Williams-Blangero et al., 1999[99]	Brazil	CS	Rural + endemic + infestation + prior control activities	n = 59	Community members	Perceived importance of CD	Any transmission pathway	NA	Any CD symptom	NA

Note: CD = Chagas disease; CS = Cross-sectional survey; NA = Not assessed; OLK = Optimal level of knowledge; PPS = Pre-post study; QC = Qualitative component

Table A6a. Characteristics and knowledge instruments of quantitative studies

Author, Year	Chagas disease familiarity/ general question	Transmission knowledge	Vector knowledge	Clinical knowledge	Sum score
Ávila Montes et al., 1998[100]	46% heard about CD	30% Vectorial 0% blood transfusions 0% congenital	98% vector recognition 97% feeds on blood 39% thatched roofs 9% accumulation of materials 3% henhouses	6% heart problems 7% fever 4% unilateral ophthalmia 6% weakness	NA
Crocco et al., 2013[93]	36% parasitic disease 27% vector transmitted 17% affecting the heart 16% dangerous 1% endemic	91% (R); 46% (U) Vectorial 0% (R); 6% (U) congenital 0% (R); 41% (U) blood transfusion	47% dog's sleeping place 63% henhouse 63% farmyard 47% feeds on chicken 59% feeds on dogs	NR	NR
Dias et al., 2016[92]	59% know someone with CD 3% reported having CD	92% vector transmits a disease 84% vector transmits CD	77% vector recognition 43% dwellings 46% cleaning and better organisation	73% CD affects heart 6% CD affects the liver 6% CD affects lungs	NA
Donovan et al., 2014[101]	90% heard about CD 16% family member with CD	2% complete understanding 74%-81% Vectorial 45%-62% blood transfusion 43%-59% congenital 32%-46% organ transplant	NA	74% "it is poss ble to have CD and not know it." 81% "CD is severe."	NA
Genero et al., 2018[97]	NA	83% Vectorial 14% congenital	86% vector recognition 82% vector habitat 82% identification of dwellings at risk 71% feeds on blood	71% CD affects the heart	6% low 38% medium 57% high
Hurtado et al., 2014[102]	84% heard about CD	70% Vectorial 27% vector faeces 9% ingestion	70% adult R. pallescens recognition 4% T. dimidiata nymphs recognition 78% palm trees 67% feeds on blood	38% any CD symptom 20% CD affects the heart	58% very poor 11% poor 4% medium 5% good 22% optimal
Manrique et al., 2011[104]	67%-97% know the name of CD	NR	41%-80% vector name 79%-91% feeds on blood	NR	Mean score: 5.6 46% insufficient 11% low 38% medium 5% optimal
Mundaray et al., 2013[105]	63% heard about CD	72% Vectorial 28% congenital 34% ingestion 34% blood transfusion	50% any vector habitat	58% fever 62% cardiomyopathy	34% low 46% medium 19% high
Navarro et al., 2017[10]	70% heard about CD 26% CD infected family member	30% 0 correct pathways 28% 1 correct pathway 33% 2-3 correct pathways 9% 4-5 correct pathways	NA	56% 0 symptoms 19% 1 symptom 14% 2 symptoms 12% 3 symptoms 53% feeling well with CD	NA

Rosecrans et al., 2014[110]	NA	8% Vectorial	93% vector recognition 73% vector feeds on blood	38% CD affects heart 61% bite swelling and pus	NA
Salm & Gertsch, 2019[89]	74%-95% (U); 82%-95% (R) heard about CD	46%-68% (U); 48%-88% (R) Vectorial	50%-66% (U); 83%-99% (R) vector recognition	NA	NA
Sanchez et al., 2014[103]	13% heard about CD	NA	NA	Among those who had heard about CD: 19% “CD is a serious disease.”	NA
Sanmartino & Crocco, 2000[96]	NR	23%-84% vector faeces 0%-25% blood transfusion 2%-22% congenital, organ transplant, ingestion	NR	14%-74% parasites cause CD	Mean score range: 36.4 - 51.0
Verdu & Ruiz, 2002[90]	14% name of CD	81% vector causes a disease	98% vector recognition	31% any health consequence of CD	NA
Villela et al., 2009[91]	NA	92% (A); 96% (C) vector transmits CD	89% (A); 67% (C) vector recognition 95% (A); 91% (C) vector transmits disease 53% (A); 41% (C) hygiene and cleaning	84.5% (A); 68.8% (C) CD affects heart; Digestive system not mentioned; Liver, eyes, kidneys mentioned	NA
Williams-Blangero et al., 1999[99]	46% “CD is a major health problem.”	73% Vectorial 12% water-borne 3% mosquito-borne	NA	42% chest pain 36% fatigue 12% digestive problems 17% no correct symptom	NA

Note: A = Adults; C = Children; CD = Chagas disease; NA = Not assessed; NR = Not reported; R = Rural; U = Urban

Table A6b. Results of knowledge assessment in quantitative studies

Author, Year	Country	Study design	Study setting	Sample size	Participants	Data collection	Transmission knowledge	Vector knowledge	Clinical knowledge	Overall evaluation of authors
Blasco-Hernández et al., 2016[108]	Spain	Grounded theory	Urban + non-endemic (Spain)	n = 14	Bolivian female migrants with CD living in Spain	Semi-structured interviews; Triangular groups; Fieldnotes	Awareness that the vector transmits CD; Some awareness of transmission through blood transfusion; Little awareness of transmission through ingestion	Reference to houses made of adobe, beds with straw mattresses, proximity to animals; Participants were familiar with the vector	Awareness that CD causes death due to heart failure or alterations in the intestine; Belief of 'the less you know, the less you suffer' was common	Highly familiar with Vectorial transmission; Poorer understanding of the symptoms, diagnosis, transmission routes and the treatment
Dell'Arciprete et al., 2014[98]	Argentina	Qualitative study	Rural + peri-urban + endemic	1: n = 14 2: n = 15	Members of two different indigenous communities; CD patients and relatives, health care workers, shamans	In-depth interviews; Observation	Triatomines are not perceived as a health risk; It has consequences on attitudes towards vector control; Due to a lack of information, people of both ethnicities do not associate the vector with CD, or with sudden death	Express of belief that young triatomines (nymphs) do not transmit the disease	CD associated with a general lack of energy, swollen eyes; Anaemia through excessive loss of blood through vector	CD is not seen as a health threat; Both groups have rates of infestation and infection that far surpass those in other groups; Their belief systems promote a way of thinking that does not attempt to identify causes
Martínez-Parra et al., 2018[107]	Colombia	Ethnographic study	Rural + urban + endemic + infestation	n = 38	CD patients + family members	Semi-structured interviews; Participant observation	Confusion about disease transmission	NA	Difficulties understanding that a parasite is the pathogen, not the vector	Patients reported confusions around disease transmission, treatment effectiveness, and development of future complications
Tineo & Ponte, 2008[109]	Venezuela	Qualitative study	Urban + non-endemic	n = 63	Students + staff + teachers	Free recall technique	Identification of the vector that transmits a causal agent; Other transmission pathways as ingestion, blood transfusion, congenital are unknown	Not part of the social representation: diversity of reservoirs, ecological relationships; Sample is unfamiliar with T. cruzi reservoir	Awareness that causal agent (the parasite) symptomatically affects the heart	The general representation revolves around the notion of the vector as an iconic image of the disease; The representation lacks fundamental aspects of the epidemiological dynamics

Valdez-Tah et al., 2015[106]	Mexico	Ethnographic study	Rural + endemic + infestation	n = 22	Community members + partly indigenous	In-depth interviews; Observation	Vector bites were considered normal events without perception of a threat; Women reported that triatomines "spread disease"; Focus on their blood-sucking behaviour and the chagoma they provoked; Less attention to CD	Knowledge and awareness of triatomines is heterogeneous; Men´s knowledge about the bugs was detailed; Related to the landscape and the vector's habits	Two local concepts exist when referring to insect bites and their effect on the skin: allergy and poison; Both concepts are used to explain why an insect produces different skin reactions or additional symptoms	Social representations are heterogeneous; Integrate different types of knowledge, popular concepts, beliefs, and biomedical or environmental information
Note: CD = Chagas Disease										

Table A6c. Characteristics and results of qualitative studies

Appendix 7

Results of the quality appraisal of studies in the literature review

Study	Ávila et al.	Crocco et al.	Dias et al.	Donovan et al.	Genero et al.	Hurtado et al.	Manrique et al.	Mundaray et al.	Navarro et al.	Rosecrans et al.	Salm & Gertsch	Sanchez et al.	Sanmartino & Crocco	Verdu & Ruiz	Villela et al.	Williams-Blangero et al.
Were the aims/objectives of the study clear?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the study design appropriate for the aim(s)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
Was the sample size justified?	N	N	N	N	Y	Y	N	N	N	N	N	N	N	N	Y	N
Was the target/reference population clearly defined?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the sample frame taken from an appropriate population base?	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y
Was the selection process likely to select participants representative of the target population?	Y	N	N	N	N	U	Y	N	N	Y	U	Y	N	U	U	U
Were measures undertaken to address and categorise Nn-responders?	N	U	N	N	N	U	U	N	U	N	U	N	N	U	N	U
Were outcome variables measured appropriate to the aims of the study?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Were the outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	Y	Y	Y	U	Y	Y	Y	N	N	Y	U	U	U	N	Y	N
Is it clear what was used to determined statistical significance and/or precision estimates?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Were the methods sufficiently described to enable them to be repeated?	N	N	Y	Y	Y	N	N	Y	N	Y	N	N	N	N	Y	N
Were the basic data adequately described?	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y
Does the response rate raise concerns about Nn-response bias?	U	U	Y	Y	U	U	U	U	U	N	U	U	U	U	U	U
If appropriate, was information about Nn-responders described?	N	N	U	N	N	U	U	U	U	Y	U	U	N	U	N	N
Were the results internally consistent?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the results for the analyses described in the methods, presented?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the authors' discussions and conclusions justified by the results?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Were the limitations of the study discussed?	N	N	N	Y	Y	N	N	Y	Y	Y	N	Y	N	N	N	N
Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	N	U	U	U	U	N	U	U	N	N	N	N	U	U	U	U
Was ethical approval or consent of participants attained?	U	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	U

Note: N = No; U = Unclear; Y = Yes

Table A7a: Quality appraisal of quantitative studies with the AXIS tol

Study	Blasco-Hernández et al.,	Dell'Arciprete et al.	Martínez-Parra et al.	Tineo & Ponte	Valdez-Tah et al.
Was there a clear statement of the aims of the research?	Y	Y	Y	Y	Y
Is a qualitative methodology appropriate?	Y	Y	Y	Y	Y
Was the research design appropriate to address the aims of the research?	Y	Y	Y	Y	Y
Was the recruitment strategy appropriate to the aims of the research?	Y	U	Y	Y	Y
Was the data collected in a way that addressed the research issue?	Y	U	Y	Y	Y
Has the relationship between researcher and participants been adequately considered?	N	N	N	N	Y
Have ethical issues been taken into consideration?	Y	Y	Y	N	Y
Was the data analysis sufficiently rigorous?	Y	U	N	Y	Y
Is there a clear statement of findings?	Y	Y	Y	Y	Y
How valuable is the research?	Valuable	Valuable	Valuable	Valuable	Valuable
Note: N = No; U = Unclear; Y = Yes					

Table A7b: Quality appraisal of qualitative studies with the CASP tool

Appendix 8

Linear regression analysis plots

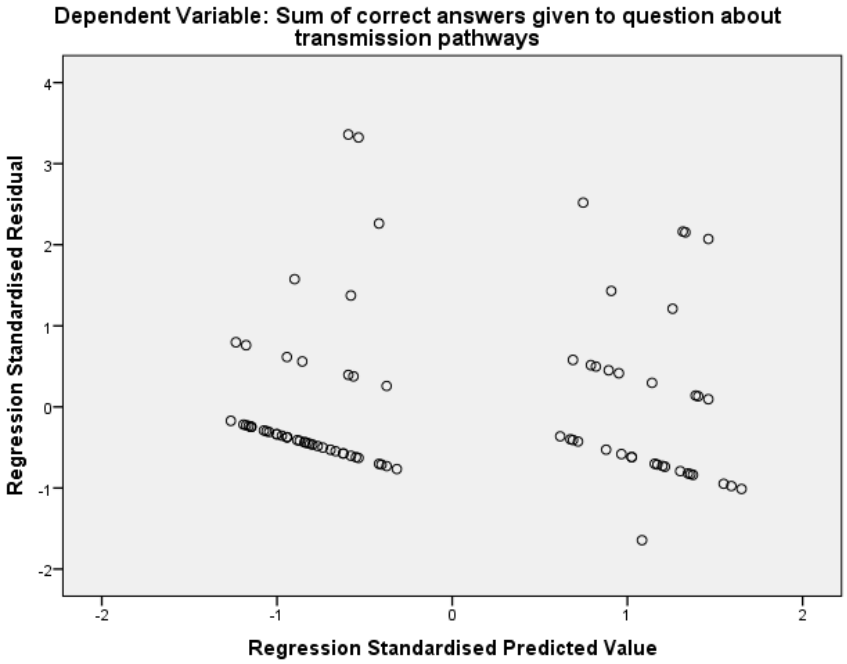

Figure A8a. Scatterplot of standardised predicted values and standardised residuals

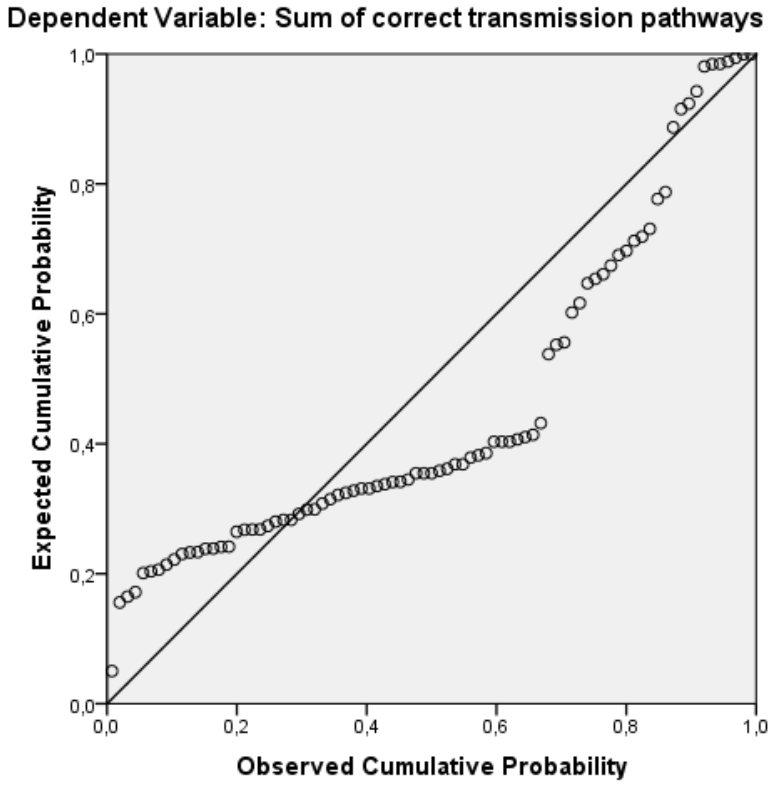

Figure A8b. Probability-Probability Plot of observed and predicted cumulative probability