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A deadly feast: Elucidating the burden of orally acquired acute Chagas disease in Latin America – Public health and travel medicine importance☆

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ABSTRACT

Over the past two decades, several countries in Latin American, particularly Brazil, Venezuela, and Colombia, have experienced multiple outbreaks of oral Chagas disease. Transmission occurs secondary to contamination of food or beverages by triatomine (kissing bug) feces containing infective *Trypanosoma cruzi* metacyclic trypomastigotes. Orally transmitted infections are acute and potentially fatal. Oral Chagas transmission carries important clinical implications from management to public health policies compared to vector-borne transmission. This review aims to discuss the contemporary situation of orally acquired Chagas disease, and its eco-epidemiology, pathogenesis, and clinical management. We also propose preventive public health interventions to reduce the burden of disease and provide important perspectives for travel medicine. Travel health advisors need to counsel intending travellers to South America on avoidance of "deadly feasts" - risky beverages such as fruit juices including guava juice, bacaba, babaçu and palm wine (*vino de palma*), açai pulp, sugar cane juice and foodstuffs such as wild animal meats that may be contaminated with *T. cruzi*.

1. Introduction

American trypanosomiasis or Chagas disease, caused by the protozoan *Trypanosoma cruzi*, remains a significant cause of illness, disability, and death [1,2]. There is evidence from multiple studies [3–40] that *T. cruzi* has existed for millennia in the Americas in an enzootic cycle involving insect vectors and wild animal reservoirs extending from the Southern U.S. to some areas of Argentina and Chile. The disease remains predominantly a major neglected tropical disease (NTD) of the poor reflecting the historical social and geopolitical realities that have prevailed in Latin America [1,2]. An estimated 6–8 million infected individuals live in South America, Central America, and Mexico. However, during the last decade, cases of Chagas disease have been identified in non-endemic areas due to migration of individuals living with the infection [3,5], or travel related acquisition of the infection [4–43].

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Table 1
Distinguishing features of orally acquired *Trypanosoma cruzi* infection versus vector-borne transmission.

Feature	Oral ingestion	Vector-borne[a]
Pattern of Illness	The cluster of acute cases in a household, migrating group, or who recently participated in festivities or meetings	While there may be more than one individual infected in the same household, their clinical manifestations do not occur in clusters and usually manifesting after many years of the initial exposure
Fever pattern	Undifferentiated febrile illness with a persistent pattern and often stepwise characterized by increasing temperature over each day	The similar pattern among those with acute Chagas disease but rarely a persistent fever unless with acute severe manifestations such as meningoencephalitis and myocarditis
Ocular/Facial manifestations	Bilateral palpebral edema in > 95% of cases Facial edema in > 90% of cases	Romaña's sign[b] Chagoma[a]
Cardiac manifestations	Early occurrence of myocardial involvement with often severe manifestations, including: - Cardiac arrhythmias (premature ventricular contractions, non-sustained ventricular tachycardia) - Congestive heart failure that may progress to cardiogenic shock - Pericardial effusion with or without pericardial tamponade - Pleural effusions	May present with acute myocarditis in 5–10% of cases, mostly in children
Epidemiological clues	Typical forms of transmission in the Amazon and many reported outbreaks in Venezuela, Brazil, French Guyana, and Colombia. Ingestion of *T. cruzi* present in fruit juices including guava juice, bacaba, babaçu and palm wine (*vino de palma*), açai pulp, sugar cane juice, wild animal meat (i.e., containing anal odoriferous glands of opossums) Some outbreaks reported in populations migrating due to the ongoing humanitarian crisis in Venezuela	Exposure to the feces of triatomine vectors leading to the entry of parasites through skin breaks or conjunctiva
Parasitic load	A complete triatomine crushed in food or beverage may contain more than 600,000 trypomastigotes	Fecal matter of a triatomine contains between 3000 and 4000 trypomastigotes per microliter
Ecological factors	Survival of *T. cruzi* in artisan fruit juices Deforestation reducing wildlife resulting in the concentration of *T. cruzi* in few animal hosts. Wildlife reduction fosters domiciliation of triatomines Population migration due to the humanitarian crisis in Venezuela favors ingestion of food and beverages with low levels of sanitation.	Deforestation reducing wildlife resulting in the concentration of *T. cruzi* in few animal hosts. Wildlife reduction fosters domiciliation of triatomines
Mortality	Much higher than vector-borne transmission 8–35%	Approximately 5–10%
Long-term sequelae	Undefined but it may produce a more rapid progression to long-term cardiac or gastrointestinal dysfunction compared to vector-borne transmission given that oral transmission is caused by a higher parasite inoculum	Approximately 30% develop cardiac involvement or gastrointestinal dysfunction within 10–30 years from the initial infection. Late-onset chronic chagasic cardiomyopathy that can manifest with: - Cardiac arrhythmias - Atrioventricular conduction abnormalities - Thromboembolic phenomena - Congestive heart failure - Left ventricular apical aneurysm Late-onset gastrointestinal mega forms: - Megaesophagus - Megacolon
Geographic distribution	An important form of transmission in the Brazilian Amazon. Other countries with reported outbreaks: French Guyana, Colombia, Brazil, and Venezuela. *Panstrongylus geniculatus* and *Rhodnius prolixus* are frequently involved in foodborne outbreaks.	*Rhodnius prolixus* is the most critical species in Central America and the upper regions of South America, while *T. dimidiata* locates from Mexico down to Ecuador and extending into other countries in South America. *T. infestans* is the primary vector in the sub-Amazonian regions.

[a] Infection occurs through a break in the skin or the site of a vector's puncture, an indurated area of erythema and swelling denominated as the chagoma and accompanied by local lymphadenopathy.

[b] Seen more commonly in children who may rub their eyes with their hands contaminated with parasite feces, and manifesting with a unilateral painless palpebral swelling that can appear after the parasite entered through the mucosal conjunctival tissue (the Romaña's sign).

Humans acquire this parasitic infection mainly by the vector-borne route that occurs through percutaneous or conjunctival exposure to the feces of feeding hematophagous Reduviidae insects of the subfamily Triatominae (most frequently: *Rhodnius prolixus, Triatoma dimidiata,* and *Triatoma infestans*) [5], also known as conenose bugs, kissing bugs (so-called from their habit of feeding around the mouths of people), or vampire bugs (in Spanish, vinchuca, chipo, pito, chinchorro, chirimacho, iquipito, chupon) (Table 1). The blood trypomastigotes (non-replicative form) and the amastigotes (replicative form) are the two stages of *T. cruzi* that are found in the mammalian host. The epimastigotes and the infective metacyclic trypomastigotes are the gut-dwelling forms in the triatomine vector [5]. The entry of contaminated triatomine feces occurs through cutaneous abrasions at the insect bite area or conjunctiva [3–7]. Untreated *T. cruzi* infection in the human host results in lifelong latent infection of specific tissues such as striated cardiac muscle and enteric ganglia [5].

In most endemic areas, vector-borne transmission is the most relevant form of human infection [3–10]. As a result, large-scale, vector-control programs, particularly in the Southern cone countries of South America have reduced the incidence of Chagas disease [3–10]. Similarly, blood bank screening practices in endemic settings have decreased the number of infections acquired through this route [5,10]. Despite many achievements in reducing the overall burden of *T. cruzi* transmission in Latin America, there have been a series of recently documented reinfestations of previously insecticide-treated communities, in parts of Venezuela, Colombia, and Bolivia [10]. Over the last few decades, the ingestion of contaminated food or beverages with complete triatomines or its feces containing metacyclic trypomastigotes have been responsible for many cases of orally acquired Chagas disease [6,7,10–15]. Orally acquired Chagas disease displays unique medical features that differ from the more common, vector-related transmission. This review article describes most current epidemiology, pathogenesis and clinical characteristics of orally acquired Chagas disease.

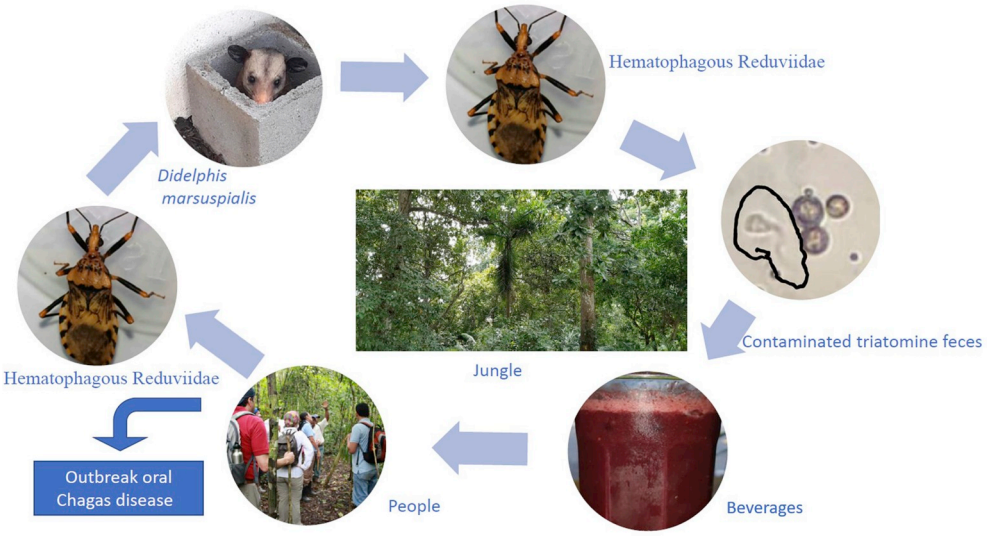

Fig. 1. The cycle of acute orally Chagas disease.
In the wild and suburban areas, mainly, opossums are a source of *T. cruzi* infection for triatomines that are able to provide infecting forms for human in their feces. In orally acquired disease, such feces can contaminate beverages by accidental deposition of triatomine feces, then becoming the source for human infection. The cycle can persist from infected humans by triatomine blood-sucking for other humans and close wild animals, including the opossum, among others. In addition, accidental ingestion of triatomines or meat and blood from infected animals, would also lead to oral transmission of *T. cruzi*.

1.1. The eco-epidemiology of orally acquired Chagas disease

There are an estimated 6-8 million people living with Chagas disease in the Americas, however the precise contribution of orally acquired Chagas disease to the overall burden of disease is challenging to ascertain except for a limited number of case series [16] and a growing number of reported foodborne outbreaks [6,7,11–15]. In the forests and rural settings of Mexico, Central, and South America, the wild cycle of *T. cruzi* transmission, requires the presence of triatomine vectors and mammalian reservoirs such as rodents, marsupials, armadillos, and primates that acquire the infection by ingestion of triatomine vectors [3,4]. Human infection occurs with higher intensity in these locations during occupational exposures or outdoor activities, and within the household where wild triatomines have adapted to reside in the crevices of poorly constructed dwellings and peridomestic areas. Indigenous groups living in these areas are at a higher risk of acquiring this parasitic infection resulting in high rates of disability and premature mortality [2,8,9]. Progressive urbanization of rural communities with increasing populations, expanding deforestation, agriculture, and livestock has led to reduced mammalian biodiversity as a food source for triatomine vectors [3,17–20]. Increasing subsistence hunting practices are also leading to substantial loss of biodiversity in these forests [17–21]. In turn, triatomines enter human dwellings attracted by light [4]. *T. cruzi* infection occurs in the human host by the percutaneous and oral routes after triatomines become domiciled vectors and while roaming in the household, searching for food sources and shelter [3,4]. Triatomine domiciliation also occurs in major urban areas and periurban areas where humans and domestic animals such as dogs, cats, rats, opossums, and others act as reservoirs of the infection [3,4,7,13]. Two critical players amplify the transmission of *T. cruzi*, the rat (*Rattus rattus*), and opossum (*Didelphis marsupialis*) [6,7]. The rat has a predilection for ingesting the insect vector *Panstrongylus geniculatus* in garbage dumping areas in urban and periurban locations close to human homes. *Panstrongylus geniculatus* is a frequent vector of transmission identified in orally acquired outbreaks [6,7].

With increasing economic disparities in Latin American countries, subsistence hunting of opossums, armadillos, and other wild animals is increasing in both urban and rural areas [18,19,21,22]. *Didelphis marsupialis* can act as reservoir and vector of *T. cruzi* transmission since the maturation cycle to the infective metacyclic trypomastigote occurs in their odoriferous anal glands (same maturation process that occurs in the triatomine intestine) [22,23]. As a result, there has been *T. cruzi* transmission by the ingestion of wild animal meat and even blood, such as opossum and armadillos [4,23,44]. Additionally, opossums may also contaminate food prepared for human consumption given their defensive ability to aerosolize secretions from the anal glands under stressful situations [4,23].

Brazil, Venezuela, Colombia, Bolivia, and French Guyana have reported outbreaks of orally acquired Chagas disease [6,7,11–15,23–27]. However, the amazon region poses the highest reported burden of *T. cruzi* oral transmission [3,11,17]. Variation of sociocultural and regional food preparation practices in households, schools, or street vendors allow contamination of food items that become vehicles of oral transmission during foodborne outbreaks [7,23–28]. Most foodborne cases have occurred after the ingestion of unpasteurized homemade or artisan fresh juices of plant origin such as sugar cane juice; and fruits such as açai berry (Brazil), guava juice (Venezuela), and palm wine (Colombia); or through the ingestion of wild-animal meat [6,7,11–15,21–29] (Table 1).

Trypanosoma cruzi can survive for many hours in these food items, either at room temperature or refrigerated [26]. Some homemade juices made from palm fruit trees may contain *T. cruzi* since triatomine insects reside in palm trees for shelter and nutritional purposes [28]. In experimental settings, *Rhodnius prolixus* has demonstrated to be a facultative phytophagous insect depending on environmental determinants, such as staying during long blood starvation periods [28]. This insect behavior may explain the frequent association of acute Chagas disease outbreaks with contaminated food in impoverished areas of Northern Brazil where palm fruits (such as the açai berry) are an important staple and palm leaves cover the roofs of human dwellings [3,4,23,29–33]. There is also some evidence that the light used to extract pulp from the açai palm tree (*Euterpe oleracea*) attracts some species of triatomines [23]. Facultative phytophagy [28] also potentially explains the transmission of *T. cruzi* infection via homemade fruit juices reported in many rural and urban outbreaks. In this context, some triatomine vectors wandering at night enter inside the juice container in the kitchens or areas of the household used for food preparation [6,7]. By the next morning, when the human host ingests the beverage, it may already contain an entire insect, a crushed one, or their feces [6,7,25,27–31] (Fig. 1). The largest reported urban outbreak of orally acquired cases of acute Chagas disease in Latin America occurred in a school in Caracas, Venezuela, and was associated with guava juice prepared the night before and left uncovered, allowing nocturnal contamination of the juice by the insect vector. More than one hundred individuals including students and staff who drank guava juice the next morning developed acute Chagas disease manifestations 5–20 days later [7,13].

Contamination of food or beverages may also occur during the food preparation of traditional artisan beverages conducted outside the household. For example, the palm wine tree in Colombia (*Attalea butyracea*) produces sap that its extracted by cutting the palm [24]. This sap ferments for many days inside a cavity in the palm tree until it becomes a whitish alcoholic beverage (palm wine) produced for human

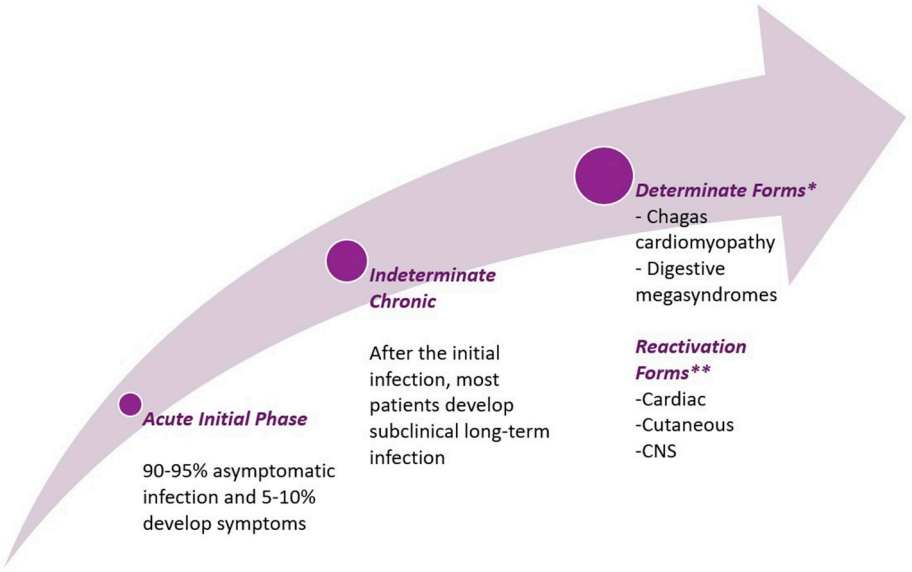

Fig. 2. The natural history of vectorial *Trypanosoma cruzi* infection.
*10–30 years after the initial infection, 30–40% of individuals develop clinical manifestations.
**Reactivation disease may also occur at any point during the indeterminate phase.

consumption. It is during the fermentation process triatomine vectors contaminate the beverage by direct invasion or by depositing its feces [24,25,27]. Similar artisan practices of palm wine occur with some variation in other regions in South America (i.e. Northern Brazil) from trees such as the bacaba (*Oenocarpus bacaba*), the chiquichique (*Leopoldinia piassaba*), the moriche or canangucha (*Mauritia minor*), and milpesillo (*Oenocarpus minur*) [29–31]. Acute manifestations of Chagas disease co-occurring in two or more individuals may constitute a foodborne outbreak [27,33] that should be notified to public health authorities in order to strengthen existing surveillance efforts to guide the institution of preventive strategies [26,27,33–38].

1.2. Pathogenesis of orally acquired chagas disease

The initial observation that *T. cruzi* infection could be acquired orally occurred in 1921, with the experimental demonstration that blood trypomastigotes can produce systemic infection when inoculated via the oral route [4]. Since wild animals possess a thick cutaneous barrier to acquiring this infection through the percutaneous vectorial route, wild mammals acquire *T. cruzi* infection by ingestion of the triatomine vectors or food contaminated with their fecal excreta [4,6,7,13,39].

Ingestion may be accidental or intentional for nutritional purposes, as in the case of small primates who ingest insect vectors [3,4]. In the human host, the initial observations regarding the potential role of oral transmission of *T. cruzi* started when the Argentinian researcher Salvador Mazza identified breastfeeding transmission of trypomastigotes in lactating mothers to their newborns in 1936 [4]. Once ingested, as part of the host-parasite interaction, metacyclic trypomastigotes express the mucin-like surface glycoprotein gp82 that provides resistance to proteolytic degradation and plays a vital role in the invasion of the gastric mucosal epithelium [34,35]. The glycoprotein gp82, which is part of the trans-sialidase/gp85 superfamily, promotes internalization of trypomastigotes by triggering intracellular transduction signaling pathways that mobilize calcium promoting changes in the gastric mucosal cell cytoskeleton [34]. In contrast, by expressing a different glycoprotein, gp90, metacyclic forms diminish the parasite's infectivity of gastric mucosal cells. However, parasite strains that express gp90 may regain their infectivity since this glycoprotein is susceptible to pepsin degradation [35]. The loss of gp90 in the gastric acid milieu allowing increasing adherence to mucin and increased entry into gastric epithelial cells may be responsible for increasing severity of clinical presentations seen in some cases [34,35].

Previous studies in humans did show entry of infective parasitic forms in the gastric epithelial cells but not in the oral and esophageal mucosa [34,35]. However, recent evidence in the mice model using bioluminescence assays and real-time quantitative PCR suggests that there is an essential degree of parasite internalization through the oral and pharyngeal mucosa in addition to the gastric mucosa [11]. Based on this evidence, it is tempting to speculate that the pathogenesis of facial and palpebral bilateral edema frequently observed in patients with the severe acute forms of orally acquired Chagas disease occurs by vascular and lymphatic congestion after *T. cruzi* enters through the oral and pharyngeal mucosa.

After oral ingestion and entry through the gastric mucosa, metacyclic trypomastigotes mature to trypomastigotes in blood and amastigotes in tissues similar to the vector-borne infection [34,35]. The overwhelming infective dose of parasites that may occur during orally acquired infection is likely responsible for the higher attack rate seen during outbreaks and the severity of the disease [36]. In contrast to the vector-borne form of *T. cruzi* infection, after oral ingestion of a high parasitic load, the host immune response has difficulty controlling systemic dissemination leading to high parasitemia levels and increased tissue invasion. In turn, these pathogenic events manifest as shorter incubation periods (average 22 days) [16,31], higher rates of early cardiac involvement, and increased clinical severity [6,7,11,12,32,33]. Many gaps remain in our understanding of the pathogenesis of *T. cruzi* infection requiring further studies, including necropsy-based clinical-pathological correlations.

1.3. Natural history and distinguishing clinical features of orally acquired Chagas disease

The natural history of Chagas disease acquired by the oral route has significant epidemiologic and clinical differences compared to the vector-borne form of human infection (Table 1). During the acute stage of vector-borne *T. cruzi* infection in the human host, there is parasitemia with systemic dissemination [5]. The number of parasites in tissues and the degree of parasitemia declines after the host immune response, leading to life-long persistence of the parasite only in specific tissues, including enteric ganglia and striated muscle [5] (Fig. 2).

The initial phase of vector mediated infection is asymptomatic in approximately 90–95% of cases; and even in symptomatic patients (mainly children), severe manifestations including acute myocarditis or meningoencephalitis develop in only a few cases [46,47]. After the initial infection (symptomatic or asymptomatic), most patients return to their previous state of health, remaining in an indeterminate stage of the infection [5,37]. Of these, approximately 30–40% progress to develop cardiac or gastrointestinal disease, or both within 10–30 years [5,37] (Fig. 2). Additionally, some individuals in the lifelong indeterminate stage develop reactivation of disease in association with immunosuppressive conditions including advanced HIV infection or solid organ transplantation [38]. Reactivation of disease produces a range of clinical presentations including fulminant myocarditis, meningoencephalitis, and cutaneous involvement [38].

In contrast, the natural history of the oral route of transmission encompasses a shorter incubation period and more severe clinical features compared to the percutaneous vector-borne transmission [6,7,10–15,29–31]. The spectrum of clinical manifestations of the acute phase is frequently symptomatic with systemic signs of infection and a more rapid and severe cardiac involvement [3,4,12,16,31,33] (Fig. 3). Additionally, the reported mortality rate of symptomatic cases acquired orally is higher than chronic infections with cardiac or gastrointestinal disease [6,7,10–15,29–31, 45]. The high attack rate during foodborne outbreaks is likely due to the ingestion of a higher parasitic load compared to those entering the skin or conjunctiva by the vector-borne route [36]. Evidence in murine models has showed a rapid penetration of the parasite through the stomach and oropharyngeal mucosa with probable replication in the nasal cavity [11].

The initial presentation of orally transmitted Chagas disease often includes generalized malaise, anorexia, and fever. Some individuals may develop abdominal pain, nausea, vomiting, and diarrhea, further confusing the clinician towards bacterial or viral gastroenteritis (Table 1) [6,7,10–15,29–31]. Similar to other foodborne outbreaks, a detailed history of potential sources of infection, such as recent ingestion of potentially contaminated meat or beverages is essential. One distinguishing clinical sign is the occurrence of edema of the face including bilateral palpebral and edema of the lower extremities [6,7,13,29–31]. Generalized lymphadenopathy and hepatosplenomegaly with jaundice may also develop. Acute myocarditis, as evidenced by autopsy studies, probably happens in most patients with acute Chagas disease manifesting with early occurrence of left ventricular systolic failure, arrhythmias (premature ventricular contractions, and non-sustained ventricular tachycardia), and pleural and pericardial effusions [25].

With an epidemiological and clinical suspicion of orally acquired acute infection, parasitological diagnosis with the use of thick and thin smears of peripheral blood offers the highest sensitivity and positive predictive value [6,7,29]. The persistent parasitemia identified during orally acquired forms of infection can assist clinicians in confirming the diagnosis and monitoring clinical response to antiparasitic therapy [6,7,13,29].

Molecular diagnosis or serological tests by different assays can assist outbreak investigations (ELISA serological testing with indirect hemagglutination or Western blot for confirmatory testing) [6,7,29]. In endemic settings, clinicians should suspect the possibility of acute orally acquired *T. cruzi* infection when one or more individuals present with undifferentiated febrile syndromes associated with bilateral palpebral edema, full facial edema, and lower extremity edema with or without manifestations of cardiac involvement. These clinical signs are essential clues in the differential diagnosis of acute febrile syndromes in patients seeking care at acute care clinical posts. Other highly prevalent infections may present with a similar clinical pattern, such as during outbreaks of dengue, leptospirosis, and others (Table 2). Patients may also present with co-infections.

1.4. Treatment and preventive interventions to reduce the burden of oral Chagas disease

Due to the rapid progression and severity of the disease, a high index of clinical suspicion is crucial in the early diagnosis given the higher mortality rate (8–35%) of acute orally acquired Chagas disease [3,4,6,7,26,29]. The establishment of antiparasitic therapy with nifurtimox or benznidazole early in the course of acute oral *T. cruzi* infection is crucial for patient recovery [5,37].

In addition to antiparasitic therapy, it is essential to institute supportive interventions, including management of left ventricular dysfunction with medical therapy to reduce cardiac afterload and promote diuresis to reduce volume overload and effusions [6,7,24,26]. Those with arrhythmias may require the use of amiodarone, and those with advanced degrees of atrioventricular blocks may need pacemakers. Unless there is definitive clinical and echocardiographic evidence of cardiac tamponade, pericardiocentesis or surgical pericardial window may increase complications and overall mortality [25]. Most patients that receive appropriate antiparasitic therapy, including benznidazole or nifurtimox, appear to recover successfully, [24]. Nevertheless, many other drugs are under evaluation, and may have shown certain anti-*T.*

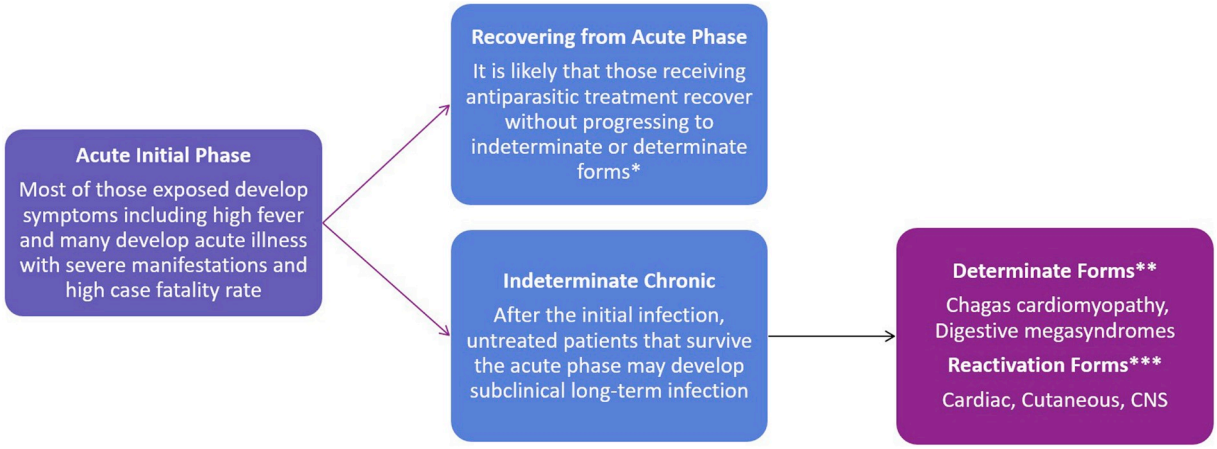

Fig. 3. The natural history of orally acquired *Trypanosoma cruzi* infection.
*There is a need to elucidate the natural history of treated and untreated *T. cruzi* infection acquired by the oral route. Due to higher parasitic load acquired by the oral route, those untreated who survive the acute phase may develop long-term cardiac or GI complications earlier than those with vector-borne acquired infection. It has been suggested that this occur in 5–10% of patients who develop symptoms and are treated after vectorial transmission. **10–30 years after the initial infection, 30–40% individuals develop clinical manifestations. ***Reactivation disease may also occur at any point during the indeterminate stage.

Table 2
Significant causes of undifferentiated febrile illness in many tropical and subtropical settings in Latin America.

Type	Disease
Virus	Dengue fever[a]
	Chikungunya[b]
	Zika[c]
	Hantavirus[d]
	Arenavirus[e]
Bacteria	Leptospirosis
	Rickettsiosis and other tick-borne bacteria (less frequent, Ehrlichiosis and Anaplasmosis)
	Enteric fever
Parasite	Malaria
	Oral acute Chagas disease
	Visceral leishmaniasis[f]

[a] Currently (2019) in epidemics across multiple countries in Latin America.
[b] Usually accompanied by bilateral-symmetric, migrating polyarthralgia.
[c] In certain areas Zika present with fever in an important proportion of patients.
[d] In the Americas, regularly presenting with pulmonary disease (HPS, Hanta pulmonary syndrome).
[e] Regularly, viral hemorrhagic fevers. Especially important in Argentina, Brazil and Bolivia, among other countries in Latin America.
[f] Areas endemic for *T. cruzi*, are commonly also endemic for *Leishmania chagasi/infantum*.

cruzi activity in the last decade, as is the case of amiodarone and itraconazole [48,49].

Recently, an experimental study in dogs using amiodarone and itraconazole suggest efficacy of this trypanocidal drug combination for the treatment of *T. cruzi* [48,49]. Treated patients require short and long-term clinical, laboratory and parasitological monitoring [6,7,24,26]. Preliminary evidence from our group suggest that untreated individuals that survive the acute phase of orally acquired infection may progress to the chronic forms of the disease faster than those infected through the vector-borne route.

Preventive efforts targeting the population at risk to improve food safety practices and early clinical diagnosis to institute effective antitrypanosomal therapy constitute the cornerstone interventions to reduce the burden of orally acquired Chagas disease, including travelers to endemic areas. While there is enough evidence-based data to contraindicate antiparasitic drugs in elderly individuals with advanced chronic chagasic cardiomyopathy, the use of antiparasitic therapy is a crucial intervention during the acute stage of foodborne infection. Ensuring the availability of sufficient antiparasitic drugs to treat multiple concomitant cases during an outbreak may require international collaboration in the deployment of drugs as occurred in Venezuela; or the establishment of stockpiles of antiparasitic drugs at a national, regional or district level to respond effectively to these public health emergencies [7,13,27,39]. Mandatory reporting and active surveillance systems of positive cases of Chagas disease with emphasis on acute cases can help to emphasize essential public health measures. Given the potential toxicity of currently available antiparasitic drugs, pharmacovigilance of treated cases is an important strategy to prevent life-threatening complications [39]. In a Venezuelan foodborne outbreak of Chagas disease, 79% of patients developed one or more adverse events. These occurred more frequently with nifurtimox compared to benznidazole. Severe adverse events, occurring in five of 179 patients treated, required treatment interruption and hospitalization including pulmonary infarction, facial paralysis, neutropenia, blurred vision, and bone marrow hypoplasia [7,13,39].

Travelers to endemic areas should avoid consuming juices or beverages that are “risky” or that have been not properly processed. Such drinks should be prepared using filtered boiled water and juices, later properly stored in refrigerators in closed bottles, or pasteurized products, to avoid the potential contamination with *T. cruzi*.

2. Conclusions and next steps

In order to reduce the morbidity and mortality of orally transmitted Chagas disease there is an urgent need to improve our understanding of the epidemiology and clinical outcomes of this mode of transmission by increased surveillance efforts and long-term follow-up cohort studies [50]. Increasing awareness of healthcare personnel of this diagnostic possibility among patients with undifferentiated febrile syndromes is crucial. Development and implementation of educational campaigns targeting at-risk populations regarding food safety practices ranging from juice and meal preparation and storage to its consumption is critical. There is a need for increased conservation efforts to reduce deforestation in Latin America [11,40]. This is not an easy task given the prevailing social inequities, collapse of indigenous economies, structural racism, forced displacements of populations, food insecurity, and limited access to education, health, and social services; all factors which predispose unsanitary food practices [17,18,20,21].

We conclude that there are critical gaps in our understanding of the oral transmission of Chagas disease that call for further research to elucidate its attributable burden of disease. This increasingly recognized form of oral transmission demands urgent attention from governments and public health institutions to foster social improvements among disenfranchised populations in Latin America [2,17,20]. Travel health advisors need to counsel intending travellers on avoidance of “deadly feasts” - risky beverages such as fruit juices including guava juice, bacaba, babaçu and palm wine (*vino de palma*), açai pulp, sugar cane juice and foodstuffs such as wild animal meat that may be contaminated with *T. cruzi*.

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CRediT authorship contribution statement

Carlos Franco-Paredes: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Wilmer E. Villamil-Gómez:** Conceptualization, Writing - review & editing. **Jonathan Schultz:** Writing - review & editing. **Andrés F. Henao-Martínez:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Gabriel Parra-Henao:** Writing - review & editing. **Anis Rassi:** Writing - review & editing. **Alfonso J. Rodríguez-Morales:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **José Antonio Suarez:** Conceptualization, Writing - review & editing.

Declaration of competing interest

All authors report no potential conflicts.

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