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Evolutionary ecology of Chagas disease; what do we know and what do we need?

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Abstract

The aetiological agent of Chagas disease, *Trypanosoma cruzi*, is a key human pathogen afflicting most populations of Latin America. This vectorborne parasite is transmitted by haematophagous triatomines, whose control by large-scale insecticide spraying has been the main strategy to limit the impact of the disease for over 25 years. While those international initiatives have been successful in highly endemic areas, this systematic approach is now challenged by the emergence of insecticide resistance and by its low efficacy in controlling species that are only partially adapted to human habitat. In this contribution, we review evidences that Chagas disease control shall now be entering a second stage that will rely on a better understanding of triatomines adaptive potential, which requires promoting microevolutionary studies and -omic approaches. Concomitantly, we show that our knowledge of the determinants of the evolution of *T. cruzi* high diversity and low virulence remains too limiting to design evolution-proof strategies, while such attributes may be part of the future of Chagas disease control after the 2020 WHO's target of regional elimination of intradomiciliary transmission has been reached. We should then aim at developing a theory of *T. cruzi* virulence evolution that we anticipate to provide an interesting enrichment of the general theory according to the specificities of transmission of this very generalist stercorarian trypanosome. We stress that many ecological data required to better understand selective pressures acting on vector and parasite populations are already available as they have been meticulously accumulated in the last century of field research. Although more specific information will surely be needed, an effective research strategy would be to integrate data into the conceptual and theoretical framework of evolutionary ecology and life-history evolution that provide the quantitative backgrounds necessary to understand and possibly anticipate adaptive responses to public health interventions.

KEYWORDS

adaptive dynamics, domiciliation, generalist parasite, insecticide resistance, local adaptation, microevolution, multihost virulence evolution, Trypanosomatidae

1 | INTRODUCTION

American trypanosomiasis, also named Chagas disease after the Brazilian physician who first described the trypanosome, its vectors and hosts (Chagas, 1909), is a key human vectorborne zoonotic disease that is endemic in 21 Latin American countries (Figure 1) and the southern United States (Bern, Kjos, Yabsley, & Montgomery, 2011; World Health Organisation, 2014), and it is now also spreading through international migrations into Europe (Perez-Molina et al., 2011), Canada (Schipper, McClarty, McRuer, Nash, & Penney, 1980), New Zealand and Australia (Jackson, Pinto, & Pett, 2014). The trypanosome develops slowly in humans with a brief acute phase followed by long-lasting chronic conditions characterized by cardiac and/or digestive pathologies leading to variable debilitating and life-threatening effects (Rassi, Rezende, Luquetti, & Rassi, 2010). The chronicity of the pathogenesis has contributed to make this trypanosomiasis a “silent” disease, thereby delaying major public health

initiatives to the 1990s, and it is now associated with a high hidden cost contributing to a global health and economic burden that makes it a major human disease with societal costs similar to those of uterine, cervical and oral cancers (Lee, Bacon, Bottazzi, & Hotez, 2013).

While Chagas disease is becoming part of public health policies in North America (CDC, 2013; PHAC, 2015), Europe (Basile et al., 2011) and Australia (Jackson et al., 2014), the vast majority of the 6–7 million people diagnosed with the disease live in Latin America with a prevalence of infection reaching up to 6.1% in Bolivia and 3.6% in Argentina (World Health Organisation, 2015b), while another 65 million people from the Americas are at risk of infection as they are daily exposed to vector transmission (World Health Organisation, 2014). The disease ecology in these endemic areas is arguably one of the most complex of all human vectorborne diseases whose transmission is further impacted by ongoing socio-economical changes (Briceño-León, 2007; Briceño-León & Méndez Galván, 2007). The causal agent of Chagas disease, the protozoan *Trypanosoma cruzi*, is a genetically diverse parasite able

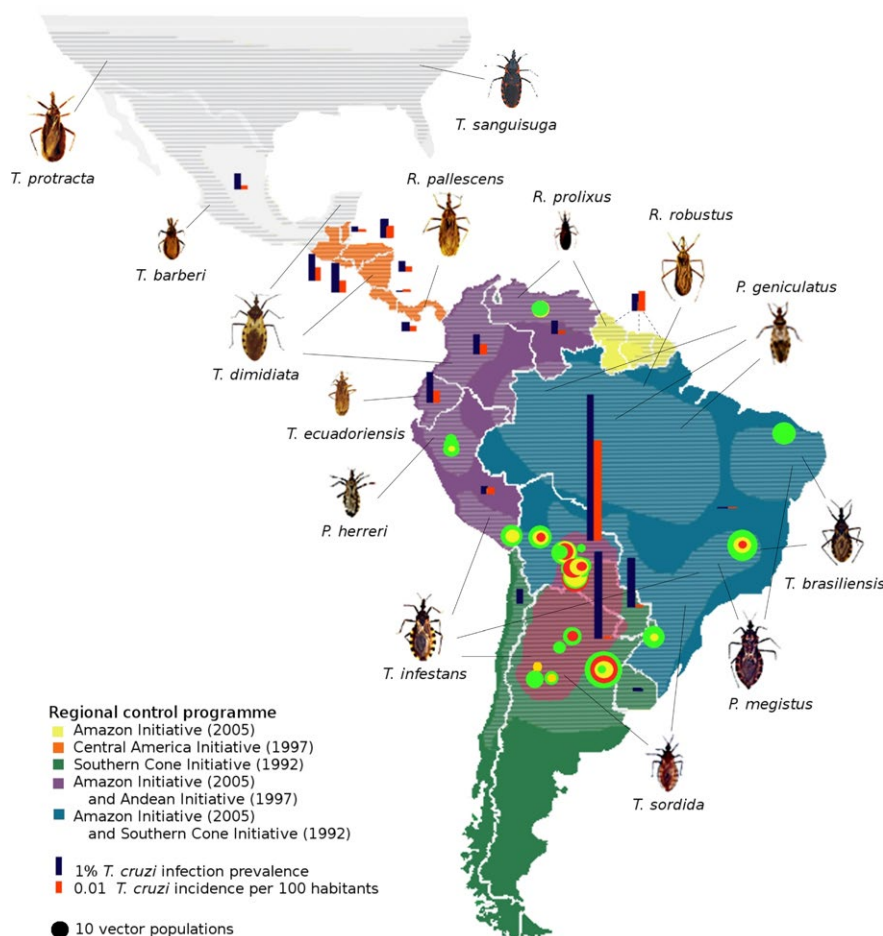


FIGURE 1 Eco-epidemiology of Chagas disease. The spatial distributions of the main triatomine vector species appear as shaded areas, while countries endemic for Chagas disease are coloured according to their contribution(s) to the main regional control programs initiated in the 1990–2000s. The last WHO’s statistics about national prevalence and incidence of the disease are given for each of these countries. The nationwide data summarized on this map are also provided in Appendix A in Supporting Information. Green, yellow and red circles stand for susceptible, resistant and highly resistant triatomine populations. The sizes of the circles are proportional to the number of populations of each province where resistance to one or more insecticides has been detected. The highly endemic Gran Chaco eco-region, where most resistance has been observed so far, is highlighted in red

to infect a broad range of vertebrates including over 100 mammal species (Jansen & Roque, 2010; World Health Organisation, 2002). The transmission of *T. cruzi* within its host (meta-)community is vectored by a large species diversity of bugs of the triatominae subfamily that are generalist haematophagous able to feed on an even broader range of vertebrate species (Gourbière, Dorn, Tripet, & Dumonteil, 2012). The complexity of these eco-epidemiological networks is such that *T. cruzi* eradication cannot be targeted and that the WHO Generic Roadmap for Neglected Tropical Diseases focuses on the regional elimination of intradomestic transmission by 2020 (World Health Organisation, 2015a). In the absence of vaccine and with the poor availability and side effects of available drugs (Chatelain, 2017), the cornerstone strategy to achieve such a goal is triatomine vector control.

This strategy lies at the heart of the WHO policy (World Health Organisation, 1998, 2010a) and of the multinational initiatives that have been launched since the 1990s to reduce human–vector contact at the regional scale, by massive campaigns of indoor insecticide spraying planned across the Andes (Salvatella, 2007), the southern cone (Silveira et al., 2002), Central America (Mancero & Ponce, 2011) and the Amazon region (World Health Organisation, 2005; Figure 1). These efforts have been successful in strongly reducing transmission due to two key “domestic” vectors, that is, *Triatoma infestans* and *Rhodnius prolixus*, that show strong levels of adaptation to human habitat (Waleckx, Gourbière, & Dumonteil, 2015). The interruption of intradomestic transmission due to *T. infestans* has been officially certified in various areas/countries, such as in Uruguay (World Health Organisation, 2012), Chile (World Health Organisation, 2000), several states of Brazil (World Health Organisation, 2006), and more recently in Argentinean provinces, and two departments of Southern Peru (World Health Organisation, 2010b). Today, the persistence of vector transmission in many other places (Patterson & Guhl, 2010) raises new issues for the future of Chagas disease's control. These emerging challenges are associated with typical evolutionary processes that could significantly change the local and/or global patterns of the disease epidemiology: (i) the rise of insecticide resistance (Mougabure-Cueto & Picollo, 2015; Pessoa, Vinãs, Rosa, & Diotaiuti, 2015), (ii) the adaptation of nondomesticated vectors to the human habitat (Almeida et al., 2009; Reyes-Lugo & Rodríguez-Acosta, 2000; Waleckx, Gourbière, et al., 2015), and (iii) the potential evolution of *T. cruzi* virulence (Bull & Luring, 2014; Pelosse et al., 2013).

In this contribution, we consider each of these three challenges in turn. For each of them, we aim at reviewing the efforts to provide evidences of the underlying evolutionary processes, and to place the control of the disease into an eco-evolutionary perspective. Along with a synthesis of the existing data, we intend to identify research lines that would significantly enhance our understanding of the evolutionary forces that shape the current and future patterns of *T. cruzi* transmission. We stress that such an eco-evolutionary knowledge is likely to become increasingly important to sustain the level of control of “domestic” vectors and to tackle the transmission due to nondomesticated triatomine species, whose epidemiological importance has definitely been uncovered in the last few years (Waleckx, Camara-Mejia, et al., 2015; Waleckx, Gourbière, et al., 2015).

2 | TRIATOMINE LIFE-HISTORY EVOLUTION AND VECTOR CONTROL CHALLENGES

The last 25 years of triatomine control have been designed under the assumption that the evolutionary potential of triatomines would be weak enough for them not to adapt to the new ecological conditions set by control interventions. This adaptive potential was a priori thought to be weak (Gorla, 1994; Schofield & Dias, 1999) for three principal reasons: the low level of triatomine genetic diversity (Mougabure-Cueto & Picollo, 2015), their long life expectancy (Guhl & Schofield, 1996; Monteiro, Escalante, & Beard, 2001) and the design of the control interventions based on low-frequency intervention with very high coverage (Bustamante Gomez, Diotaiuti, & Gorla, 2016). We review below field and laboratory studies on the development of insecticide resistance and the adaptation potential of vectors to human habitat as evidences that triatomine adaptive evolution can be much faster than anticipated and may jeopardize control efforts.

2.1 | Insecticide resistance

The development of insecticide resistance is a major issue wherever chemical control has been intended (Brown, 1986; Liu, 2015; Mallet, 1989; Rivero, Vézilier, Weill, Read, & Gandon, 2010). Populations of key vectors such *Anopheles* and *Culex* mosquitoes have been resistant to insecticides for over 60 years (Gjullin & Peters, 1952; Jones et al., 2012; Ranson & Lissenden, 2016), and similar resistance has also appeared in *Aedes* mosquitoes (Georghiou, 1986; Vontas et al., 2012). Unsurprisingly, given these past experiences, evidences of pyrethroid resistance are mounting in triatomines, especially in *T. infestans* and *R. prolixus* that have been heavily targeted by international control initiatives.

2.1.1 | Insecticide resistance in triatomines; where, when, who and to what extent?

Although insecticide resistance had been reported before the major international initiatives were launched (González Valdivieso, Sanchez Diaz, & Nocerino, 1971), its regular assessment began in the mid-1990s. We compiled measures of pyrethroid resistance in 378 populations studied since then (see Appendix B in Supporting Information), among which 149 (39%) were considered as “resistant.” The most documented foci of resistance are populations of *T. infestans* from northern Argentina (43.6%) and Bolivia (45.6%) with only a few additional cases reported from populations of *T. infestans* in Brazil and Peru, *R. prolixus* in Venezuela, *Triatoma sordida* in Brazil and *Panstrongylus herreri* in Peru (Figure 1). These highly endemic areas being under more investigations than many other places in Latin America, insecticide resistance may actually be spread over a larger spatial range than suggested by Figure 1 (although at different levels, see below). The highest levels of resistance are mostly observed in and around the Chaco region where 79 field populations of *T. infestans* have been shown to be highly resistant (i.e., $RR_{50} > 50$ or mortality $< 30\%$). In these areas, the level of

resistance can be up to 2,000 times higher than the level in reference strains (Sierra, Capriotti, Fronza, Mougabure-Cueto, & Ons, 2016), and it has already led to control failures (Picollo et al., 2005). Interestingly, we could not detect any temporal change in the levels of insecticide resistance reported since 2000 (Figure 2a,b) or with the number of years of control (Figure 2c,d). This suggests, as previously mentioned (Bustamante Gomez et al., 2016), that natural tolerance was already present to various levels at a large scale, although the highest levels remain concentrated in and around the Chaco area, where resistant and susceptible individuals still coexist at the local scale of a village or even a single household (Germano, Picollo, & Mougabure-Cueto, 2013). The majority of resistant populations of *T. infestans* were found resistant to deltamethrin (73.9%) with high levels of resistance also observed to other pyrethroids in Argentinian and Bolivian populations (Figure 2c,d), but there currently is little evidence of multiple resistances (Fabro et al., 2012; Germano & Picollo, 2014; Yon et al., 2004).

2.1.2 | A priori evolutionary thoughts and evolutionary questions

Insecticide resistance has emerged in triatomines, according to the general trend observed in many insects (Mallet, 1989; Rivero et al.,

2010) and despite the a priori evolutionary thoughts mentioned above. Whether the massive spraying of pyrethroids through international initiatives was worth is out of question given the success in controlling some of the most epidemiologically relevant triatomine populations. However, the evidences above raise issues about the sustainability of such vector control. We now need to reconsider our initial evolutionary thoughts in the light of more quantitative data and concepts to characterize triatomines' true evolutionary potential and possibly identify evolution-proof spraying strategies that will minimize the development of insecticide resistance while still providing efficient vector control.

Genetic diversity and evolutionary potential

That triatomines have a low adaptive potential due to their low genetic diversity is a statement that should be considered with caution. The correlation between genetic diversity measured at neutral molecular markers (typically used in triatomine genetics, see Gourbière et al., 2012 for a review) and short-term adaptive potential is indeed highly debatable, mostly because such markers retain information from a tiny part of the genome and as they can lose genetic variability at a very different rate than adaptive loci (Reed & Frankham, 2001). By contrast, the ability to adapt to rapidly happening environmental

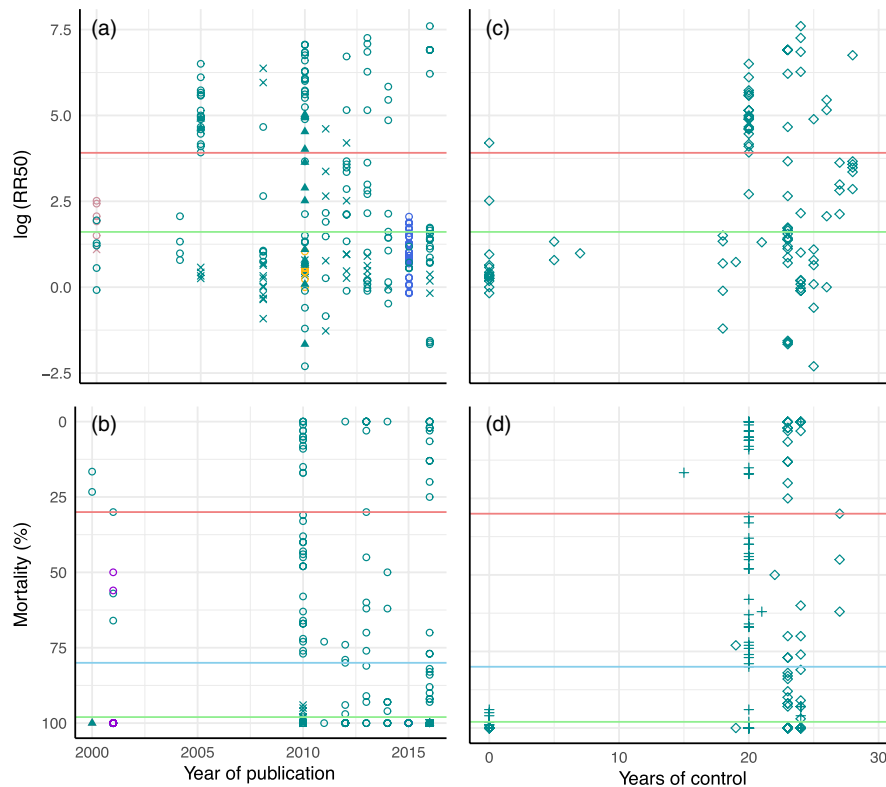


FIGURE 2 Levels of insecticide resistance reported in triatomines population with respect to their date of detection (a,b) and the number of years of control preceding detection (c,d). The level of resistance is measured as the logarithm of RR_{50} (a and c) or as a percentage of mortality (b and d). The green and pink lines are standard thresholds differentiating between susceptible, resistant and highly resistant triatomines populations. In b and d, no specific status is given to populations lying between the blue and pink lines. Colours indicate different species: green (*Triatoma infestans*), yellow (*Triatoma brasiliensis*), blue (*Triatoma sordida*), pink (*Rhodnius prolixus*) and violet (*Panstrongylus herreri*). Shapes correspond to different types of resistance in a and b; circles (pyrethroids), X (nonpyrethroids) and triangles (insecticide synergy), and they indicate countries in c and d; crosses (Bolivia) and lozenge (Argentina). Data are provided in Appendix B in Supporting Information

changes induced by human activities is increasingly recognized as a complex combination of genetic and epigenetic factors (Fernández et al., 2014; Rey, Danchin, Mirouze, Loot, & Blanchet, 2016), and it has been hypothesized that epigenetic could contribute to triatomine speciation (Costa et al., 2016; Dujardin, Costa, Bustamante, Jaramillo, & Catala, 2009). Interestingly, it has recently been shown that the spatial distribution of highly resistant populations coincides with the distribution of an intermediate cytogenetic group of *T. infestans* and further correlates with local environmental variables (Bustamante Gomez et al., 2016). This environmental determinism could, as suggested by the authors, be the outcome of an evolutionary dynamics involving some trade-offs between resistance genes and key ecological traits. Alternatively, it could reflect the effects of abiotic factors on the epigenetic components and/or the role of transposable elements in the regulation of gene expression (Rey et al., 2016). The importance of the regulation of (detoxification) gene expression was indeed recently proposed to explain that populations with similar frequencies of *kdr* mutations affecting the target sites of pyrethroid present different levels of resistance (Sierra et al., 2016). Meanwhile, it has been suggested that today's patterns of pyrethroid resistance reflect the existence of "naturally tolerant populations" of *T. infestans* rather than selective sweeps associated with insecticide spraying (Mougabure-Cueto & Picollo, 2015). This is indeed consistent with the reports of resistance profiles in sylvatic populations (Bustamante Gomez et al., 2016; Depickère et al., 2012; Roca-Acevedo et al., 2011), the broad spatial distribution of resistance (Figure 1, Mougabure-Cueto & Picollo, 2015) and the apparent absence of temporal changes in the observed levels of resistance (Figure 1b). Undoubtedly, triatomine insecticide resistance is a complex and plastic trait as it involves different mechanisms (González Audino, Vassena, Barrios, Zerba, & Picollo, 2004; Mougabure-Cueto & Picollo, 2015; Roca-Acevedo, Picollo, Capriotti, Sierra, & Santo-Orihuela, 2015) with a polygenic determinism (Pessoa et al., 2015). This trait shall now be investigated through functional genomics approaches (as genuinely initiated by Traverso et al., 2017), if one is to uncover the true nature of its variations, and propose some mechanistic explanations to the intriguing associations of the highest level of resistance with a specific genetic background and environmental variables (Bustamante Gomez et al., 2016).

Fitnesses are composite measures

A critical difficulty in assessing our evolutionary a priori and the evolutionary questions raised above is the lack of integrative measures that would allow comparing the fitness of resistant and susceptible individuals with respect to trait values over their entire life cycle, that is, the duration, survival and fecundity rates of each developmental stages, and the effect of insecticide on those different traits. Most experimental studies indeed focus on a single stage and typically measure effects of insecticide on survival of eggs (6%), first and fifth instars (86%, 4%) or adults (4%) of triatomines caught in their domestic (35%), peridomestic (58%) and sylvatic (7%) habitats (data from Appendix B in Supporting Information). Some pioneering attempts provide interesting estimates of both fecundity and longevity of the different

stages from colonies with different levels of resistance to deltamethrin (Germano & Picollo, 2014; Pires, Barbosa, & Diotaiuti, 2000). More resistant populations laid a lower number of eggs (Germano & Picollo, 2014) of higher weight (Pires et al., 2000). Meanwhile, those studies show an extension of egg or duration of instar stages in resistant individuals with compensation in others, so that there is overall no effect of resistance on the length of the complete life cycle. Although these lower reproductive outputs and developmental delays were interpreted as costs of resistance, they only affect the fitness of resistant and susceptible individuals when exposed to insecticide. Just as Germano and Picollo's (2014) data provide evidences of trade-off between the duration of different instar stages, insecticide resistance could be linked through trade-offs with the rates of survival and adult life stage, but this was not evaluated. Expressions of fitness with respect to life-history traits of individuals with developmental stages have been developed for a long time (Caswell, 2001, chapters 3–4) allowing to account for various trade-offs between such traits (Roff, 2002, chapter 4; Roff, 2010, chapters 2–3). To provide quantitative studies about the evolution of resistance in triatomines now requires such integrative fitness measures to be calculated for resistant and susceptible individuals in both treated and nontreated conditions as the evolution of resistance usually involves some form of spatially heterogeneous or temporally variable selection with a selective disadvantage of resistant individuals in nontreated environment. Triatomines are typically exposed to lethal doses inside domiciles and sublethal doses in peridomiciles (Bustamante Gomez, Caldas Pessoa, Luiz Rosa, Espinoza Echeverria, & Gonçalves Diotaiuti, 2015; Fronza, Toloza, Picollo, Spillmann, & Mougabure-Cueto, 2016). According to existing models, sublethal doses are likely to limit the evolution of resistance as selective pressures are then relaxed on earlier life stages and mostly affect the older and more infected vector individuals (Read, Lynch, & Thomas, 2009). Accordingly, the peridomestic habitat could provide a reservoir for re-infestation (Cecere et al., 2013; Gürtler, 2009) but with less resistant individuals, which could potentially impede the spread of resistant genes. Similarly, the effect of temporal heterogeneity in control interventions could be assessed. In such context, an interesting point raised by Germano and Picollo (2014) is that insecticide spraying might be seen as a strong random environmental variation. Such variability is well known to select for bet-hedging strategies and adaptive developmental delays (Gourbière & Menu, 2009 and references therein) that could explain prolonged developmental times in triatomine nymphs (Menu, Ginoux, Rajon, Lazzari, & Rabinovich, 2010).

2.2 | Domiciliation

There is a large diversity of triatomine species (Gourbière et al., 2012; Lent & Wgodzinsky, 1979; Schofield & Galvão, 2009) whose epidemiological importance is linked to their level of adaptation to human environment, that is, their level of domiciliation. Understanding the ability of triatomine species/populations to occupy wild and/or human habitat and its evolvability is thus essential in both optimizing today's control strategies and anticipating future epidemiological trends.

2.2.2 | Triatomine domiciliation potential

Although it is generally thought that anthropogenic pressure and damage to triatomine biotopes promote dispersion towards human dwellings and domiciliation of sylvatic triatomines, the evolutionary processes and driving mechanisms of adaptation to human environments remain poorly understood. On the one hand, taking into account the high morphologic plasticity of Triatominae associated with a rapid adaptation to different ecotopes (Dujardin, Steinden, Chavez, Machane, & Schofield, 1999; Dujardin et al., 2009), as well as the high diversity of human habitats, and the catholic feeding habits observed for many species of triatomines (Rabinovich et al., 2011), it is safe assuming that any triatomine population can infest human dwellings in particular settings. On the other hand, only a small fraction of triatomines are able to establish sustainable domestic colonies there, suggesting that these have evolved a set of traits which confers the ability to exploit domestic habitat (Abad-Franch & Monteiro, 2007). According to Schofield, Diotaiuti and Dujardin (1999), domiciliation involves both genetic and phenetic simplification as a result of a strong inside dwelling intraspecific competition after invading populations reach the carrying capacity of the domestic habitat. They speculated that such simplified genotypes would be the most efficient in obtaining blood and avoiding to “waste energetic resources to produce genes or gene products that may not be used.” While such adaptive view has been influential, including for vector control (see Section 2.1), its ecological foundations remain loosely documented. First, there is no quantitative evidence of the specificity and presumably higher stability of the “domestic” habitat. If there are probably less demographic changes of the blood hosts than in sylvatic ecotopes, and maybe less temperature variations (this clearly depends on human dwelling type and wild nests we are comparing), humans also tend to remove insects from its habitat, so stability may be very subjective. Second, the link between changes in ecological traits and selective advantage to triatomines in a domestic habitat is lacking. The authors used an eclectic mix of evidences to back their proposal about morphological and genetic changes observed in the transition from natural to artificial habitat. These included a progressive simplification of the sensory system in accordance with increasing habitat stability, a relaxed bilateral symmetry, a general reduction in body size, mainly in female bugs, leading to a corresponding reduction in sexual dimorphism (as females are on average larger than males in Triatominae), a decrease in total DNA per cell, a reduction in variability and polymorphism of isoenzymes, and a reduction in gene sequence variability (Schofield et al., 1999). Unfortunately, these observations have not been accompanied with any studies on the fitness of these different morpho- and genotypes in artificial environments to effectively link simplified genotypes or phenotypes with increased competitive ability in domestic habitats. In addition, most of the observed changes have not been supported by subsequent studies. For example, while Panzera et al. (2004) reported a reduction in DNA content in *T. infestans* from the Andes to the lowlands in South America, Hernandez, Abrahan, Moreno, Gorla,

and Catala (2008) reported an increasing complexity of the antennal sensilla pattern of the same insects from the lowlands to the Andes. Antennal sensilla patterns have also been shown to depend on many parameters including species, populations of a same species, sex and microhabitat (Arroyo, Esteban, Catala, & Angulo, 2007; Catala, Maida, Caro-Riano, Jaramillo, & Moreno, 2004; Dujardin et al., 2009; Hernandez et al., 2008), so that a simplification of the sensory system in the transition from sylvatic to domestic habitat (which provide plenty of different microhabitats) is a too simplistic idea and cannot be established as a rule. Similarly, the reduction in sexual dimorphism, which has been proposed as a marker of domiciliation in Triatominae (Dujardin et al., 1999), or the levels of fluctuating asymmetry—which is expected to be lower in stable habitats (Marquez & Saldamando-Benjumea, 2013; Nattero, Dujardin, del Pilar Fernández, & Gürtler, 2015) while the model of domiciliation of Triatominae mentioned above paradoxically predicts a relaxed bilateral symmetry as a consequence of habitat stability leading to a demographic increase and subsequent competition for food (Schofield et al., 1999), do not show consistent enough patterns, and should also be interpreted with caution (Dujardin et al., 1999; Marquez & Saldamando-Benjumea, 2013; Nattero et al., 2015; Sandoval Ramirez et al., 2015). Consequently, the morphological characters generally studied in Triatominae appear too variable to trustworthy be used to infer the level of domiciliation of triatomine species/populations or as markers of potential for domiciliation.

As mentioned above, a high plasticity is also observed in terms of blood hosts for many triatomine species (Rabinovich et al., 2011). This feature suggests that triatomines can easily adapt to new blood sources if their natural hosts disappear (as can occur when human and its domestic animals invade new areas), and potentially use human/domestic animals without a real evolutionary cost. Some studies have measured different life-history traits of triatomines in relation to different blood hosts (Emmanuelle-Machado et al., 2002; Gomes, Azambuja, & Garcia, 1990; Guarneri, Araujo, Diotaiuti, Gontijo, & Pereira, 2011; Guarneri, Pereira, & Diotaiuti, 2000; Lunardi, Gomes, Peres Camara, & Arrais-Silva, 2015; Martinez-Ibarra, Grant-Guillen, Nogueira-Torres, & Trujillo-Contreras, 2004; Martinez-Ibarra et al., 2006; Medone, Balsobre, Rabinovich, Marti, & Menu, 2015; Nattero, Leonhard, Rodriguez, & Crocco, 2011; Nattero, Rodriguez, & Crocco, 2013), as well as blood host preferences (Crocco & Catala, 1997; Gürtler et al., 2009; Jiron & Zeledon, 1982). This kind of studies can shed light on the attractiveness of human and/or domestic animals as blood hosts, as well as the performances and advantages/disadvantages to feed on them, and can thus help predicting the potential for domiciliation of different triatomine populations (Guarneri et al., 2011). Nevertheless, results need again to be interpreted with caution and extrapolation to natural situations may be difficult, as many traits affect fitness and results can depend on the traits studied. For example, while Nattero et al. (2011) suggested a better reproductive success for *T. infestans* feeding on mammalian rather than avian blood, Medone et al. (2015) reported a better population growth for *T. infestans* feeding on hen rather than human blood. Moreover, while better performances of the studied traits when feeding on human/domestic animals may suggest that a

triatomine population will gain advantage to invade human dwellings, it will not necessarily happen. Many factors cannot be reproduced in the laboratory, including host behaviour in its natural habitat. Inversely, this is not because lower performances are observed when feeding on human that invasion of human dwellings will not happen. The association with blood hosts depends on the benefit/cost ratio for triatomines, and a nonoptimal association can be preferred or even vital on some occasions, as evidenced by the fact that feeding patterns are modified depending on the availability and density of vectors and hosts (Gürtler et al., 2009). In such a context, data-driven modelling approaches could be used to concomitantly derivate fitness measures of vectors and help predicting domiciliation potential by expanding standard evolutionary ecology theories rooted in source–sink dynamical models (Gourbière & Gourbière, 2002; Nouvellet, Cucunubá, & Gourbière, 2015; Rascalou, Pontier, Menu, & Gourbière, 2012).

3 | *TRYPANOSOMA CRUZI* DIVERSITY AND VIRULENCE EVOLUTION

While triatomine vectors blood feed on a variety of vertebrate hosts including amphibians, reptiles, birds and mammals, *T. cruzi* infection is restricted to mammalian species. For example, complement-mediated lysis of the parasites rapidly occurs in birds, making them refractory to *T. cruzi* infection (Lima & Kierszenbaum, 1984; Minter-Goedbloed & Croon, 1981). *Trypanosoma cruzi* can nonetheless be considered a very generalist parasite, able to infect a large range of mammalian species covering very different orders, including Marsupialia, Rodentia, Lagomorpha, Chiroptera, Carnivora and Primata. While the infection in these different orders may have variable outcomes, there are also many common features in the acquisition and the within-host dynamic of *T. cruzi* that may contribute to explain its overall high diversity and

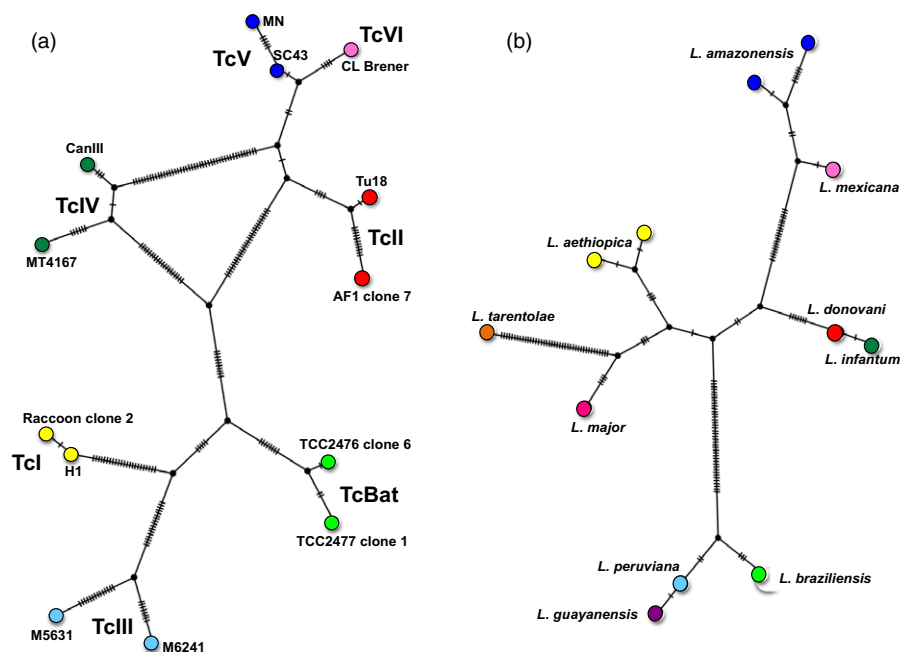
low virulence that are described below. We refer here to virulence as a parasite-induced loss of host's fitness. This broad definition encompasses both the empirical assessments of *T. cruzi* sublethal effects (see Section 3.1) and the theoretical acceptance of virulence as a rate of pathogen-induced host mortality (see Section 3.2).

3.1 | *T. cruzi* diversity and its determinants

Trypanosoma cruzi represents one of the best model organisms following a predominant clonal evolution model, with rare recombination and/or hybridization events (Tibayrenc & Ayala, 2015). The high genetic diversity of the parasite is believed to have arisen from this clonal model, leading to its subdivision into seven discrete typing units (DTUs TcI to TcVI and TcBat), which are highly stable across the Americas and over time (Zingales et al., 2009, 2012), and correspond to a (near-) clade genetic structuration of the parasite as a species (Tibayrenc & Ayala, 2015). This level of genetic diversity among *T. cruzi* DTUs is comparable to that observed among some *Leishmania* species (Yeo et al., 2011; and Figure 3). While TcI to TcIV are considered monophyletic and ancient clades, TcV and TcVI are more recent natural hybrids of TcII and TcIII DTUs (Lewis et al., 2011). However, with improved genotyping methods, a growing number of studies suggest that recombination and hybridization may be much more frequent than previously acknowledged, challenging the current model of clonal evolution (Messenger & Miles, 2015), and more studies will be required to clarify this issue.

Many studies have attempted to associate this genetic variability of the parasite with specific vertebrate hosts and transmission cycles, restricted geographic distribution of strains and DTUs, and the biological and clinical characteristics of the infection (Messenger, Miles, & Bern, 2015). For example, it was believed that TcI DTU was largely predominant in Mexico and to some extent in Central America (over 95% of the

FIGURE 3 Genetic diversity of *Trypanosoma cruzi* and *Leishmania* spp. TCS haplotype networks for *T. cruzi* DTUs (a) and *Leishmania* species (b) were constructed based on sequence alignments of the mini-exon intergenic sequence and HSP70 gene, respectively, using PopArt. *T. cruzi* strains and corresponding DTUs (TcI to TcVI and TcBat) are indicated, as well as *Leishmania* species. Ticks on network branches indicate the number of mutations from one haplotype to the next. The mini-exon sequences were 210–250 bp in length, with 122 segregating sites, and 99 parsimony informative sites for the *T. cruzi* network. *Leishmania* HSP70, sequences were 1,245 bps in length, with 110 segregating sites, and 79 parsimony informative sites



strains), but recent studies have documented the presence of non-Tcl parasite strains in triatomines from different regions in Mexico and Central America at high frequencies (Ibanez-Cervantes et al., 2013; Pennington, Paiz, Grajeda, & Cordon-Rosales, 2009; Torres-Montero, López-Monteon, Dumonteil, & Ramos-Ligonio, 2012), and a high proportion of patients appear to be infected with non-Tcl parasite strains (Risso et al., 2011). Similarly in the southern United States, initial work reported only Tcl and TcIV DTUs (Roelling et al., 2008), but recent studies also indicate the presence of TcII DTUs in rodents (Herrera, Licon, Nation, Jameson, & Wesson, 2015), as well as the predominant presence of TcII-TcV-TcVI in autochthonous human cases (Garcia et al., 2017). Together, these observations indicate clearly that *T. cruzi* genotype distribution in Central and North America is still poorly understood (Brenière, Waleckx, & Barnabe, 2016).

Other studies have suggested an association between *T. cruzi* DTUs and their biological properties and the pathogenesis of *T. cruzi* infection (Andrade & Magalhães, 1997; Carneiro, Romanha, & Chiari, 1991; Cencig, Coltel, Truysens, & Carlier, 2013; Lewis, Francisco, Taylor, Jayawardhana, & Kelly, 2016), raising hopes that infection outcome in humans may be predicted by the infecting DTU. However, these studies all suffer from the examination of a very limited number of strains, making such generalization poorly supported. Genotyping studies in large cohorts of patients with different clinical profiles may provide stronger evidence of such an association, but so far have been unable to provide evidence of associations between clinical outcomes and parasite DTUs (Martinez-Perez et al., 2016; Perez-Molina et al., 2014; Zafra, Mantilla, Jacome, Macedo, & Gonzalez, 2011), and contrasting results associating hosts and parasite DTUs have been described (Cura et al., 2010; Llewellyn et al., 2009; Monje-Rumi et al., 2015). A major limitation is that current PCR genotyping methods are poorly sensitive for the successful genotyping of parasites in chronically infected patients because of the very low amounts of parasite DNA present, so that genotypes can only be identified in about 50% of the patients (Cura et al., 2012, 2015; Garcia et al., 2017). The use of multiple consecutive blood samples from patients may increase the success rate of the genotyping to up to 70% of the patients (Martinez-Perez et al., 2016). Importantly, DTU classification is mostly based on the analysis housekeeping gene sequences such as ribosomal RNA genes and metabolic enzymes, that are unlikely to have a strong relevance for the virulence of the parasite, and alternative genetic markers derived from proteins playing a key role in the biological events of *T. cruzi* infection may be more likely to reveal potential associations between genotypes and the biological characteristics of parasite strains (De Pablos & Osuna, 2012).

Recent studies are also focusing on the genetic diversity within DTUs (Brenière et al., 2016). Within hosts of the order Didelphimorpha, haplotype and nucleotide diversity of Tcl are of the same magnitude as within all other wild mammals combined, strongly suggesting a longer and closer association between *T. cruzi* and Didelphimorpha (Brenière et al., 2016). These observations suggest a genetic structuration of *T. cruzi* influenced by the coevolution and adaptation of the parasite to specific hosts and transmission cycles, which should be examined further to establish the epidemiologic relevance of specific *T. cruzi* genotypes in human Chagas disease. Nonetheless, ecological host fitting may also represent an important mechanism allowing the parasite to

maintaining its genetic diversity and ample range of vertebrate hosts (Agosta, Janz, & Brooks, 2010). Indeed, under this scenario, the phenotypic plasticity of parasites allows them to be pre-adapted to new resources/hosts. A detailed genetic study revealed a limited gene flow between *T. cruzi* from different transmission cycles and a low level of genetic structure among strains from similar ecotopes in Bolivia, taken as evidence of ecological host fitting underlying the diversification of the parasite (Messenger et al., 2015). It is in fact likely that the complex interactions between *T. cruzi* and its vertebrate hosts are shaped by a combination of multiple nonexclusive evolutionary and ecological mechanisms (Agosta et al., 2010), and untangling their relative contributions remains challenging. Further studies are thus needed to clearly understand the different evolutionary forces underlying *T. cruzi* parasite diversity and the epidemiology of Chagas disease.

Finally, current approaches focus almost exclusively on detecting the dominant parasite genotype in biological samples (triatomine vectors and vertebrate hosts), so that the multiclonality of infections is overlooked. One of the rare studies analysing the multiclonality of *T. cruzi* infection in mammalian hosts revealed concurrent infections with up to 10 parasite genotypes in the same host and suggested the occurrence of diversifying selection on the parasite (Llewellyn et al., 2011). The analysis of sequence variation in GP63, a major surface glycoprotein involved in parasite infectivity to mammalian cells, revealed a large number of gene variants present in Chagasic patients, also suggesting a large parasite genetic diversity within hosts (Llewellyn et al., 2015). However, because this gene is present in multiple copy number in the parasite genome, the clonal structure of the infecting parasite population could not be established in that study. Also, no significant associations could be made between GP63 antigenic diversity and epidemiological and clinical parameters. However, strong selection could be evidenced, with a significant excess of nonsynonymous substitutions, suggesting that this may be a key factor contributing to parasite genetic diversity (Llewellyn et al., 2015). The multiclonality of infection in humans is also evidenced in longitudinal studies of patients follow-up, a large proportion of which present changes in the dominant DTU identified before and after drug treatment, suggesting that cryptic mixed infections and heterogeneous drug response may be occurring (Martinez-Perez et al., 2016). Multiclonal infections may thus be the norm rather than the exception, and the interactions among parasite genotypes within hosts are still mostly unknown, although they may lead to different infection profiles (Ragone et al., 2015) and have important evolutionary implications. Overall, a better understanding of the multiclonality of infection is clearly needed for a detailed understanding of parasite infection dynamics and of the evolutionary forces that modulate parasite genetic diversity (Lewis & Kelly, 2016).

3.2 | The evolution of *T. cruzi* virulence

3.2.1 | The secret and lazy life-history of *T. cruzi*; silent, dormant and persistent

The transmission and the epidemiology of *T. cruzi* are influenced by the long-term dynamics of host infection that is associated with the

very peculiar life history of this protozoan parasite. Although oral transmission has been reported in humans and nonhuman hosts (Henriques, Henriques-Pons, Meuser-Batista, Ribeiro, & de Souza, 2014; de Noya & González, 2015; Sánchez & Ramírez, 2013; Silva-dos-Santos et al., 2017), typical infection starts with an acute phase where the parasite enters the host through microlesions of the skin before multiplying in the bloodstream and spreading to other tissues. In humans, this infective stage lasts for 4–8 weeks and it is usually asymptomatic, although it might present as a febrile illness with local reaction at the site of infection (Rassi et al., 2010). Most individuals survive this acute stage and enter a chronic asymptomatic stage. The blood parasitemia then falls, and *T. cruzi* parasitizes myocytes located within cardiac, skeletal or smooth muscle tissues. Parasite persistence may then involve different mechanisms that potentially include continuous intracellular replication, dormant forms of *T. cruzi* and intermittent reactivation (Lewis & Kelly, 2016). Over the course of infection, those combine to induce local and global inflammatory responses that, together with the parasite-mediated autoimmune response (Teixeira, Nascimento, & Sturm, 2006), determine the timing and intensity of Chagas disease pathology. Most patients actually never develop any clinical symptoms, and only 30%–40% of infected humans show cardiac (20%–30%), digestive (10%–15%) or cardiogastrointestinal pathological manifestations that typically emerge 10–30 years after initial infection (Rassi et al., 2010). Overall, *T. cruzi* shall thus be considered of low virulence as in most infections, it persists inside its host over its lifespan causing little harm. Although our knowledge on the pathogenesis of *T. cruzi* in nonhuman hosts is limited, the dynamics of experimental infections in mouse (Henriques et al., 2014; Vorraro et al., 2014) and the high prevalence of infection in various reservoirs (Cortez et al., 2006; Herrera et al., 2005; Orozco et al., 2013) suggest that *T. cruzi* infection may there rely on the same pillars: silence, dormancy and persistence. In an evolutionary context, one spontaneously wonders why no strain of *T. cruzi* was able to evolve a higher level of virulence? Basic ingredients of existing theories suggest that it should indeed have done so. Vectorborne pathogens are expected to exhibit stronger virulence than directly transmitted diseases as their impact on host mobility is not associated with a reduction in transmission that remained possible through the vectors (Boots & Sasaki, 1999; Ewald, 1993, 2004; Gandon, 2004). Although very high levels of vector domiciliation can be associated with severe restriction of gene flow and dispersal (even at the scale of individual households, Noireau, Zegarra, Ordonez, Gutierrez, & Dujardin, 1999; Brenière, Lopez, Vargas, & Barnabé, 1997; Brenière et al., 1998), in most places triatomines disperse between human dwellings and surrounding habitats so that the parasite is likely to be spread out of infected hosts to reach various other host individuals and/or species, which should have provided many opportunities for virulence to evolve to a higher level. In addition, *T. cruzi* shows a high level of genetic diversity with several well-identified phylogenetic lineages and an important heterogeneity inside of each lineage (see above), which has been shown to favour the evolution of virulent strains because of within-host competition (see Alizon, Hurford, Mideo, and Van Baalen (2009) for a review). The restrained life history of *T. cruzi* is puzzling, and one can only hope

to resolve this apparent paradox with a better understanding of the evolutionary pressures that shape its evolution.

3.2.2 | Evolutionary paradox or evolutionary adaptation?

There is virtually no effort specifically devoted at identifying the key factors driving the evolution of *T. cruzi* virulence through classical theoretical approaches. The only contribution sets under the light of life-history evolution is by Pelosse et al. (2013), and it shows that vector's risk spreading strategies can speed up the invasion of virulent strains in a stochastically variable environment. Although truly inspiring, this paper relies on numerical analyses that do not seek to provide the simple (analytical) foundations for a broad theory of *T. cruzi* virulence evolution. We thus focus here on exploiting theoretical results that were obtained in the context of *T. cruzi* eco-epidemiology with the aim of illustrating that they can readily be used to provide general predictions on *T. cruzi* adaptive evolution, which will fit into the overall theory of virulence evolution. Expressions of the basic reproductive number (R_0) have been developed to look at *T. cruzi* population dynamics and can indeed be used as fitness measures in a simple “optimality” approach (Bull & Lauring, 2014; Parker & Smith, 1990). From the expressions of R_0 found in the literature (see Appendix C in Supporting Information), we established a “core” R_0 :

$$R_0 = \sqrt{\frac{\beta_h \cdot c_h(N_h, N_v)}{(\mu_h + \alpha_h)} \cdot \frac{\beta_v \cdot c_v(N_h, N_v)}{(\mu_v + \alpha_v)}},$$

that gives the rate of emergence of a *T. cruzi* strain according to the (i) per contact probabilities of transmission from vector/host to host/vector (β_h, β_v), (ii) contact rates between susceptible host/vector and infected vector/host ($c_h(N_h, N_v), c_v(N_h, N_v)$), death rates of host and vector (μ_h, μ_v), and (iii) virulence, that is, additional mortality to host and vector (α_h, α_v). Assuming a typical transmission–virulence trade-off, it comes $\beta_h = \varepsilon \cdot \alpha_h / (1 + \alpha_h)$, ε stands for the maximal probability of stercorarian transmission, and a linear relationship between virulences, that is, $\alpha_v = \nu \cdot \alpha_h$. An analytical expression of the optimal level of virulence to host (α_h^*) can then be derived searching for the maximal value of R_0 :

$$\alpha_h^* = \sqrt{\frac{\mu_h \mu_v}{\mu_v + \nu(1 + \mu_h)}},$$

that allows establishing the first basic predictions about the effects of key features of *T. cruzi* transmission on the evolution of its virulence.

A first specificity of *T. cruzi* life history comes from its stercorarian mode of transmission. The pathogen multiplies within the gut of triatomines, but it is not able to reach their salivary glands so that transmission occurs through the vector faeces. The per bite probability of transmission from infected vector to susceptible host is thus unusually low, with estimates of the orders of 10^{-4} to 10^{-3} on humans (Nouvellet, Dumonteil, & Gourbière, 2013; Rabinovich, Wisnivesky-Colli, Solarz, & Gürtler, 1990) and 10^{-4} to 10^{-2} on

reservoirs (Basombrío et al., 1996; Rabinovich, Schweigmann, Yohai, & Wisnivesky-Colli, 2001). According to the expression of α_h^* , this low probability of transmission is expected not to have any impact on the evolution of *T. cruzi*, basically because the (in)efficacy of the transmission processes (e) is similar for all strains. Such (in)efficacy has been related with the time elapsing between feeding and defecation, and a “defecation index” allows comparing the transmission potential of different triatomine species (Loza-Murguía & Noireau, 2010; Reisenman, Gregory, Guerenstein, & Hildebrand, 2011). Hypothetically, different strains could thus be transmitted with different efficacies if they had different capacities in manipulating (or at least affecting) their vector's behaviour. In the last few years, *T. cruzi* has indeed been shown to affect the dispersal of *T. dimidiata* (Nouvellet, Ramirez-Sierra, Dumonteil, & Gourbière, 2011; Ramirez-Sierra, Herrera-Aguilar, Gourbière, & Dumonteil, 2010) and *R. prolixus* (Marlière et al., 2015). Even more intriguingly, infected bugs have been shown to bite 45% more often than uninfected individuals, and the time before defecation to be reduced by 30% by infection (Botto-Mahan, Cattán, & Medel, 2006). While this neat paper did not provide any information on the infecting strain of *T. cruzi*, experiments could presumably be repeated to quantify heterogeneities in the impact of various strains of parasites. The above theory could then be adapted in a data-driven manner to gain further insights into the contribution of the stercorarian mode of transmission to the low level of virulence of *T. cruzi*.

A second specificity of *T. cruzi* is its ability to infect a broad range of vertebrate species. Both the expression of α_h^* and the general theory of virulence (Dieckmann, 2002; Otto & Day, 2007) predict shorter lived hosts to lead to greater virulence. As *T. cruzi* is able to infect a vast diversity of vertebrate hosts, its “average host” is likely to be of relatively short life expectancy, so that more virulent strains should outcompete less virulent ones in exploiting such hosts before they die. Noteworthy, these conclusions are based on single host modelling that does not account for a reduction in between strains competition that could be associated with a broad range of host species. Still, the above theory suggests that a larger number of host individuals (N_h) would increase R_0 , but will not affect the optimal level of virulence, which, again, is mostly because the fitness of all strains is uniformly affected. Hypothetically, a larger number of host species may lead to evolutionary branching and host specialization, or it may yield the evolution of more generalist strategies (Brown, Cornforth, & Mideo, 2012; Gandon, 2004; Leggett, Buckling, Long, & Boots, 2013). However, the analyses of triatomines' bloodmeal sources have demonstrated that they are generalist haematophagous species feeding on an even broader range of vertebrates than *T. cruzi* is able to infect. Accordingly, the most likely evolutionary scenario is that between-host species transmission is frequent and, in such conditions, virulence is expected to evolve almost independently of the abundance of the host species, and to be primarily determined by within- and between-hosts constraints on parasite life-history (Gandon, 2004). To genuinely understand such constraints and ultimately the effects of host biodiversity on the virulence of *T. cruzi* now requires a specific modelling of the pathogen rooted in empirically informed descriptions of its ecological networks.

A third specificity of *T. cruzi* transmission is the longevity and nymphal haematophagy of its triatomine vectors, so that infection rates increase gradually during the entire triatomine lifespan (Buitrago et al., 2010) that typically is one order of magnitude longer than other mosquito or fly vectors (Rascalou et al., 2012). A common wisdom in modelling vectorborne infection is to consider that pathogens have no effect on their vectors (Elliot, Adler, & Sabelis, 2003). Under such assumption ($\nu = 0$), the expected level of *T. cruzi* virulence α_h^* would not depend on triatomine lifespan. However, significant effects of *T. cruzi* infection have been reported on the behaviour and/or life-history of various triatomine species, which include *T. infestans* (Schaub, 1988, 1989), *R. prolixus* (Elliot, Rodrigues, Lorenzo, Martins-Filho, & Guarneri, 2015; Peterson, Bartsch, Lee, & Dobson, 2015), *T. dimidiata* (Ramirez-Sierra et al., 2010), *P. megistus* (Lima et al., 1992) and *Mepraia spinolai* (Botto-Mahan, 2009; Botto-Mahan et al., 2006). This suggests that vectors could be considered as alternative hosts rather than a merely neutral compartment. According to the expression of α_h^* (with $\nu \neq 0$), virulence is then expected to decrease with vector life expectancy, so that the unusual lifespan of triatomine may actually be a good candidate hypothesis to explain *T. cruzi* low virulence.

The above predictions are first steps into the development of a theory of *T. cruzi* evolution, and they illustrate how standing eco-epidemiological models can be informative. Although such optimization of R_0 accounting for potential trade-off between pathogen's life-history traits is a natural approach to lay the foundation of the desired theory, it sensu stricto compares the ability of different strains to invade a naive host-vector population (Bull & Ebert, 2008). The outcomes of optimality study often provide satisfactory predictions on longer term evolution were various virulent strains can invade each other in more typical mutation-substitution dynamics (Cressler, McLeod, Rozins, Van Den Hoogen, & Day, 2015). However, complexes dynamical feedbacks can also emerge when virulent strains are confronted one with another (Dieckmann, 2002) and when host populations experiment recurrent invasions of new parasite variants before equilibrium has been reached (Bull & Ebert, 2008). Understanding the determinants of *T. cruzi* virulence will undoubtedly require combining such approaches, with the ultimate challenges of designing evolution-proof control strategies to avoid that this ubiquitous pathogen widely spreads across the Americas becomes an even more substantial public health concern.

4 | CONCLUSION

After the success of international initiatives in reducing the abundance of key domestic vector species in highly endemic areas, new challenges are emerging for the future of Chagas disease control. These new challenges will require a microevolutionary thinking that is slowly growing to assess the evolutionary potential of *T. cruzi* and its triatomine vectors and their adaptive response to control interventions. The eco-epidemiological relationships that build-up the selective pressures at work have been assiduously studied over the last century, so that, combined with concepts and modelling inspired

from life-history evolution, a good evolutionary understanding could be rapidly gained. Such basic knowledge will naturally find itself at the heart of future strategies that will undoubtedly target the long-term sustainability of today's achievements in highly endemic areas and the further reduction in disease incidence in other areas where secondary vectors may be adapting to the human habitat. In such a context, the development of solid eco-epidemiological studies on a large diversity of triatomine vector species should be encouraged to provide opportunities for comparative analyses that will undoubtedly improve our evolutionary understanding of *T. cruzi* and Chagas disease transmission.

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DATA ARCHIVING STATEMENT

We will not be archiving data because this manuscript does not have associated data.

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REFERENCES

- Abad-Franch, F. (2016). A simple, biologically sound, and potentially useful working classification of Chagas disease vectors. *Memorias do Instituto Oswaldo Cruz*, 111(10), 649–651. <https://doi.org/10.1590/0074-02760160203>
- Abad-Franch, F., & Monteiro, F. A. (2007). Biogeography and evolution of Amazonian triatomines (Heteroptera: Reduviidae): Implications for Chagas disease surveillance in humid forest ecoregions. *Memorias do Instituto Oswaldo Cruz*, 102(Suppl 1), 57–70. <https://doi.org/10.1590/S0074-02762007005000108>
- Agosta, S. J., Janz, N., & Brooks, D. R. (2010). How specialists can be generalists: Resolving the "parasite paradox" and implications for emerging infectious disease. *Zoologia*, 27(2), 151–162. <https://doi.org/10.1590/S1984-46702010000200001>
- Alizon, S., Hurford, A., Mideo, N., & Van Baalen, M. (2009). Virulence evolution and the trade-off hypothesis: History, current state of affairs and the future. *Journal of Evolutionary Biology*, 22(2), 245–259. <https://doi.org/10.1111/j.1420-9101.2008.01658.x>
- Almeida, C. E., Folly-Ramos, E., Peterson, A. T., Lima-Neiva, V., Gumiel, M., Duarte, R., ... Costa, J. (2009). Could the bug *Triatoma sherlocki* be vectoring Chagas disease in small mining communities in Bahia, Brazil? *Medical and Veterinary Entomology*, 23(4), 410–417. <https://doi.org/10.1111/j.1365-2915.2009.00822.x>
- Andrade, S. G., & Magalhães, J. B. (1997). Biodemes and zymodemes of *Trypanosoma cruzi* strains: Correlations with clinical data and experimental pathology. *Revista da Sociedade Brasileira de Medicina Tropical*, 30, 27–35. <https://doi.org/10.1590/S0037-86821997000100006>
- Arroyo, C. M., Esteban, L., Catala, S., & Angulo, V. M. (2007). Antennal phenotype variation in sylvatic, peridomestic and domestic populations of *Triatoma dimidiata* (Hemiptera: Reduviidae) from Santander, Colombia. *Biomedica*, 27(1), 92–100. <https://doi.org/10.7705/biomedica.v27i1.252>
- Barbu, C., Dumonteil, E., & Gourbière, S. (2009). Optimization of control strategies for non-domiciliated *Triatoma dimidiata*, Chagas disease vector in the Yucatan Peninsula, Mexico. *PLoS Neglected Tropical Diseases*, 3(4), e416. <https://doi.org/10.1371/journal.pntd.0000416>
- Barbu, C., Dumonteil, E., & Gourbière, S. (2011). Evaluation of spatially targeted strategies to control non-domiciliated *Triatoma dimidiata* vector of Chagas disease. *Plos Neglected Tropical Diseases*, 5(5), e1045. <https://doi.org/10.1371/journal.pntd.0001045>
- Basile, L., Jansa, J. M., Carlier, Y., Salamanca, D. D., Angheben, A., Bartoloni, A., ... Working Group on Chagas Disease (2011). Chagas disease in European countries: the challenge of a surveillance system. *Chagas Disease in Europe*, 18.
- Basombrío, M. A., Gorla, D., Catalá, S., Segura, M. A., Mora, M. C., Gómez, L., & Nasser, J. (1996). Number of vector bites determining the infection of guinea pigs with *Trypanosoma cruzi*. *Memorias Do Instituto Oswaldo Cruz*, 91(4), 421–424. <https://doi.org/10.1590/S0074-02761996000400006>
- Bermudez, H., Balderrama, F., & Torrico, F. (1993). Identification and characterization of sylvatic foci of *Triatoma infestans* in Central Bolivia. *American Journal of Tropical Medicine and Hygiene*, 49(Suppl), 371.
- Bern, C., Kjos, S., Yabsley, M. J., & Montgomery, S. P. (2011). *Trypanosoma cruzi* and Chagas' Disease in the United States. *Clinical Microbiology Reviews*, 24(4), 655–681. <https://doi.org/10.1128/CMR.00005-11>
- Boots, M., & Sasaki, A. (1999). "Small worlds" and the evolution of virulence: Infection occurs locally and at a distance. *Proceedings of the Royal Society of London B: Biological Sciences*, 266(1432), 1933–1938. <https://doi.org/10.1098/rspb.1999.0869>
- Botto-Mahan, C. (2009). *Trypanosoma cruzi* induces life-history trait changes in the wild kissing bug *Mepraia spinolai*: Implications for parasite transmission. *Vector-Borne and Zoonotic Diseases*, 9, 505–510. <https://doi.org/10.1089/vbz.2008.0003>
- Botto-Mahan, C., Cattán, P. E., & Medel, R. (2006). Chagas disease parasite induces behavioural changes in the kissing bug *Mepraia spinolai*. *Acta Tropica*, 98(3), 219–223. <https://doi.org/10.1016/j.actatropica.2006.05.005>
- Brenière, S. F., Bosseno, M. F., Vargas, F., Yaksic, N., Noireau, F., Noel, S., ... Tibayrenc, M. (1998). Smallness of the panmictic unit of *Triatoma infestans* (Hemiptera: Reduviidae). *Journal of Medical Entomology*, 35, 911–917. <https://doi.org/10.1093/jmedent/35.6.911>
- Brenière, S. F., Lopez, J., Vargas, F., & Barnabé, C. (1997). Genetic variability and microdistribution of *Triatoma infestans* genotypes and *Trypanosoma cruzi* clones in Arequipa region (Peru). *Memórias do Instituto Oswaldo Cruz*, 92, 401–408. <https://doi.org/10.1590/S0074-02761997000300018>
- Brenière, S. F., Salas, R., Buitrago, R., Bremond, P., Sosa, V., Bosseno, M.-F., ... Barnabe, C. (2013). Wild populations of *Triatoma infestans* are highly connected to intra-peridomestic conspecific populations in the Bolivian Andes. *PLoS ONE*, 8(11), e80786. <https://doi.org/10.1371/journal.pone.0080786>
- Brenière, S. F., Waleckx, E., & Barnabe, C. (2016). Over six thousand *Trypanosoma cruzi* strains classified into discrete typing units (DTUs): Attempt at an inventory. *PLoS Neglected Tropical Diseases*, 10(8), e0004792. <https://doi.org/10.1371/journal.pntd.0004792>
- Briceño-León, R. (2007). Chagas disease and globalization of the Amazon. *Cadernos De Saude Publica*, 23(Suppl 1), S33–S40. <https://doi.org/10.1590/S0102-311X2007001300005>
- Briceño-León, R., & Méndez Galván, J. (2007). The social determinants of Chagas disease and the transformations of Latin America. *Memorias Do Instituto Oswaldo Cruz*, 102(Suppl 1), 109–112. <https://doi.org/10.1590/S0074-02762007005000095>

- Brown, A. W. A. (1986). Insecticide resistance in mosquitoes: A pragmatic review. *Journal of the American Mosquito Control Association*, 2, 123–140.
- Brown, S. P., Cornforth, D. M., & Mideo, N. (2012). Evolution of virulence in opportunistic pathogens: Generalism, plasticity, and control. *Trends in Microbiology*, 20(7), 336–342. <https://doi.org/10.1016/j.tim.2012.04.005>
- Buitrago, R., Waleckx, E., Bosseno, M. F., Zoveda, F., Vidaurre, P., Salas, R., ... Brenière, S. F. (2010). First report of widespread wild populations of *Triatoma infestans* (Reduviidae, Triatominae) in the valleys of La Paz, Bolivia. *American Journal of Tropical Medicine and Hygiene*, 82(4), 574–579. <https://doi.org/10.4269/ajtmh.2010.09-0325>
- Bull, J. J., & Ebert, D. (2008). Invasion thresholds and the evolution of non-equilibrium virulence: Nonoptimal virulence. *Evolutionary Applications*, 1(1), 172–182. <https://doi.org/10.1111/j.1752-4571.2007.00003.x>
- Bull, J. J., & Luring, A. S. (2014). Theory and empiricism in virulence evolution. *PLoS Pathogens*, 10(10), e1004387. <https://doi.org/10.1371/journal.ppat.1004387>
- Bustamante Gomez, M., Caldas Pessoa, G. D., Luiz Rosa, A. C., Espinoza Echeverria, J., & Gonçalves Diotaiuti, L. (2015). Inheritance and heritability of deltamethrin resistance under laboratory conditions of *Triatoma infestans* from Bolivia. *Parasites & Vectors*, 8(1), 595. <https://doi.org/10.1186/s13071-015-1211-9>
- Bustamante Gomez, M., Diotaiuti, L. G., & Gorla, D. E. (2016). Distribution of pyrethroid resistant populations of *Triatoma infestans* in the Southern Cone of South America. *PLoS Neglected Tropical Diseases*, 10(3), e0004561.
- Carneiro, M., Romanha, A. J., & Chiari, E. (1991). Biological characterization of *Trypanosoma cruzi* strains from different zymodemes and schizodemes. *Memorias do Instituto Oswaldo Cruz*, 86, 387–393. <https://doi.org/10.1590/S0074-02761991000400002>
- Caswell, H. (2001). *Matrix population models: Construction, analysis, and interpretation* (2nd ed.). Sunderland, MA: Sinauer Associates.
- Catala, S. S., Maida, D. M., Caro-Riano, H., Jaramillo, N., & Moreno, J. (2004). Changes associated with laboratory rearing in antennal sensilla patterns of *Triatoma infestans*, *Rhodnius prolixus*, and *Rhodnius pallescens* (Hemiptera, Reduviidae, Triatominae). *Memorias do Instituto Oswaldo Cruz*, 99(1), 25–30. <https://doi.org/10.1590/S0074-02762004000100005>
- CDC (2013, September). Chagas disease in the Americas 2013. CS242221-A. Center for Global Health, Department of health and human services USA. Retrieved from <https://www.cdc.gov/parasites/chagas/resources/chagasdiseaseintheamericas.pdf>
- Cecere, M. C., Vazquez-Prokopec, G. M., Ceballos, L. A., Boragno, S., Zárate, J. E., Kitron, U., & Gürtler, R. E. (2013). Improved chemical control of Chagas disease vectors in the dry Chaco region. *Journal of Medical Entomology*, 50(2), 394–403. <https://doi.org/10.1603/ME12109>
- Cencig, S., Coltel, N., Truyens, C., & Carlier, Y. (2013). Fertility, gestation outcome and parasite congenital transmissibility in mice infected with TcII and TcVI genotypes of *Trypanosoma cruzi*. *PLoS Neglected Tropical Diseases*, 7(6), e2271. <https://doi.org/10.1371/journal.pntd.0002271>
- Chagas, C. (1909). Nova tripanozomíaze humana: Estudos sobre a morfologia e o ciclo evolutivo do *Schizotrypanum cruzi* n. gen., n. sp., agente etiológico de nova entidade morbida do homem. *Memorias do Instituto Oswaldo Cruz*, 1(2), 159–218. <https://doi.org/10.1590/S0074-02761909000200008>
- Chatelain, E. (2017). Chagas disease research and development: Is there light at the end of the tunnel? *Computational and Structural Biotechnology Journal*, 15, 98–103. <https://doi.org/10.1016/j.csbj.2016.12.002>
- Cortez, M. R., Pinho, A. P., Cuervo, P., Alfaro, F., Solano, M., Xavier, S. C. C., ... Jansen, A. M. (2006). *Trypanosoma cruzi* (Kinetoplastida Trypanosomatidae): Ecology of the transmission cycle in the wild environment of the Andean valley of Cochabamba, Bolivia. *Experimental Parasitology*, 114(4), 305–313. <https://doi.org/10.1016/j.exppara.2006.04.010>
- Costa, J., Bargues, M. D., Neiva, V. L., Lawrence, G. G., Gumiel, M., Oliveira, G., ... Dujardin, J. P. (2016). Phenotypic variability confirmed by nuclear ribosomal DNA suggests a possible natural hybrid zone of *Triatoma brasiliensis* species complex. *Infection, Genetics and Evolution*, 37, 77–87. <https://doi.org/10.1016/j.meegid.2015.10.025>
- Cressler, C. E., McLeod, D. V., Rozins, C., Van Den Hoogen, J., & Day, T. (2015). The adaptive evolution of virulence: A review of theoretical predictions and empirical tests. *Parasitology*, 143(07), 915–930. <https://doi.org/10.1017/S003118201500092X>
- Crocco, L., & Catala, S. (1997). Host preferences of *Triatoma sordida*. *Annals of Tropical Medicine and Parasitology*, 91(8), 927–930. <https://doi.org/10.1080/00034983.1997.11813220>
- Cura, C. I., Duffy, T., Lucero, R. H., Bisio, M., Peneau, J., Jimenez-Coello, M., ... Schijman, A. G. (2015). Multiplex real-time PCR assay using TaqMan probes for the identification of *Trypanosoma cruzi* DTUs in biological and clinical samples. *PLoS Neglected Tropical Diseases*, 9(5), e0003765. <https://doi.org/10.1371/journal.pntd.0003765>
- Cura, C. I., Lucero, R. H., Bisio, M., Oshiro, E., Formichelli, L. B., Burgos, J. M., ... Schijman, A. G. (2012). *Trypanosoma cruzi* discrete typing units in Chagas disease patients from endemic and non-endemic regions of Argentina. *Parasitology*, 139(4), 516–521. <https://doi.org/10.1017/S0031182011002186>
- Cura, C. I., Mejía-Jaramillo, A. M., Duffy, T., Burgos, J. M., Rodriguez, M., Cardinal, M. V., ... Schijman, A. G. (2010). *Trypanosoma cruzi* I genotypes in different geographical regions and transmission cycles based on a microsatellite motif of the intergenic spacer of spliced-leader genes. *International Journal for Parasitology*, 40(14), 1599–1607. <https://doi.org/10.1016/j.ijpara.2010.06.006>
- De Pablos, L. M., & Osuna, A. (2012). Multigene families in *Trypanosoma cruzi* and their role in infectivity. *Infection and Immunity*, 80, 2258–2264. <https://doi.org/10.1128/IAI.06225-11>
- Depickère, S., Buitrago, R., Siñani, E., Baune, M., Monje, M., Lopez, R., ... Brenière, S. F. (2012). Susceptibility and resistance to deltamethrin of wild and domestic populations of *Triatoma infestans* (Reduviidae: Triatominae) in Bolivia: New discoveries. *Memorias do Instituto Oswaldo Cruz*, 107(8), 1042–1047. <https://doi.org/10.1590/S0074-02762012000800013>
- Dieckmann, U. (2002). *Adaptive dynamics of infectious diseases: In pursuit of virulence management*. (International Institute for Applied Systems Analysis, Ed.). Cambridge; New York: Cambridge University Press. <https://doi.org/10.1017/CBO9780511525728>
- Dujardin, J. P., Costa, J., Bustamante, D., Jaramillo, N., & Catala, S. (2009). Deciphering morphology in Triatominae: The evolutionary signals. *Acta Tropica*, 110(2–3), 101–111. <https://doi.org/10.1016/j.actatropica.2008.09.026>
- Dujardin, J. P., Schofield, C. J., & Panzera, F. (2002). *Los vectores de la enfermedad de Chagas*. Brussels, Belgium: Académie Royale des Sciences d'Outre-Mer.
- Dujardin, J. P., Steinden, M., Chavez, T., Machane, M., & Schofield, C. (1999). Changes in the sexual dimorphism of triatominae in the transition from natural to artificial habitats. *Memorias do Instituto Oswaldo Cruz*, 94(4), 565–569. <https://doi.org/10.1590/S0074-02761999000400024>
- Dumonteil, E., Gourbière, S., Barrera-Perez, M., Rodriguez-Felix, E., Ruiz-Pina, H., Banos-Lopez, O., ... Rabinovich, J. E. (2002). Geographic distribution of *Triatoma dimidiata* and transmission dynamics of *Trypanosoma cruzi* in the Yucatan Peninsula of Mexico. *American Journal of Tropical Medicine and Hygiene*, 67(2), 176–183. <https://doi.org/10.4269/ajtmh.2002.67.176>
- Dumonteil, E., Ramirez-Sierra, M. J., Ferral, J., Euan-Garcia, M., & Chavez-Nunez, L. (2009). Usefulness of community participation for the fine temporal monitoring of house infestation by non-domiciliated triatomines. *Journal of Parasitology*, 95(2), 469–471. <https://doi.org/10.1645/ge-1712.1>
- Elliot, S. L., Adler, F. R., & Sabelis, M. W. (2003). How virulent should a parasite be to its vector? *Ecology*, 84(10), 2568–2574. <https://doi.org/10.1890/02-8013>

- Elliot, S. L., Rodrigues, J. O., Lorenzo, M. G., Martins-Filho, O. A., & Guarneri, A. A. (2015). *Trypanosoma cruzi*, etiological agent of Chagas disease, is virulent to its triatomine vector *Rhodnius prolixus* in a temperature-dependent manner. *PLOS Neglected Tropical Diseases*, 9(3), e0003646. <https://doi.org/10.1371/journal.pntd.0003646>
- Emmanuelle-Machado, P., Koerich, L. B., Joukoski Dde, B., Carvalho-Pinto, C. J., Grisard, E. C., & Steindel, M. (2002). Biology of *Triatoma klugi* Carcavallo, Jurberg, Lent & Galvao 2001 (Heteroptera: Reduviidae) under laboratory conditions: Effects of distinct blood sources and susceptibility to *Trypanosoma cruzi* and *Trypanosoma rangeli*. *Memorias do Instituto Oswaldo Cruz*, 97(4), 583–587. <https://doi.org/10.1590/S0074-02762002000400025>
- Ewald, P. W. (1993). The evolution of virulence. *Scientific American*, 268(4), 86–93. <https://doi.org/10.1038/scientificamerican0493-86>
- Ewald, P. W. (2004). Evolution of virulence. *Infectious Disease Clinics of North America*, 18(1), 115. [https://doi.org/10.1016/S0891-5520\(03\)00099-0](https://doi.org/10.1016/S0891-5520(03)00099-0)
- Fabro, J., Sterkel, M., Capriotti, N., Mougabure-Cueto, G., Germano, M., Rivera-Pomar, R., & Ons, S. (2012). Identification of a point mutation associated with pyrethroid resistance in the para-type sodium channel of *Triatoma infestans*, a vector of Chagas' disease. *Infection, Genetics and Evolution*, 12(2), 487–491. <https://doi.org/10.1016/j.meegid.2011.12.006>
- Fernández, A. F., Toraño, E. G., Urdinguio, R. G., Lana, A. G., Fernández, I. A., & Fraga, M. F. (2014). The epigenetic basis of adaptation and responses to environmental change: Perspective on human reproduction. In W. V. Holt, J. L. Brown, & P. Comizzoli (Eds.), *Reproductive sciences in animal conservation* (Vol. 753, pp. 97–117). New York, NY: Springer New York.
- Fronza, G., Toloza, A. C., Picollo, M. I., Spillmann, C., & Mougabure-Cueto, G. A. (2016). Geographical variation of deltamethrin susceptibility of *Triatoma infestans* (Hemiptera: Reduviidae) in Argentina with emphasis on a resistant focus in the Gran Chaco. *Journal of Medical Entomology*, 53(4), 880–887. <https://doi.org/10.1093/jme/tjw056>
- Gandon, S. (2004). Evolution of multihost parasites. *Evolution*, 58(3), 455–469. <https://doi.org/10.1111/j.0014-3820.2004.tb01669.x>
- Garcia, M. N., Burroughs, H., Gorchakov, R., Gunter, S. M., Dumonteil, E., Murray, K. O., & Herrera, C. P. (2017). Molecular identification and genotyping of *Trypanosoma cruzi* DNA in autochthonous Chagas disease patients from Texas, USA. *Infection, Genetics and Evolution*, 49, 151–156. <https://doi.org/10.1016/j.meegid.2017.01.016>
- Georghiou, G. P. (1986). The magnitude of the resistance problem. In Committee on Strategies for the Management of Pesticide Resistant Pest Populations & National Research Council (Ed.), *Pesticide resistance: Strategies and tactics for management* (pp. 11–44). Washington, DC: National Academies Press. Retrieved from <http://public.eblib.com/choice/publicfullrecord.aspx?p=3377048>
- Germano, M. D., & Picollo, M. I. (2014). Reproductive and developmental costs of deltamethrin resistance in the Chagas disease vector *Triatoma infestans*. *Journal of Vector Ecology*, 40(1), 59–65.
- Germano, M. D., Picollo, M. I., & Mougabure-Cueto, G. A. (2013). Microgeographical study of insecticide resistance in *Triatoma infestans* from Argentina. *Acta Tropica*, 128(3), 561–565. <https://doi.org/10.1016/j.actatropica.2013.08.007>
- Gjullin, C. M., & Peters, R. (1952). Recent studies of mosquito resistance to insecticides in California. *Mosquito News. American Mosquito Control Association*, 12, 001–007.
- Gomes, J. E., Azambuja, P., & Garcia, E. S. (1990). Comparative studies on the growth and reproductive performances of *Rhodnius prolixus* reared on different blood sources. *Memorias do Instituto Oswaldo Cruz*, 85(3), 299–304. <https://doi.org/10.1590/S0074-02761990000300006>
- González Audino, P., Vassena, C., Barrios, S., Zerba, E., & Picollo, M. I. (2004). Role of enhanced detoxication in a deltamethrin-resistant population of *Triatoma infestans* (Hemiptera, Reduviidae) from Argentina. *Memorias Do Instituto Oswaldo Cruz*, 99(3), 335–339. <https://doi.org/10.1590/S0074-02762004000300018>
- González Valdivieso, P., Sanchez Diaz, B., & Nocerino, F. (1971). Susceptibility of *R. prolixus* to chlorinated hydrocarbon insecticides in Venezuela. Retrieved from <http://apps.who.int/iris/handle/10665/188269>
- Gorla, D. (1994). Perspectivas biológicas y ecológicas para el desarrollo de resistencia en Triatomíneos. *Acta Toxicol Argent*, 2(1), 48–51.
- Gourbière, S., Dorn, P., Tripet, F., & Dumonteil, E. (2012). Genetics and evolution of triatomines: From phylogeny to vector control. *Heredity*, 108(3), 190–202. <https://doi.org/10.1038/hdy.2011.71>
- Gourbière, S., Dumonteil, E., Rabinovich, J. E., Minkoue, R., & Menu, F. (2008). Demographic and dispersal constraints for domestic infestation by non-domiciliated Chagas disease vectors in the Yucatan peninsula, Mexico. *American Journal of Tropical Medicine and Hygiene*, 78(1), 133–139.
- Gourbière, S., & Gourbière, F. (2002). Competition between unit-restricted fungi: A metapopulation model. *Journal of Theoretical Biology*, 217(3), 351–368. <https://doi.org/10.1006/jtbi.2002.3033>
- Gourbière, S., & Menu, F. (2009). Adaptive dynamics of dormancy duration variability: Evolutionary trade-off and priority effect lead to suboptimal adaptation. *Evolution*, 63(7), 1879–1892. <https://doi.org/10.1111/j.1558-5646.2009.00731.x>
- Guarneri, A. A., Araujo, R. N., Diotaiuti, L., Gontijo, N. F., & Pereira, M. H. (2011). Feeding performance of *Triatoma brasiliensis* (Hemiptera: Reduviidae) on habitual hosts: *Trichomys laurentius* (Rodentia: Echimyidae) and humans. *Vector-Borne and Zoonotic Diseases*, 11(4), 443–445. <https://doi.org/10.1089/vbz.2010.0086>
- Guarneri, A. A., Pereira, M. H., & Diotaiuti, L. (2000). Influence of the blood meal source on the development of *Triatoma infestans*, *Triatoma brasiliensis*, *Triatoma sordida*, and *Triatoma pseudomaculata* (Heteroptera, Reduviidae). *Journal of Medical Entomology*, 37(3), 373–379. <https://doi.org/10.1093/jmedent/37.3.373>
- Guhl, F., & Schofield, C. J. (1996). Population genetics and control of Triatominae. *Parasitology Today*, 12(5), 1996.
- Gürtler, R. E. (2009). Sustainability of vector control strategies in the Gran Chaco Region: Current challenges and possible approaches. *Memorias do Instituto Oswaldo Cruz*, 104, 52–59. <https://doi.org/10.1590/S0074-02762009000900009>
- Gürtler, R. E., Ceballos, L. A., Ordonez-Krasnowski, P., Lanati, L. A., Stariolo, R., & Kitron, U. (2009). Strong host-feeding preferences of the vector *Triatoma infestans* modified by vector density: Implications for the epidemiology of Chagas disease. *PLoS Neglected Tropical Diseases*, 3(5), e447. <https://doi.org/10.1371/journal.pntd.0000447>
- Hashimoto, K., & Schofield, C. J. (2012). Elimination of *Rhodnius prolixus* in Central America. *Parasites & Vectors*, 5, 45. <https://doi.org/10.1186/1756-3305-5-45>
- Henriques, C., Henriques-Pons, A., Meuser-Batista, M., Ribeiro, A. S., & de Souza, W. (2014). In vivo imaging of mice infected with bioluminescent *Trypanosoma cruzi* unveils novel sites of infection. *Parasites & Vectors*, 7(1), 89. <https://doi.org/10.1186/1756-3305-7-89>
- Hernandez, L., Abraham, L., Moreno, M., Gorla, D., & Catala, S. (2008). Phenotypic variability associated to genomic changes in the main vector of Chagas disease in the southern cone of South America. *Acta Tropica*, 106(1), 60–67. <https://doi.org/10.1016/j.actatropica.2008.01.006>
- Herrera, L., D'Andrea, P. S., Xavier, S. C. C., Mangia, R. H., Fernandes, O., & Jansen, A. M. (2005). *Trypanosoma cruzi* infection in wild mammals of the National Park "Serra da Capivara" and its surroundings (Piauí, Brazil), an area endemic for Chagas disease. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 99(5), 379–388. <https://doi.org/10.1016/j.trstmh.2004.07.006>
- Herrera, C. P., Licon, M. H., Nation, C. S., Jameson, S. B., & Wesson, D. M. (2015). Genotype diversity of *Trypanosoma cruzi* in small rodents and *Triatoma sanguisuga* from a rural area in New Orleans, Louisiana. *Parasites & Vectors*, 8(1), 123. <https://doi.org/10.1186/s13071-015-0730-8>
- Ibanez-Cervantes, G., Martinez-Ibarra, A., Noguera-Torres, B., Lopez-Orduna, E., Alonso, A. L., Perea, C., ... Leon-Avila, G. (2013). Identification

- by Q-PCR of *Trypanosoma cruzi* lineage and determination of blood meal sources in triatomine gut samples in Mexico. *Parasitology International*, 62(1), 36–43. <https://doi.org/10.1016/j.parint.2012.09.003>
- Jackson, Y., Pinto, A., & Pett, S. (2014). Chagas disease in Australia and New Zealand: Risks and needs for public health interventions. *Tropical Medicine & International Health*, 19(2), 212–218. <https://doi.org/10.1111/tmi.12235>
- Jansen, A. M., & Roque, A. L. R. (2010). Domestic and wild mammalian reservoirs. In J. Telleria & M. Tibayrenc (Eds.), *American Trypanosomiasis: Chagas disease one hundred years of research* (pp. 249–276). London, UK: Elsevier. Retrieved from <http://linkinghub.elsevier.com/retrieve/pii/B9780123848765000113>
- Jiron, L. F., & Zeledon, R. (1982). Feeding preferences in 3 species of Triatominae (Hemiptera: Reduviidae) in experimental conditions. *Revista de Biología Tropical*, 30(2), 151–159.
- Jones, C. M., Machin, C., Mohammed, K., Majambere, S., Ali, A. S., Khatib, B. O., ... Kelly-Hope, L. A. (2012). Insecticide resistance in *Culex quinquefasciatus* from Zanzibar: Implications for vector control programmes. *Parasites & Vectors*, 5(1), 78. <https://doi.org/10.1186/1756-3305-5-78>
- Lee, B. Y., Bacon, K. M., Bottazzi, M. E., & Hotez, P. J. (2013). Global economic burden of Chagas disease: A computational simulation model. *The Lancet Infectious Diseases*, 13(4), 342–348. [https://doi.org/10.1016/S1473-3099\(13\)70002-1](https://doi.org/10.1016/S1473-3099(13)70002-1)
- Leggett, H. C., Buckling, A., Long, G. H., & Boots, M. (2013). Generalism and the evolution of parasite virulence. *Trends in Ecology & Evolution*, 28(10), 592–596. <https://doi.org/10.1016/j.tree.2013.07.002>
- Lent, H., & Wgodzinsky, P. (1979). Revision of the triatominae (hemiptera: reduviidae), and their significance as vectors of Chagas disease. *Bulletin of the American Museum of Natural History*, 163(3), 123–520.
- Lewis, M. D., Francisco, A. F., Taylor, M. C., Jayawardhana, S., & Kelly, J. M. (2016). Host and parasite genetics shape a link between *Trypanosoma cruzi* infection dynamics and chronic cardiomyopathy. *Cellular Microbiology*, 18(10), 1429–1443. <https://doi.org/10.1111/cmi.12584>
- Lewis, M. D., & Kelly, J. M. (2016). Putting infection dynamics at the heart of Chagas disease. *Trends in Parasitology*, 32(11), 899–911. <https://doi.org/10.1016/j.pt.2016.08.009>
- Lewis, M. D., Llewellyn, M. S., Yeo, M., Acosta, N., Gaunt, M. W., & Miles, M. A. (2011). Recent, independent and anthropogenic origins of *Trypanosoma cruzi* hybrids. *PLoS Neglected Tropical Diseases*, 5(10), e1363. <https://doi.org/10.1371/journal.pntd.0001363>
- Lima, M. F., & Kierszenbaum, F. (1984). Lysis of vector-transmissible, metacyclic forms of *Trypanosoma cruzi* by avian serum. *Journal of Parasitology*, 70(1), 155–156. <https://doi.org/10.2307/3281944>
- Lima, M. M., Pereira, J. B., Santos, D., Albuquerque, J. A., Pinto, Z. T., & Braga, M. V. (1992). Development and reproduction of *Panstrongylus megistus* (Hemiptera: Reduviidae) infected with *Trypanosoma cruzi*, under laboratory conditions. *Annals of the Entomological Society of America*, 85(4), 458–461. <https://doi.org/10.1093/aesa/85.4.458>
- Liu, N. (2015). Insecticide resistance in mosquitoes: Impact, mechanisms, and research directions. *Annual Review of Entomology*, 60(1), 537–559. <https://doi.org/10.1146/annurev-ento-010814-020828>
- Llewellyn, M. S., Messenger, L. A., Luquetti, A. O., Garcia, L., Torrico, F., Tavares, S. B., ... Miles, M. A. (2015). Deep sequencing of the *Trypanosoma cruzi* GP63 surface proteases reveals diversity and diversifying selection among chronic and congenital Chagas disease patients. *PLoS Neglected Tropical Diseases*, 9(4), e0003458. <https://doi.org/10.1371/journal.pntd.0003458>
- Llewellyn, M. S., Miles, M. A., Carrasco, H. J., Lewis, M. D., Yeo, M., Vargas, J., ... Gaunt, M. W. (2009). Genome-scale multilocus microsatellite typing of *Trypanosoma cruzi* discrete typing unit I reveals phylogeographic structure and specific genotypes linked to human infection. *PLoS Pathogens*, 5(5), e1000410. <https://doi.org/10.1371/journal.ppat.1000410>
- Llewellyn, M. S., Rivett-Carnac, J. B., Fitzpatrick, S., Lewis, M. D., Yeo, M., Gaunt, M. W., & Miles, M. A. (2011). Extraordinary *Trypanosoma cruzi* diversity within single mammalian reservoir hosts implies a mechanism of diversifying selection. *International Journal for Parasitology*, 41(6), 609–614. <https://doi.org/10.1016/j.ijpara.2010.12.004>
- Loza-Murguía, M., & Noireau, F. (2010). Vectorial capacity of *Triatoma guayanae* (Wygodzinsky & Abalos) (Hemiptera: Reduviidae) compared with two other species of epidemic importance. *Neotropical Entomology*, 39(5), 799–809. <https://doi.org/10.1590/S1519-566X2010000500020>
- Lunardi, R. R., Gomes, L. P., Peres Camara, T., & Arrais-Silva, W. W. (2015). Life cycle and vectorial competence of *Triatoma williamsi* (Galvão, Souza e Lima, 1965) under the influence of different blood meal sources. *Acta Tropica*, 149, 220–226. <https://doi.org/10.1016/j.actatropica.2015.05.023>
- Mallet, J. (1989). The evolution of insecticide resistance: Have the insects won? *Trends in Ecology & Evolution*, 4(11), 336–340. [https://doi.org/10.1016/0169-5347\(89\)90088-8](https://doi.org/10.1016/0169-5347(89)90088-8)
- Mancero, T., & Ponce, C. (2011). *Iniciativa de los países de América Central, para la interrupción de la transmisión vectorial y transfusional de la enfermedad de Chagas (IPCA). Historia de 12 años de una iniciativa subregional 1998–2010*. (PAHO). Argus Business.
- Marlière, N. P., Latorre-Estivalis, J. M., Lorenzo, M. G., Carrasco, D., Alves-Silva, J., Rodrigues, J., ... Guraneri, A. (2015). Trypanosomes modify the behavior of their insect hosts: Effects on locomotion and on the expression of a related gene. *PLoS Neglected Tropical Diseases*, 9(8), e0003973. <https://doi.org/10.1371/journal.pntd.0003973>
- Marquez, E. J., & Saldamando-Benjumea, C. I. (2013). *Rhodnius prolixus* and *Rhodnius robustus*-like (Hemiptera, Reduviidae) wing asymmetry under controlled conditions of population density and feeding frequency. *Journal of Biosciences*, 38(3), 549–560. <https://doi.org/10.1007/s12038-013-9332-9>
- Martinez-Ibarra, J. A., Alejandre-Aguilar, R., Torres-Morales, A., Trujillo-Garcia, J. C., Noguera-Torres, B., & Trujillo-Contreras, F. (2006). Biology of three species of the *Meccus phyllosomus* complex (Hemiptera: Reduviidae: Triatominae) fed on blood of hens and rabbits. *Memorias do Instituto Oswaldo Cruz*, 101(7), 787–794. <https://doi.org/10.1590/S0074-02762006000700014>
- Martinez-Ibarra, J. A., Grant-Guillen, Y., Noguera-Torres, B., & Trujillo-Contreras, F. (2004). Influence of the blood meal source on the biology of *Meccus longipennis* (Hemiptera: Reduviidae) under laboratory conditions. *Journal of the American Mosquito Control Association*, 20(3), 328–330.
- Martinez-Perez, A., Poveda, C., Ramirez, J. D., Norman, F., Girones, N., Guhl, F., ... Lopez-Velez, R. (2016). Prevalence of *Trypanosoma cruzi*'s discrete typing units in a cohort of Latin American migrants in Spain. *Acta Tropica*, 157, 145–150. <https://doi.org/10.1016/j.actatropica.2016.01.032>
- Medone, P., Balsalobre, A., Rabinovich, J. E., Marti, G. A., & Menu, F. (2015). Life history traits and demographic parameters of *Triatoma infestans* (Hemiptera: Reduviidae) fed on human blood. *Journal of Medical Entomology*, 52(6), 1282–1290. <https://doi.org/10.1093/jme/tjv138>
- Menu, F., Ginoux, M., Rajon, E., Lazzari, C. R., & Rabinovich, J. E. (2010). Adaptive developmental delay in Chagas disease vectors: An evolutionary ecology approach. *Plos Neglected Tropical Diseases*, 4(5), e691. <https://doi.org/10.1371/journal.pntd.0000691>
- Messenger, L. A., & Miles, M. A. (2015). Evidence and importance of genetic exchange among field populations of *Trypanosoma cruzi*. *Acta Tropica*, 151, 150–155. <https://doi.org/10.1016/j.actatropica.2015.05.007>
- Messenger, L. A., Miles, M. A., & Bern, C. (2015). Between a bug and a hard place: *Trypanosoma cruzi* genetic diversity and the clinical outcomes of Chagas disease. *Expert Review of Anti-Infective Therapy*, 13(8), 995–1029. <https://doi.org/10.1586/14787210.2015.1056158>
- Minter-Goedbloed, E., & Croon, J. J. (1981). The susceptibility of chickens to *Trypanosoma* (Schizotrypanum) *cruzi*. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 75(3), 350–353. [https://doi.org/10.1016/0035-9203\(81\)90090-0](https://doi.org/10.1016/0035-9203(81)90090-0)

- Monje-Rumi, M. M., Brandan, C. P., Ragone, P. G., Tomasini, N., Lauthier, J. J., Alberti D'Amato, A. M., ... Diosque, P. (2015). *Trypanosoma cruzi* diversity in the Gran Chaco: Mixed infections and differential host distribution of TcV and TcVI. *Infection, Genetics and Evolution*, 29, 53–59. <https://doi.org/10.1016/j.meegid.2014.11.001>
- Monteiro, F. A., Escalante, A. A., & Beard, C. B. (2001). Molecular tools and triatomine systematics: A public health perspective. *Trends in Parasitology*, 17(7), 344–347. [https://doi.org/10.1016/S1471-4922\(01\)01921-3](https://doi.org/10.1016/S1471-4922(01)01921-3)
- Mougabure-Cueto, G., & Picollo, M. I. (2015). Insecticide resistance in vector Chagas disease: Evolution, mechanisms and management. *Acta Tropica*, 149, 70–85. <https://doi.org/10.1016/j.actatropica.2015.05.014>
- Nattero, J., Dujardin, J.-P., del Pilar Fernández, M., & Gürtler, R. E. (2015). Host-feeding sources and habitats jointly affect wing developmental stability depending on sex in the major Chagas disease vector *Triatoma infestans*. *Infection, Genetics and Evolution*, 36, 539–546. <https://doi.org/10.1016/j.meegid.2015.08.032>
- Nattero, J., Leonhard, G., Rodriguez, C. S., & Crocco, L. (2011). Influence of the quality and quantity of blood ingested on reproductive parameters and life-span in *Triatoma infestans* (Klug). *Acta Tropica*, 119(2–3), 183–187. <https://doi.org/10.1016/j.actatropica.2011.05.015>
- Nattero, J., Rodriguez, C. S., & Crocco, L. (2013). Effects of blood meal source on food resource use and reproduction in *Triatoma patagonica* Del Ponte (Hemiptera: Reduviidae). *Journal of Vector Ecology*, 38(1), 127–133. <https://doi.org/10.1111/j.1948-7134.2013.12018.x>
- Noireau, F., Brenière, F., Ordonez, J., Cardozo, L., Morochi, W., Gutierrez, T., ... Wisnivesky-Colli, C. (1997). Low probability of transmission of *Trypanosoma cruzi* to humans by domiciliary *Triatoma sordida* in Bolivia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 91(6), 653–656. [https://doi.org/10.1016/S0035-9203\(97\)90508-3](https://doi.org/10.1016/S0035-9203(97)90508-3)
- Noireau, F., Zegarra, M., Ordonez, J., Gutierrez, T., & Dujardin, J. P. (1999). Genetic structure of *Triatoma sordida* (Hemiptera: Reduviidae) domestic populations from Bolivia: Application on control interventions. *Memorias do Instituto Oswaldo Cruz*, 94, 347–351. <https://doi.org/10.1590/S0074-02761999000300011>
- Nouvellet, P., Cucunubá, Z. M., & Gourbière, S. (2015). Ecology, evolution and control of chagas disease: A century of neglected modelling and a promising future. In R. M. Anderson & M. G. Basáñez (Eds.), *Advances in parasitology* (Vol. 87, pp. 135–191). New York, NY: Academic Press. <http://www.sciencedirect.com/science/article/pii/S0065308X14000050>
- Nouvellet, P., Dumonteil, E., & Gourbière, S. (2013). The improbable transmission of *Trypanosoma cruzi* to human: The missing link in the dynamics and control of Chagas disease. *Plos Neglected Tropical Diseases*, 7(11), e2505. <https://doi.org/10.1371/journal.pntd.0002505>
- Nouvellet, P., Ramirez-Sierra, M. J., Dumonteil, E., & Gourbière, S. (2011). Effects of genetic factors and infection status on wing morphology of *Triatoma dimidiata* species complex in the Yucatán peninsula, Mexico. *Infection, Genetics and Evolution*, 11(6), 1243–1249. <https://doi.org/10.1016/j.meegid.2011.04.008>
- de Noya, B. A., & González, O. N. (2015). An ecological overview on the factors that drives to *Trypanosoma cruzi* oral transmission. *Acta Tropica*, 151, 94–102. <https://doi.org/10.1016/j.actatropica.2015.06.004>
- Orozco, M. M., Enriquez, G. F., Alvarado-Otegui, J. A., Cardinal, M. V., Schijman, A. G., Kitron, U., & Gürtler, R. E. (2013). New sylvatic hosts of *Trypanosoma cruzi* and their reservoir competence in the humid Chaco of Argentina: A longitudinal study. *American Journal of Tropical Medicine and Hygiene*, 88(5), 872–882. <https://doi.org/10.4269/ajtmh.12-0519>
- Otto, S. P., & Day, T. (2007). *A biologist's guide to mathematical modeling in ecology and evolution*. Princeton, NJ: Princeton University Press.
- Panzer, F., Dujardin, J. P., Nicolini, P., Caraccio, M. N., Rose, V., Tellez, T., ... Perez, R. (2004). Genomic changes of Chagas disease vector, South America. *Emerging Infectious Diseases*, 10(3), 438–446. <https://doi.org/10.3201/eid1003.020812>
- Parker, G. A., & Smith, J. M. (1990). Optimality theory in evolutionary biology. *Nature*, 348(6296), 27–33. <https://doi.org/10.1038/348027a0>
- Patterson, J. S., & Guhl, F. (2010). Geographical distribution of Chagas disease. In J. Telleria, M. Tibayrenc (Eds.), *American Trypanosomiasis Chagas disease: One hundred years of research* (pp. 83–114). London: Elsevier.
- Pelosse, P., Kribs-Zaleta, C. M., Ginoux, M., Rabinovich, J. E., Gourbière, S., & Menu, F. (2013). Influence of vectors' risk-spreading strategies and environmental stochasticity on the epidemiology and evolution of vector-borne diseases: The example of Chagas' disease. *PLoS ONE*, 8(8), e70830. <https://doi.org/10.1371/journal.pone.0070830>
- Pennington, P. M., Paiz, C., Grajeda, L. M., & Cordon-Rosales, C. (2009). Short report: Concurrent detection of *Trypanosoma cruzi* lineages I and II in domestic *Triatoma dimidiata* from Guatemala. *American Journal of Tropical Medicine and Hygiene*, 80(2), 239–241.
- Perez-Molina, J., Perez-Ayala, A., Parola, P., Jackson, Y., Odolini, S., & Lopez-Velez, R. (2011). EuroTravNet: imported Chagas disease in nine European countries, 2008 to 2009. *Chagas Disease in Europe*, 52.
- Perez-Molina, J. A., Poveda, C., Martinez-Perez, A., Guhl, F., Monge-Maillo, B., Fresno, M., ... Girones, N. (2014). Distribution of *Trypanosoma cruzi* discrete typing units in Bolivian migrants in Spain. *Infection, Genetics and Evolution*, 21, 440–442. <https://doi.org/10.1016/j.meegid.2013.12.018>
- Pessoa, G. C. D., Vinãs, P. A., Rosa, A. C. L., & Diotaiuti, L. (2015). History of insecticide resistance of Triatominae vectors. *Revista Da Sociedade Brasileira de Medicina Tropical*, 48(4), 380–389. <https://doi.org/10.1590/0037-8682-0081-2015>
- Peterson, J. K., Bartsch, S. M., Lee, B. Y., & Dobson, A. P. (2015). Broad patterns in domestic vector-borne *Trypanosoma cruzi* transmission dynamics: Synanthropic animals and vector control. *Parasites & Vectors*, 8, 537. <https://doi.org/10.1186/s13071-015-1146-1>
- PHAC (2015). Surveillance of Chagas disease (American trypanosomiasis). Public Health Agency of Canada. Retrieved from <https://www.canada.ca/en/public-health/services/diseases/chagas-disease-american-trypanosomiasis/surveillance-chagas-disease-american-trypanosomiasis.html>
- Piccolo, M. I., Vassena, C., Orihuela, P. S., Barrios, S., Zaidemberg, M., & Zerba, E. (2005). High resistance to pyrethroid insecticides associated with ineffective field treatments in *Triatoma infestans* (Hemiptera: Reduviidae) from Northern Argentina. *Journal of Medical Entomology*, 42(4), 637–642. <https://doi.org/10.1093/jmedent/42.4.637>
- Pires, H. H. R., Barbosa, S. E., & Diotaiuti, L. (2000). Comparative developmental and susceptibility to insecticide of Bolivian and Brazilian populations of *Triatoma infestans*. *Memórias do Instituto Oswaldo Cruz*, 95(6), 883–888. <https://doi.org/10.1590/S0074-0276200000600025>
- Rabinovich, J. E., Kitron, U. D., Obed, Y., Yoshioka, M., Gottdecker, N., & Chaves, L. F. (2011). Ecological patterns of blood-feeding by kissing-bugs (Hemiptera: Reduviidae: Triatominae). *Memorias Do Instituto Oswaldo Cruz*, 106(4), 479–494. <https://doi.org/10.1590/S0074-02762011000400016>
- Rabinovich, J. E., Schweigmann, N., Yohai, V., & Wisnivesky-Colli, C. (2001). Probability of *Trypanosoma cruzi* transmission by *Triatoma infestans* (Hemiptera: Reduviidae) to the opossum *Didelphis albiventris* (Marsupialia: Didelphidae). *The American Journal of Tropical Medicine and Hygiene*, 65(2), 125–130. <https://doi.org/10.4269/ajtmh.2001.65.125>
- Rabinovich, J. E., Wisnivesky-Colli, C., Solarz, N. D., & Gürtler, R. E. (1990). Probability of transmission of Chagas disease by *Triatoma infestans* (Hemiptera: Reduviidae) in an endemic area of Santiago del Estero, Argentina. *Bulletin of the World Health Organization*, 68(6), 737.
- Ragone, P. G., Perez Brandan, C., Monje Rumi, M., Tomasini, N., Lauthier, J. J., Cimino, R. O., ... Diosque, P. (2015). Experimental evidence of biological interactions among different isolates of *Trypanosoma cruzi* from the Chaco Region. *PLoS ONE*, 10(3), e0119866. <https://doi.org/10.1371/journal.pone.0119866>
- Ramirez-Sierra, M. J., Herrera-Aguilar, M., Gourbière, S., & Dumonteil, E. (2010). Patterns of house infestation dynamics by non-domiciliated *Triatoma dimidiata* reveal a spatial gradient of infestation in rural villages and potential insect manipulation by *Trypanosoma cruzi*. *Tropical Medicine & International Health*, 15(1), 77–86. <https://doi.org/10.1111/j.1365-3156.2009.02422.x>

- Ranson, H., & Lissenden, N. (2016). Insecticide resistance in African Anopheles mosquitoes: A worsening situation that needs urgent action to maintain malaria control. *Trends in Parasitology*, 32(3), 187–196. <https://doi.org/10.1016/j.pt.2015.11.010>
- Rascalou, G., Pontier, D., Menu, F., & Gourbière, S. (2012). Emergence and prevalence of human vector-borne diseases in sink vector populations. *PLoS ONE*, 7(5), e36858. <https://doi.org/10.1371/journal.pone.0036858>
- Rassi, A., Rezende, J. M., Luquetti, A. O., & Rassi, A. Jr (2010). Clinical phases and forms of Chagas disease. In J. Telleria, M. Tibayrenc (Eds.), *American Trypanosomiasis (Chagas disease). One hundred years of research* (1st ed., pp. 709–741). Burlington, MA: Elsevier Inc.
- Read, A. F., Lynch, P. A., & Thomas, M. B. (2009). How to make evolution-proof insecticides for malaria control. *PLoS Biology*, 7(4), e1000058.
- Reed, D. H., & Frankham, R. (2001). How closely correlated are molecular and quantitative measures of genetic variation? A meta-analysis. *Evolution*, 55(6), 1095–1103. <https://doi.org/10.1111/j.0014-3820.2001.tb00629.x>
- Reisenman, C. E., Gregory, T., Guerenstein, P. G., & Hildebrand, J. G. (2011). Feeding and defecation behavior of *Triatoma rubida* (Uhler, 1894) (Hemiptera: Reduviidae) under laboratory conditions, and its potential role as a vector of Chagas disease in Arizona, USA. *The American Journal of Tropical Medicine and Hygiene*, 85(4), 648–656. <https://doi.org/10.4269/ajtmh.2011.11-0137>
- Rey, O., Danchin, E., Mirouze, M., Loot, C., & Blanchet, S. (2016). Adaptation to global change: A transposable element-epigenetics perspective. *Trends in Ecology & Evolution*, 31(7), 514–526. <https://doi.org/10.1016/j.tree.2016.03.013>
- Reyes-Lugo, M., & Rodríguez-Acosta, A. (2000). Domiciliation of the sylvatic Chagas disease vector *Panstrongylus geniculatus* Latreille, 1811 (Triatominae: Reduviidae) in Venezuela. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 94, 508. [https://doi.org/10.1016/S0035-9203\(00\)90068-3](https://doi.org/10.1016/S0035-9203(00)90068-3)
- Risso, M. G., Sartor, P. A., Burgos, J. M., Briceño, L., Rodríguez, E. M., Guhl, F., ... Leguizamón, M. S. (2011). Immunological identification of *Trypanosoma cruzi* lineages in human infection along the endemic area. *American Journal of Tropical Medicine and Hygiene*, 84(1), 78–84. <https://doi.org/10.4269/ajtmh.2011.10-0177>
- Rivero, A., Vézilier, J., Weill, M., Read, A. F., & Gandon, S. (2010). Insecticide control of vector-borne diseases: When is insecticide resistance a problem? *PLoS Pathogens*, 6(8), e1001000. <https://doi.org/10.1371/journal.ppat.1001000>
- Roca-Acevedo, G. R., Cueto, G. M., Germano, M., Orihuela, P. S., Cortez, M. R., Noireau, F., ... Vassena, C. (2011). Susceptibility of sylvatic *Triatoma infestans* from Andean valleys of Bolivia to deltamethrin and fipronil. *Journal of Medical Entomology*, 48(4), 828–835. <https://doi.org/10.1603/me10208>
- Roca-Acevedo, G., Picollo, M. I., Capriotti, N., Sierra, I., & Santo-Orihuela, P. L. (2015). Examining mechanisms of pyrethroid resistance in eggs of two populations of the Chagas' Disease vector *Triatoma infestans* (Hemiptera: Reduviidae). *Journal of Medical Entomology*, 52(5), 987–992. <https://doi.org/10.1093/jme/tjv078>
- Roelling, D. M., Brown, E. L., Barnabe, C., Tibayrenc, M., Steurer, F. J., & Yabsley, M. J. (2008). Molecular typing of *Trypanosoma cruzi* isolates, United States. *Emerging Infectious Diseases*, 14(7), 1123–1125. <https://doi.org/10.3201/eid1407.080175>
- Roff, D. A. (2002). *Life history evolution*. Sunderland, MA: Sinauer Associates.
- Roff, D. A. (2010). *Modeling evolution: An introduction to numerical methods* (pp. 59–221). Oxford, UK: Oxford University Press.
- Salvatella, R. (2007). Andean subregional Chagas disease area and the Andean initiative of Chagas disease. *Memórias do Instituto Oswaldo Cruz*, 102, 39–40. <https://doi.org/10.1590/S0074-02762007005000105>
- Sánchez, L. V., & Ramírez, J. D. (2013). Congenital and oral transmission of American trypanosomiasis: An overview of physiopathogenic aspects. *Parasitology*, 140(2), 147–159. <https://doi.org/10.1017/S0031182012001394>
- Sandoval Ramirez, C. M., Nieves Blanco, E. E., Gutiérrez Marin, R., Jaimes Mendez, D. A., Ortiz Rodríguez, N., Otálora-Luna, F., & Aldana, E. J. (2015). Morphometric analysis of the host effect on phenotypical variation of *Belminus ferroae* (Hemiptera: Triatominae). *Psyche*, 2015, 1–12.
- Schaub, G. A. (1988). Developmental time and mortality of larvae of *Triatoma infestans* infected with *Trypanosoma cruzi*. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 82(1), 94–96. [https://doi.org/10.1016/0035-9203\(88\)90273-8](https://doi.org/10.1016/0035-9203(88)90273-8)
- Schaub, G. A. (1989). Does *Trypanosoma cruzi* stress its vectors? *Parasitology Today*, 5(6), 185–188. [https://doi.org/10.1016/0169-4758\(89\)90142-7](https://doi.org/10.1016/0169-4758(89)90142-7)
- Schipper, H., McClarty, B. M., McRuer, K. E., Nash, R. A., & Penney, C. J. (1980). Tropical diseases encountered in Canada: 1. Chagas' disease. *Canadian Medical Association Journal*, 122(2), 165–172.
- Schofield, C. J., & Dias, J. C. (1999). The southern cone initiative against Chagas disease. *Advances in Parasitology*, 42, 1–27.
- Schofield, C. J., Diotaiuti, L., & Dujardin, J. P. (1999). The process of domestication in Triatominae. *Memorias Do Instituto Oswaldo Cruz*, 94, 375–378. <https://doi.org/10.1590/s0074-02761999000700073>
- Schofield, C. J., & Galvão, C. (2009). Classification, evolution, and species groups within the Triatominae. *Acta Tropica*, 110(2–3), 88–100. <https://doi.org/10.1016/j.actatropica.2009.01.010>
- Schofield, C. J., Jannin, J., & Salvatella, R. (2006). The future of Chagas disease control. *Trends in Parasitology*, 22(12), 583–588. <https://doi.org/10.1016/j.pt.2006.09.011>
- Sierra, I., Capriotti, N., Fronza, G., Mougabure-Cueto, G., & Ons, S. (2016). Kdr mutations in *Triatoma infestans* from the Gran Chaco are distributed in two differentiated foci: Implications for pyrethroid resistance management. *Acta Tropica*, 158, 208–213. <https://doi.org/10.1016/j.actatropica.2016.03.014>
- Silva-dos-Santos, D., Barreto-de-Albuquerque, J., Guerra, B., Moreira, O. C., Berbert, L. R., Ramos, M. T., ... Meis, J. (2017). Unraveling Chagas disease transmission through the oral route: Gateways to *Trypanosoma cruzi* infection and target tissues. *PLoS Neglected Tropical Diseases*, 11(4), e0005507. <https://doi.org/10.1371/journal.pntd.0005507>
- Silveira, A. C., de Rojas Arias, A., Segura, E., Guillén, G., Russomando, G., Schenone, H., ... Salvatella, R. (2002). El control de la enfermedad de Chagas en los países del cono sur de América. *História de una iniciativa internacional*. 1991/2001.
- Silveira, A. C., & Vinhaes, M. (1999). Elimination of vector-borne transmission of Chagas disease. *Memorias do Instituto Oswaldo Cruz*, 94(Suppl 1), 405–411. <https://doi.org/10.1590/S0074-02761999000700080>
- Teixeira, A. R., Nascimento, R. J., & Sturm, N. R. (2006). Evolution and pathology in Chagas disease: A review. *Memórias do Instituto Oswaldo Cruz*, 101(5), 463–491. <https://doi.org/10.1590/S0074-02762006000500001>
- Tibayrenc, M., & Ayala, F. J. (2015). The population genetics of *Trypanosoma cruzi* revisited in the light of the predominant clonal evolution model. *Acta Tropica*, 151, 156–165. <https://doi.org/10.1016/j.actatropica.2015.05.006>
- Torres-Montero, J., López-Monteón, A., Dumonteil, E., & Ramos-Ligonio, A. (2012). House infestation dynamics and feeding sources of *Triatoma dimidiata* in central Veracruz, Mexico. *The American journal of tropical medicine and hygiene*, 86(4), 677–682. <https://doi.org/10.1371/journal.pntd.0000780.t001>
- Torrico, R. A. (1946). Hallazgo de *Eratyrus mucronatus*, infestación natural de vinchucas de cerro y eu *Triatoma sordida* en Cochabamba. *An Lab Central Cochabamba*, 1, 19–23.
- Traverso, L., Lavore, A., Sierra, I., Palacio, V., Martínez-Barnetche, J., Latorre-Estivalis, J. M., ... Rivera-Pomar, R. V. (2017). Comparative and functional triatomine genomics reveals reductions and expansions in insecticide resistance-related gene families. *PLOS Neglected*

- Tropical Diseases*, 11(2), e0005313. <https://doi.org/10.1371/journal.pntd.0005313>
- Vontas, J., Kioulos, E., Pavlidi, N., Morou, E., della Torre, A., & Ranson, H. (2012). Insecticide resistance in the major dengue vectors *Aedes albopictus* and *Aedes aegypti*. *Pesticide Biochemistry and Physiology*, 104(2), 126–131. <https://doi.org/10.1016/j.pestbp.2012.05.008>
- Vorraro, F., Cabrera, W. H. K., Ribeiro, O. G., Jensen, J. R., De Franco, M., Ibañez, O. M., & Starobinas, N. (2014). *Trypanosoma cruzi* infection in genetically selected mouse lines: Genetic linkage with quantitative trait locus controlling antibody response. *Mediators of Inflammation*, 2014, 1–15. <https://doi.org/10.1155/2014/952857>
- Waleckx, E., Camara-Mejia, J., Jesus Ramirez-Sierra, M., Cruz-Chan, V., Rosado-Vallado, M., Vazquez-Narvaez, S., ... Dumonteil, E. (2015). An innovative ecohealth intervention for Chagas disease vector control in Yucatan, Mexico. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 109(2), 143–149. <https://doi.org/10.1093/trstmh/tru200>
- Waleckx, E., Depickere, S., Salas, R., Aliaga, C., Monje, M., Calle, H., ... Brenière, S. F. (2012). New discoveries of sylvatic *Triatoma infestans* (Hemiptera: Reduviidae) throughout the Bolivian Chaco. *American Journal of Tropical Medicine and Hygiene*, 86(3), 455–458. <https://doi.org/10.4269/ajtmh.2012.11-0205>
- Waleckx, E., Gourbière, S., & Dumonteil, E. (2015). Intrusive versus domiciliated triatomines and the challenge of adapting vector control practices against Chagas disease. *Memorias Do Instituto Oswaldo Cruz*, 110(3), 324–338. <https://doi.org/10.1590/0074-02760140409>
- Waleckx, E., Pasos-Alquicira, R., Ramirez-Sierra, M. J., & Dumonteil, E. (2016). Sleeping habits affect access to host by Chagas disease vector *Triatoma dimidiata*. *Parasites & Vectors*, 9(1), 568. <https://doi.org/10.1186/s13071-016-1852-3>
- Waleckx, E., Salas, R., Huamán, N., Buitrago, R., Bosseno, M. F., Aliaga, C., ... Brenière, S. F. (2011). New insights on the Chagas disease main vector *Triatoma infestans* (Reduviidae, Triatominae) brought by the genetic analysis of Bolivian sylvatic populations. *Infection, Genetics and Evolution*, 11(5), 1045–1057. <https://doi.org/10.1016/j.meegid.2011.03.020>
- World Health Organisation (1998). WHA51.14 Elimination of transmission of Chagas disease. Retrieved from http://apps.who.int/gb/archive/pdf_files/WHA51/ea42.pdf
- World Health Organisation (2000). Chagas disease, Chile. Certification of interruption of transmission. *Releve Épidémiologique Hebdomadaire*, (2), 9–12. Retrieved from <http://apps.who.int/iris/handle/10665/231033>
- World Health Organisation (2002). *Control of Chagas disease: second report of the WHO Expert Committee*. Geneva: WHO. Retrieved from <http://apps.who.int/iris/handle/10665/42443>
- World Health Organisation (2005). International Meeting on Surveillance and Prevention of Chagas Disease in the Amazon Region. Implementation of the Intergovernmental Initiative for Surveillance and Control of Chagas Disease in the Amazon Region (AMCHA). Manaus, Amazonas State, Brazil, 19–22 September 2004. OPS/DPC/CD/321/05.
- World Health Organisation (2006). Newsbriefs. Brazil marks Chagas milestone. *The Newsletter of the Pan American Health Organization*. Retrieved from http://www.paho.org/hq/index.php?option=com_content&view=article&id=10244:paho-celebrates-112th-anniversary&Itemid=2&lang=en
- World Health Organisation (2010a). WHA63.20 Chagas disease: control and elimination. Retrieved from http://www.who.int/neglected_diseases/mediacentre/WHA_63.20_Eng.pdf
- World Health Organisation (2010b). Perú – Moquegua logró interrumpir transmisión de milenaria enfermedad de chagas en su región. Retrieved from http://www.paho.org/per/index.php?option=com_content&view=article&id=1082:moquegua-logro-interrumpir-transmision-milenaria-enfermedad-chagas-region&Itemid=900
- World Health Organisation (2012). Uruguay – Uruguay es el 1o país de América Latina libre del insecto que transmite el mal de chagas. Retrieved from http://www.paho.org/uru/index.php?option=com_content&view=article&id=525:uruguay-1o-pais-america-latina-libre-insecto-que-transmite-mal-chagas-&Itemid=340
- World Health Organisation (2014). Small bites big threats. Chagas. World Health Day. Retrieved from www.paho.org/WorldHealthDay2014
- World Health Organisation (2015a). Generic Framework for control, elimination and eradication of neglected tropical diseases. Retrieved from http://www.who.int/neglected_diseases/resources/NTD_Generic_Framework_2015.pdf
- World Health Organisation (2015b). Chagas disease in Latin America: An epidemiological update based on 2010 estimates. *Weekly Epidemiological Record*, 90, 33–34. Retrieved from <http://www.who.int/wer/2015/wer9006/en/>
- Yeo, M., Mauricio, I. L., Messenger, L. A., Lewis, M. D., Llewellyn, M. S., Acosta, N., ... Miles, M. A. (2011). Multilocus sequence typing (MLST) for lineage assignment and high resolution diversity studies in *Trypanosoma cruzi*. *PLoS Neglected Tropical Diseases*, 5(6), e1049. <https://doi.org/10.1371/journal.pntd.0001049>
- Yon, C., Balta, R., García, N., Troyes, M., Cumpa, H., & Valdivia, A. (2004). Susceptibilidad y resistencia de *Triatoma infestans* y *Panstrongylus herreri* a los insecticidas piretroides, Perú 2001. *Revista Peruana de Medicina Experimental Y Salud Publica*, 21(3), 179–182.
- Zafra, G., Mantilla, J. C., Jacome, J., Macedo, A. M., & Gonzalez, C. I. (2011). Direct analysis of genetic variability in *Trypanosoma cruzi* populations from tissues of Colombian chagasic patients. *Human Pathology*, 42(8), 1159–1168. <https://doi.org/10.1016/j.humpath.2010.11.012>
- Zingales, B., Andrade, S. G., Briones, M. R., Campbell, D. A., Chiari, E., Fernandes, O., ... Schijman, A. G. (2009). A new consensus for *Trypanosoma cruzi* intraspecific nomenclature: Second revision meeting recommends TcI to TcVI. *Memorias do Instituto Oswaldo Cruz*, 104(7), 1051–1054. <https://doi.org/10.1590/S0074-02762009000700021>
- Zingales, B., Miles, M. A., Campbell, D. A., Tibayrenc, M., Macedo, A. M., Teixeira, M. M., ... Sturm, N. R. (2012). The revised *Trypanosoma cruzi* subspecific nomenclature: Rationale, epidemiological relevance and research applications. *Infection, Genetics and Evolution*, 12(2), 240–253. <https://doi.org/10.1016/j.meegid.2011.12.009>

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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