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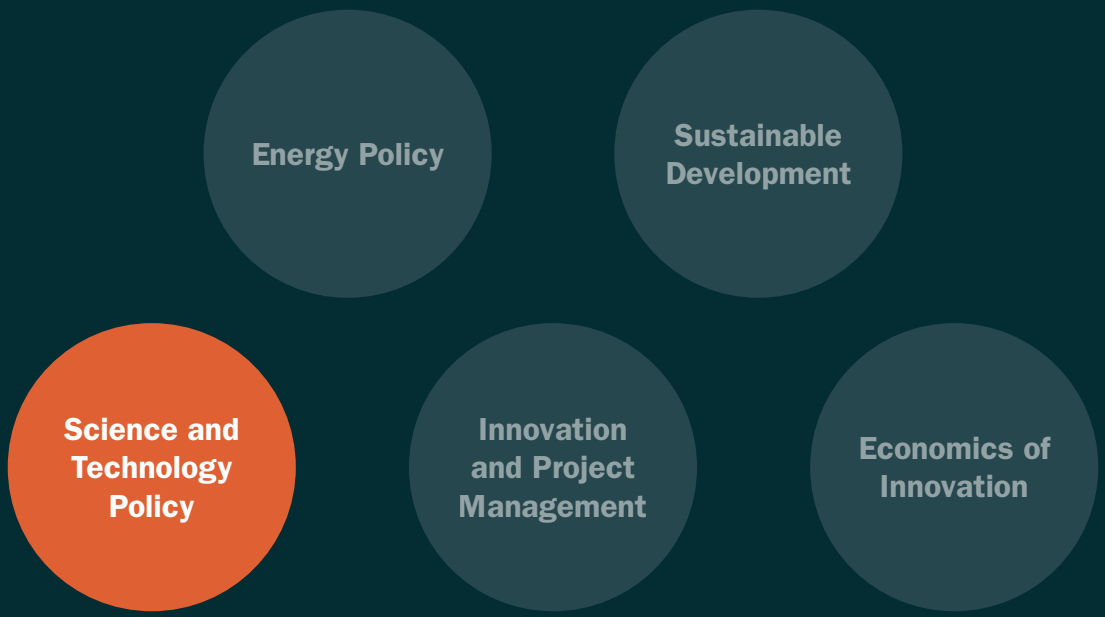


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# Exploring the links between research demand and supply: The case of Chagas

Valeria Arza[†] and Agustina Colonna[‡]

## Blurb

**We identify societal needs for research on Chagas disease based on qualitative analysis in Argentina and explore quantitatively research supply and the factors that matter for alignment**

## Abstract

This paper contributes to the literature assessing how scientific research can improve its contribution societal needs. Our context of analysis is scientific research on the socio-environmental problems associated to Chagas, a neglected tropical disease. We use mixed methods in our approach. We identify societal needs and perceived demand for Chagas research based on secondary evidence and interviews with key informants in Argentina, while research supply is identified through a bibliometric analysis on research production worldwide and in Argentina since the 1990s. We find three areas of research demands: i) vector control, ii) early diagnosis and reduction in congenital transmission and iii) social science research to improve policy outcomes. We identify that research supply in these three areas has evolved differently and is steered by diverse factors. While vector control seems to be attended by local research systems, severe deficits turn up in the social sciences both locally and globally. There has been increasing attention worldwide in diagnosis and congenital transmission, with international cooperation as an important driver, although Argentinean research seems not to be intensively participating in these networks. We claim that different policy pathways derive from an analysis that takes into consideration perceived demand and supply of research in different areas.

**Keywords**: Chagas Disease; Research Priorities; Research demand-supply analysis; Societal needs; Argentina

## 1. Introduction

Over the past decades there has been a general recognition of the role of science in promoting economic growth and improving living standards (Salter & Martin, 2001) and a call for a better alignment between

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the production of science and societal needs related to inclusion and sustainability (Nelson, 2011). Science, technology and innovation policy has an important role in steering this alignment (Schot & Steinmueller, 2018) but there is yet little evidence to guide the process.

Misalignments between research supply and societal demand are particularly salient regarding diseases prevalent in poor countries (Evans et al., 2014; Yegros-Yegros et al., 2020). This is the case for the neglected tropical diseases which affect the world's poorest population (WHO, 2015a), and cause an enormous burden to the health and economic development of low-income countries (Hotez et al., 2007). In the case of these diseases, the global market demand does not work properly as an incentive to steer private investment (Kyle & McGahan, 2012) and the academia does not respond promptly because their incentive schemes are biased towards topics defined internationally (Miller, 2007; Wallace & Ràfols, 2018).

In this paper we investigate how scientific production contributes to providing solutions to Chagas, one of the neglected tropical diseases particularly present in Latin America. The problem of Chagas holds various dimensions apart from health: education and access to information is key for prevention; better infrastructure such as roads and hospitals is important for early detection and treatment; and changes in ecological systems due to production activities and climate change have moved the vector which transmits the disease towards new areas. Research on Chagas is more concentrated on some of these dimensions than others, and this concentration varies across regions and time. We aim to analyze how this distribution of research topics, which proxies the supply of scientific knowledge, is aligned to the perceived demand for knowledge on Chagas. We look to answer the following questions: Which are the research areas within Chagas where there are greatest needs? Which are the areas with the highest supply of knowledge? How does this supply vary according to space and time? What policies may improve the alignment between demand and supply?

We attempt to identify what societal demands are most salient in 2019 based on interviews to experts and secondary evidence. We link these demands to research areas from a bibliometric analysis of publications during the period 1990-2019 and analyze how research in the demanded areas varies across regions and time. We also evaluate the role of collaborative research in this scenario. Our study allows to identify what research is still missing to improve societal impact and what policies may contribute to alignment between demand and supply of research on Chagas.

The paper is organized as follows: section 2 presents a literature review on the relation of scientific production with societal needs; section 3 characterizes the context of analysis by describing Chagas research and political context; section 4 presents our methodology for assessing supply and demand of scientific knowledge in Chagas-related problems; section 5 presents the results and section 6 extends the discussion on demand and supply of scientific knowledge and concludes.

## 2. Literature review

The social implications of knowledge production and its alignment with societal needs are topics which have gained increasing relevance in the last decades (Ciarli & Ràfols, 2019; Gibbons, 1999; Sarewitz & Pielke, 2007). The conception of science has evolved to become more closely linked to societal problems and the global and local challenges facing humanity. More importance has been given to its applicability, rather than considering science as an activity independent of social processes and as a "free play of intellects" (Bush, 1945a), or as a mechanism for strategic national positioning during wars (Sarewitz, 2017). Consequently, the social accountability of science has become more relevant (Gibbons et al., 1995; Spaapen & van Drooge, 2011). Increasing attention has been concentrated on evaluating scientific production in a

more comprehensive manner, including social, economic, environmental and political impacts. (Gibbons et al., 1995; Schot & Steinmueller, 2018; Spaapen & van Drooge, 2011).

However, the distribution of scientific progress has been usually uneven between different actors and sectors and has not necessarily met social needs of marginalized groups of society. For example, advances in agriculture have prioritized productivity at the expense of local needs (Dalrymple, 2006; Herdt, 2012) and there has been relatively little investment in research for diseases that affect poor populations (Evans et al., 2014).

Thus, there seems to be a gap between research priorities and social demands, at least in some areas of knowledge. Since shifts in the conception of science tend to be tightly related to changes in the instruments, institutions and procedures which guide scientific activity (Velho 2011), science policy framing is important to improve the balancing of priorities. Schot and Steinmueller (2018) refer to three different policy frames. The first frame was informed by the linear model of innovation, which suggested that applied private R&D would follow from scientific discoveries produced in the public sphere (Bush, 1945b). . The second frame sustains that relevant knowledge was meant to be produced in the context of application and the State should then help to create the necessary infrastructure for interactions, coordination and learning especially among research centers, industry and governmental bodies (Lundvall, 2010; Gibbons, 1994; Etzkowitz and Leydesdorff, 2000). The third frame, in turn, originates from a deep questioning of previous framings for not having engaged with the idea that science and innovation always involves certain directionality. This view sustains that power dynamics explain why transformative change towards more inclusive and sustainable societies have not yet been achieved (Schot & Steinmueller, 2018). Transformative change towards sustainability then needs a process of systemic change and policies must promote appraisals and negotiation over diverse sets of pathways by multiple groups of stakeholders (Stirling, 2008).

Thus, to promote the third frame it becomes very important to understand who carries out scientific research, which topics or problems are prioritized over others, what strategies and methods are applied, how knowledge is shared, how the research process is regulated and steered (European Commission, 2009) and to contrast all these against the main societal needs.

In this line, bibliometric techniques have recently emerged to evaluate the impact of scientific production and its alignment with societal needs. For example, Cassi et al. (2017) study scientific research in obesity using topic modelling and identify the demand using political discourse in the European Parliament. Ciarli and Ràfols (2019) analyze demand and supply of research in the case of rice using co-word analysis and agricultural data. Some of these studies using bibliometric techniques also analyze collaboration patterns across institutions and countries through co-authorship networks and funding data to assess whether these characteristics correlate with any particular research areas or affect scientific impact (Melin and Persson 1996).

Particularly, in the health area Fonseca et al. (2018) study collaboration between Low/Middle Income Countries and High Income countries in HIV research. They find that the research focus varies according to the income of the collaborating countries, and the funding origins of the research. Wallace and Ràfols (2018) study whether the research supply since the 2003 outbreak of the avian influenza matched the expectations on how research could meet societal outcomes as informed by key stakeholders (scientific experts and policy makers) interviewees. They find that the research agenda did not respond to those concerns but was guided by excellence (in the case of academic research) or investment opportunities (for private sector research). Several studies assess inequalities in global health systems. For instance, Evans et al. (2014) contrast disability-adjusted life years (DALYs) for several medical conditions with the production on medical articles and find that there was no positive associations. Similarly, Yegros-Yegros

et al. (2020) find a clear mismatch between the societal health needs (assessed by indicators on global health burden produced by WHO) and research supply (based on MEDLINE publications). Although at national level there seems to be some balance in priorities, global imbalances persist because most research is done in high-income countries. Confraria and Wang (2020) find that sub-Saharan African research capacity, although being significantly smaller when compared with other regions, organized its priorities according to their disease burden, even when collaborating internationally. Thus, supporting local research systems, could be a route to reduce global health inequality.

The case of Chagas disease is particularly interesting to study regarding research agendas and needs. Chagas mainly affects marginalized populations in Latin America, thus incentives for research in the area are weak. However, in the past five decades, its importance across the international scientific community has grown significantly (Bortz & Thomas, 2019). Thus, although this problem is mainly concentrated in Latin America, science carried out worldwide can be relevant to tackle the problems related to Chagas, particularly in the fields which are less context dependent (Yegros-Yegros et al. 2020). It is highly relevant to study whether international research in the topic is being correctly directed to make the best use of scientific resources across countries. Following the literature stated above, we provide a novel assessment of the relation between demand of supply of knowledge in the case of Chagas combining qualitative and bibliometric methodologies.

Most previous studies on scientific production of Chagas based on interviews, literature reviews and official statistics have argued that that local research agendas are strongly aligned with the problems that grant greater visibility and international scientific legitimacy rather than producing knowledge which can be easily applied to tackle local problems (Kreimer and Zabala 2006). As a consequence, the authors claim that despite the great number of articles published in scientific journals, the development of medical treatments and other solutions to Chagas are almost inexistent. Bortz and Thomas (2019), who analyze scientific production in Chagas based on interviews, non-participatory observations and documentary analysis, hold this position as well, stating that the need to fit with international requirements has prevented R&D projects from being easily implemented in the local Latin American context, where the disease is most present.

Thus, this paper contributes to the literature on scientific production on Chagas through the novel combination of qualitative and quantitative bibliometric methodologies in this area. In addition, it contributes to literature on research evaluation, particularly in neglected diseases, by providing an in-depth analysis how research agendas are aligned with the main problems in this field through the study of demand and supply factors. Our qualitative approach to study the demand also allows for a different more in-depth r delineation of societal needs with respect to past literature, which followed a quantitative approach. We also contribute to science policy by providing useful policy recommendations on how to best align the perceived demands with research supply, which differs according to the research field.

## 3. Context

### 3.1 Chagas, a neglected disease

Chagas is an infectious disease which affects 6 million people and causes over 14,000 deaths each year worldwide (WHO, 2015b), with a DALYs of 232 thousand in 2017 (*Global Burden of Disease Study*, 2017)[1]. The disease is caused by a parasite (*Trypanosoma Cruzi*) and has three main forms of transmission: vectoral transmission through an insect known as *vinchuca* (or *kissing bug* in English), vertical transmission through mother-fetus infection, and through blood transfusion. Each year 30000 new people are infected by the *vinchuca* in Latin America and 9000 new-borns are infected during pregnancy (WHO, 2020b). It is

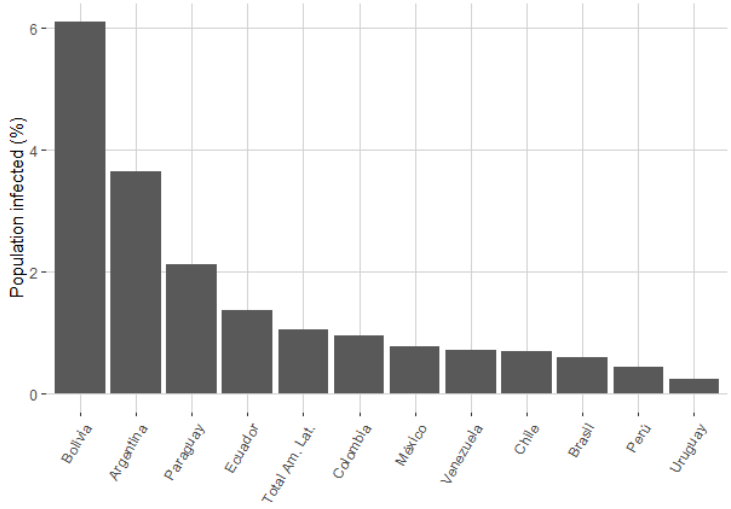
[1] As a comparison, DALYs index in 2017 was 45000 thousand for Malaria and 2.24 thousand for Zika virus.

considered a neglected tropical disease because it has received little attention by the international scientific and policy community for many years, despite being an important health burden in many low- and middle-income countries with no effective solution.

The disease evolves in two phases: the acute phase and the chronic phase. The first stage lasts between one and two months and is usually asymptomatic. The first period of the chronic phase is also asymptomatic and can last several years. Later in the chronic phase, heart failures may develop and, to a lesser extent, digestive and nervous problems that cause the main organs to have organic failures. Despite the scientific advances, existing drugs (Benznidazole and Nifurtimox) are mostly effective only during the acute phase of the disease and the first stage of the chronic phase, while effectiveness drops considerably during later stages of the chronic phase (DNDi, 2018). Thus, early diagnosis is extremely important. Additionally, there are no vaccines to prevent Chagas.

Argentina ranks first in Latin America in terms of quantity of infected people (1,5 million of people, 3.5% of population in 2010) and is the second highest in terms of incidence (3.5% of the population, in 2010, behind Bolivia with 6.1% of its infected population) (See Figure 1, (WHO, 2015b).

*Figure 1: Prevalence of Chagas, % of population infected*




Source: World Health Organization data, 2015

Until some time ago, Chagas was considered a strictly Latin American health problem, directly linked to the distribution and density of several species of *vinchucas* in the so-called endemic areas, traditionally affecting the poor rural population. However, as a result of the increasing rural-urban and international migration and vertical transmission, the disease has expanded globally. Chagas has started to be a problem in urban areas as well, and some cases has been found in Europe and the United States[2]. This phenomenon has favored the international visibility of Chagas as an issue that deserves close attention and has increased the support from multilateral organizations to combat Chagas.

Chagas is increasingly considered a multidimensional phenomena (Sanmartino (Coord.), 2015) involving medical, social and environmental aspects. Although vector control and better diagnosis and treatment are

[2] At least 300.000 cases of chronic Chagas disease have been found in the United States (Montgomery et al., 2016) and 42.000 in Spain

still important matters, social needs in Chagas go beyond them and include issues related to discrimination, access to infrastructure, land use and policy articulation

In 2005 the World Health Organisation (WHO) recognized Chagas as a neglected tropical disease (WHO, 2020a). In 2015 it was included in the 2030 Sustainable Development Agenda, since in target 3.3 of the Sustainable Development Goals refers to the neglected tropical diseases which the global community looks to eradicate (United Nations, 2015). Finally, in 2016 Chagas was included in the of list diseases prioritized by the Pan American Health Organization's (PAHO) plan ETMI-Plus which promotes the elimination of mother-to-child transmission of certain diseases.

### 3.2 Scientific and political context of Chagas

The history of Chagas as research problem has been marked by different periods in which the disease has been differently framed. This has led to the prioritization of various disciplinary fields, solutions and public policies around Chagas (Kreimer & Zabala, 2006; Zabala, 2010)

A first period in Chagas research started 1908, with the identification of the causative agent (the parasite), the vector and a series of clinical manifestations by Carlos Chagas. This phase was characterized by the construction or definition of the disease, where the main actors involved were a small group of scientists interested in developing the links between the pathogen and a set of clinical symptoms.

The second moment corresponds to the period of 1940-50 in which Chagas started to be recognized as a relevant public health issue and social problem. This led to the development of various Latin American national control plans (including Argentina, which launched the National Chagas Program in 1961) around the disease in the fields of health, epidemiological control, scientific research and housing (Kreimer & Zabala, 2006; Sanmartino (Coord.), 2015). During this period, research was focused on the eradication of the vector of the disease.

Since the 1970s there has been growing interest in Chagas across the scientific community. During this third moment, Chagas evolved from being framed as a health problem and social issue to be conceived as a relevant "biological problem" which resulted in the development of various lines of research in the field of molecular biology (Bortz & Thomas, 2019). During this period, the main object of interest shifted from being the vector to the parasite causing the disease. Hence research on Chagas has shown a strong concentration in the fields of Molecular Biology and Biochemistry. Additionally, in these years research on Chagas has gained wider international reputation and support through initiatives such as the "Special Program for Research and Training in Tropical Diseases" (TDR) in 1975, co-sponsored by the WHO, UNDP and World Bank (Coutinho, 1999) and the creation of the Drugs for Neglected Diseases initiative (DNDi) in 2003.

More recently, due to the elimination of blood transmission and the decreasing rate of vector transmission in the last decade, the emphasis in the field of Chagas policies and research has shifted from rural settings and housing deficits to congenital transmission (the current main source of infection in Argentina). Consequently, activities in Chagas have shifted from rural areas to maternities, and more emphasis has been placed on early detection and treatment than vector control (Bortz & Thomas, 2019).

In sum, although since the 1940s Chagas is acknowledge as a social problem and symbolically associated to Latin American structural inequalities (Zabala, 2010), academic research has mostly focused on biological aspects related to the parasite, the vector and some medical aspects (Kreimer & Zabala, 2006). These authors claim that research is predominantly basic science, highly specialized research, published in scientific publications well integrated into international networks but with little local articulation and poor capacity to generate effective policy solutions.

## 4. Methodology

We evaluate to what extent local priorities in research have been addressed by local (Argentine) or by global research supply, and whether collaboration, particularly international partnerships, could contribute to improve alignment between demand and supply. We follow a mixed-method approach combining qualitative and quantitative methods which promote a deeper the understanding of our research topic (Johnson et al., 2007). We carry out qualitative analysis to characterize societal needs and research demand. Then, we assess global and local research supply in Chagas research using bibliometric methods to identify diversity of topics being studied by different countries and regions. We will contrast demand and supply and will attempt to identify different policy strategies to improve the balance between research demand and supply.

The exercise consists of a procedure with four steps. In first place we identify and interpret the demands of Chagas research with a qualitative approach. We study the needs in Chagas research in the particular case of Argentina through interviews with key actors in Chagas research and policy and analysis of sources produced by civil society organizations representing groups of people suffering from Chagas. In second place we apply a quantitative bibliometric analysis of Chagas research using microdata on academic publications. The main topics in Chagas research are identified through topic modelling (Landauer et al., 2007). In third place, we associate some of these topics to the identified demands. We study the distribution of topics across regions to assess specialization patterns and over time periods, to evaluate the dynamics in relation to the identified needs Thirdly, we use econometric techniques to identify what variables are relevant in determining whether a publication is related to a specific topic, particularly those with greater demand.

It is important to mention that although our demand analysis focuses on the case of Argentina, the bibliometric study of research supply is done at both a global and local scale. We follow this approach because the research agenda is globally produced and quality research done worldwide can contribute to solve Chagas-related problems in Argentina since researchers and policy makers could use, adapt and apply that knowledge in policies, technologies and further research. However, we also identify research produced by Argentinean institutions, as many aspects relevant for problem solving (e.g. articulation between different actors in policy design and implementation) greatly depend on localized capabilities (Herdt, 2012).

### 4.2 Qualitative methodology: measuring demand of Chagas research

Three main sources of information were used to measure the demand of Chagas research:

We interviewed key informants in Chagas in the first semester of 2019. These were actors with long trajectory in the field of Chagas coming from various contexts including policy, science and NGOs. They all held a deep understanding of the issues related to Chagas and the state of research in the area. Key informants were chosen combining the use of secondary information sources such as newspaper articles, government reports, and choosing actors who had many publications on Chagas in different fields. Additionally, we consider diversity when selecting the group of key informants. In particular, we aimed to include informants from sociological research, biological research, medical research, education, philanthropic organizations and public policy. We include at least key informant for each of them, interviewing a total of eight key informants.

We also interviewed members of five different research projects in Chagas, completing thirteen interviews in total, mostly during the second semester of 2019. These were scientific researchers from public, private and civil society sectors. The selection of projects for interviews was based on three criteria: those that were repeatedly mentioned in our key informants' interviews, those performed by organizations ranking highest

in terms of publications, and disciplinary diversity (i.e. we aimed to include projects belonging to a variety of disciplines). Their perspective was essential to capture the view of people with experience carrying out research in this field on what the priorities in Chagas are nowadays.

During the interviews, respondents mentioned what they thought to be the research areas which need to be emphasized in order to find solutions to Chagas. They were also asked on the policies they believe necessary, and the main obstacles in research and implementation (which are also an indicator of the needs in the field).

Finally, throughout 2019 and early 2020 we analyzed secondary sources of information including reports and social media web pages produced by organizations of people suffering from Chagas (people infected or living in areas with high infection rates) such as the International Federations of Associations of people affected by Chagas (FINDECHAGAS) and a documentary produced by a Chagas educational project in collaboration with rural associations in Argentina (Sanmartino, 2015). Their view was extremely important to understand the needs of the people directly suffering the consequences of the disease

### 4.1 Quantitative methodology: measuring supply of Chagas research

*Data sources*

The main data source used for our quantitative analysis consists of a database containing information on publications (Title, Abstract, Keywords, Authors, Affiliations) and their citations from the Web of Science (WoS) bibliographic database produced by Thomson Reuters (*Web of Science*, 2019). Given that WoS has an underrepresentation of research from the global south, publications in non-English languages and grey literature, we are aware that this database adds limitations to the study[3].

We restrict the publications in our database to those within the field of Chagas research. Specifically, we download microdata on publications containing the terms "*chagas**" or *"trypanosoma cruzi"* or *"t. cruzi"* or "*kissing bug*" or "*vinchuca*" or *"triatoma infestans"* or "*tripanosomiasis americana*" or "*triatominae*" [4] in their title, abstract, or keywords.

The database holds 25711 publications from 1980 to 2020. Of this sample, 19383 publications have an abstract available[5] (which is used for topic modeling). The distribution of publications on Chagas is unequal through the time period covered: in our corpus the average publications per year was 345 from 1980 to 1999; and 942 from 2000 to 2019. One important caveat is that Argentinean research could be under-represented in WoS, since some may be published in Spanish in academic journals not indexed in WoS. This may be particularly important in the case of Social Science.

*Topic modelling*

[3] Although Scielo (https://scielo.org/es/) provides a better coverage of Latin American publications, the downloadable database does not contain important information on each publication that WoS does (such as institutions involved and abstract), which would limit our analysis greatly.

[4] The query used for the publication search was based on (i) most frequent terms in Pubmed publications under Mesh term "Chagas disease" (ii) consultation of experts and (iii) authors' own research on the topic. *Tripanosomiasis americana is* another form of referring to Chagas disease. *Trypanosoma cruzi* and *t. cruzi* refer to the parasite causing Chagas (and its abbreviation). *Kissing bug* and *vinchuca* refer to the vector transmitting the disease, and, *triatominae* and *triatoma infestans* are the scientific names of the family of insects and the main species within this family which transmit the disease.

[5] Abstracts are only available for publications from 1990 onwards

Our main analysis consists of identifying different topics within Chagas research, and studying how they vary across regions and time periods.

We use the method of topic modelling to discover common *topics* across a collection of documents. In particular, we use Latent Dirichlet allocation (LDA) for fitting the topic model. This methodology considers each document as a distribution of topics, and each topic as a distribution of words. This allows documents to relate to several topics with different levels of intensity , rather than being separated into discrete groups. (Cassi et al., 2017; Robinson & Silge, 2017). Each topic in LDA is a multinomial distribution over the terms in the vocabulary of the corpus. We refer to the probability of term *n* being generated by topic *m* as $Beta_{mn}$. Documents are related to topics by estimating the proportion of words from each abstract that are generated from each topic. We refer to $Gamma_{im}$ as the probability of document *i* belonging to topic *m*.

We apply topic modelling to our sub-sample of publications containing an abstract (19383). After eliminating stop words, terms appearing in less than 25 documents, and carrying out a lemmatization of the terms, we reach a total of 5521 terms. We decide to divide our corpus into twelve topics as we consider that this provides a good summary of the most important areas within Chagas research. We analyze the topics with the interactive visualization provided by LDAvis program (Sievert & Shirley, 2014). This tool allows to rank terms within topics according to their relevance, which takes into account a term's *frequency* within a topic, as well as its *exclusivity*[6], the degree to which its occurrences are limited to only a particular topic. It also positions the topics as circles in a two-dimensional space by computing the distance between topics using Jensen-Shannon divergence.

### 4.3 Joining demand and supply of research

*Linking demand and supply*

The matching between demand and supply was done through a correspondence between perceived needs identified qualitatively and research topics identified through topic modelling based on similar studies (Ciarli & Ràfols, 2019) and consultation with experts in the field. To simplify interpretations, we group the twelve topics into five larger groups where some groups represent research areas which are higher in demand[7]. This grouping is based on the their linguistic similarity of the topics (i.e. the similarity of important terms across topics) and citing networks (the distributions of the $Gamma_{im}$ for the publications citing or being cited by the top 5% of publications with the highest $Gamma_{im}$ in each topic).

We first study the distribution of research topics across regions and time. This allows us to see which scientific areas have gained (and lost) most relevance in the past years. In the case of Argentinean and also aggregated international supply we can relate them to the identified Argentinean demand. It also gives us a first interpretation on the relative and absolute country specialization (as a proxy for their research capabilities in different areas) allowing us to identify where research supply for different topics comes from.

*Drivers of research*

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[6] The relevance score for term n in topic m is = $\lambda \log(Beta_{mn}) + (1-\lambda) \log(\frac{Beta_{mn}}{p_n})$, where $p_n$ denotes the marginal probability of term *n* in the corpus and λ determines the weight given to the probability of term *n* under topic *m* relative to its exclusivity. We use λ=0.6 which has been shown to produce optimal results (Sievert & Shirley, 2014).

[7] We decide to first divide the corpus into 12 topics to achieve a better, more detailed, understanding of the topics dealt with within Chagas research. After achieving this understanding, we group them into five larger groups for a simpler analysis. This procedure allows the reader to understand exactly which topics are included in each of the five broader groups, allowing for richer conclusions.

We use an econometric approach to study what factors drive research and correlate highly with topics of greater demand. We then proceed to run five linear regressions, one for each group of topics *n* of the form:

$$G_{it}^{n} = \beta * X_{it} + f_t + \varepsilon_{it}$$

For publication *i* of year *t*. Where $G_{it}^{n}$ is the sum of $Gamma_{im}$ relating publication *i* to topics in Group *n*. $X_{it}$ is a vector of variables characterizing publication *i* (specified below), $f_t$ are time fixed effects on the year of publication, and $\varepsilon_{it}$ is a random error[8].

The explanatory variables in our regressions are:

- *Inter-institution collaboration:* Computed as number of institutions involved in the publication
- *Inter-country collaboration:* Number of countries of the institutions involved in the publication
- *Country concentration index*: Reflects the distribution of institutions from different countries in the publication and is computed as a "Herfindahl index"[9] where a lower index represents a more equal distribution of institutions across countries (e.g. 3 institutions from one country A and 3 institutions from country B) and a higher index represents a higher concentration of institutions in one country (e.g. 5 institutions from one country A and 1 institution from country B).
- *Interdisciplinarity:* computed as the number of different scientific disciplines (WoS categories) where the authors of the publication specialize[10]. Thus, this indicator reflects whether researchers with different specializations are collaborating in the publication.
- *Citations:* total number of times the publication has been cited
- *Number of Institutions from Argentina participating in the publication:* this variable reflects the presence of Argentine institutions in the study. Given that the qualitative exercise focuses on Argentina, this variable is relevant to measure where research in Argentina is concentrating on
- *Dominant region:* this categorical variable indicates the region with the greatest number of institutions participating in the publication. We divide countries into four regions: Europe, Latin America, North America (USA & Canada) and Rest (we join the rest of the countries into one group because they have significantly fewer number of publications)[11]

Descriptive statistics and correlations between these variables can be seen in the Appendix, Tables A1 and A2.

## 5. Results

### 5.1 Demands for scientific knowledge

The accurate identification of supply and demand factors frequently constitutes an important methodological issue (Wooldridge, 2002). For instance, although vaccine development and effective drugs

[8] We consider robust-clustered standard errors at the year level

[9] $\sum {S_i}^2$ where $S_i$ is the share of institutions from country i in the total number of institutions involved in the publication

[10] The field where each author specializes is computed as the top WoS category of the articles the author has published in the last five years (year X-4 to X)

[11] Although we have included a descriptive analysis of the relative and absolute specialization of four countries, we include this variable to analyze these results on regional specialization controlling for other factors characterizing the publication

for the chronic phase of Chagas are clear research areas where progress is needed, these were scarcely mentioned in interviews or secondary evidence. We believe people express what they expect in the context of what is most likely to occur in the short-medium term, while the examples above may be relevant for progress in the longer term. With these caveats, we have found three key areas where there is great potential for research to contribute to find solutions:

a. Alternatives for vector control

Two problematic changes were mentioned by experts in the field regarding the changes in the behavior of the kissing bug, which affects vectoral transmission. Firstly, while kissing bugs were traditionally found in rural settings, they have started to be found in urban areas. This is likely to be because of the recent changes in natural ecosystems (due to production activities and climate change) which have led to changes in the kissing bugs' habitat.

Another important problem mentioned by two experts in ecology and entomology is the recent resistance that kissing bugs have developed to existing insecticides. This has generated a great demand for the development of new methods to eliminate the vectors.

Both issues require research to search for alternatives for vector control, which is also a problem highlighted by people living in endemic areas. Affected people state that the fumigation of their areas is a priority for them because they live in areas with a high presence of kissing bugs. However, they highly criticize the housing program put forward by the argentine government which looked to eradicate all the adobe houses (known as "ranchos") to help prevent the presence of kissing bugs. People were forced to leave their homes and all their belongings behind to settle in government-built houses, which seems to have a negative emotional and cultural consequence. They believed this sacrifice was unnecessary as they state that keeping the houses clean is sufficient to prevent kissing bugs from settling in the houses. This poses the need to research on other mechanisms which could be useful for the control of vectoral infection which have fewer negative effects on people's livelihoods.

b. Development of rapid diagnosis methods and reduction of congenital transmission

Multiple sources of information stress the need for rapid diagnosis methods for Chagas that can be implemented in areas with poor infrastructure. This is mainly for two reasons: on the one hand, congenital transmission today is one of the main issues in Chagas, and scientists have firm evidence that treatment on Chagas is much more effective on newborns (in the case of congenital transmission) and in the initial phases of the disease. Thus, early, rapid, easy and accessible detection methods are key. As one of our interviewees expresses this idea:

*You have to focus on the development of rapid tests (...) Chagas treatment today is very long (...) if you attack Chagas in children, we will decrease Chagas in Argentina (...).We fail in asking people (living in poor areas) to come (to health centers) and not us going to them.*(Policy maker in Chagas)

Thus, research on the development of easy and accessible diagnosis methods which can be easily distributed to health centers around the territory is extremely useful.

c. More research in social sciences and policy implementation

It was repeatedly mentioned that there were shortcomings in public policy, particularly lack of integration in policy schemes to fully address the multiple socio-environmental dimensions related to Chagas problems. Fragmentation was also multisided: there were references to lack of articulation across different jurisdictions (municipalities, provinces and national state), policy areas (education, health, housing, infrastructure, sanitation, etc.) and intermittency in policy attention to Chagas (e.g. national program on Chagas, created in 1961 suffered from many interruptions across time). These problems may be partially

rooted in lack of relevant knowledge in the public policy arena but also on political frictions which are not explained by knowledge shortages.

Yet, it was mentioned in multiple interviews from individuals with various backgrounds, that research on Chagas needs to further include the social perspective of the problem, especially in the policy arena. Research on all the other socioeconomic characteristics such as marginalization, discrimination, and social vulnerability were mentioned as central to the fight against this problem. Put very clearly by an important member of a public organization working on Chagas:

*"The day we start seeing Chagas as a social problem, we will be able to start reducing Chagas in our country."* (Policy maker)

Within this social perspective, some key issues were raised such as the need for research on how to implement policies related to Chagas in the most effective manner or the need for research on how to best approach education in Chagas in order to cover the important gaps in information about this problem across a great part of the population. In the words of an expert in the field of Chagas on this issue:

*Education in Chagas has been underestimated (…) as if it were not real research (…). In this problematic (Chagas) we need an approach to education with a scientific methodology* (Researcher in Chagas)

*It has been extremely complicated to find research teams in the social sciences which are interested in Chagas, they have other priorities.* (Researcher in Chagas)

In addition, we identified a strong need for studies on science, technology and innovation policy. In particular, to improve the digital infrastructure for collating and sharing scientific outputs. As Chagas is a neglected disease there is low availability of accurate and reliable data because the matter is not given sufficient attention and resources. Thus, research projects aimed at generating such data are fundamental.

In the case of Argentina, fundamentally there is a need for basic data on the number of people suffering this disease, the deaths caused by Chagas, and their distribution across the country. Another example of the data needed is experimental evidence on clinical trials which is fundamental for drug discovery:

*"One of the problems is that (…) the linking is based on experimental evidence (…) to link genomic research with drug development (…) there is not much information available in terms of experimental data (…) that is the critical bottleneck (for the development of drugs for Chagas)"* (Researcher in drug discovery)

### 5.2 Supply of scientific production

#### 5.2.1 Descriptive statistics

We first display a series of descriptive statistics on the set of publications to understand the geographical and disciplinary distribution of the dataset.

*Regional distribution*

The top publishing country in Chagas is Brazil, which is followed by the United States and Argentina. Other top countries are Spain, France, England and Mexico.. The ranking of Chagas research across countries has been quite stable through the time period considered and the top three countries (Brazil, USA, Argentina) are constant when dividing the corpus into ten-year time frames.

As expected, international collaboration in Chagas research across years has increased: while in the past 20 years, over 32% of articles have been published by institutions belonging to more than one country, this proportion was 16% before 2000 and only 8% before 1990.

*Table 1: Participation of Latin America and Argentina in Chagas research 1980-2019*

| Country of affiliation of authors | Only Argentina | At least one Argentina | Only Latam | At least one Latam |
|---|---|---|---|---|
| Number | 2106 | 3353 | 10813 | 15256 |
| (proportion) | (8%) | (13%) | (42%) | (59%) |

Table 1 shows the number and proportion of publications in our dataset coming from Latin American countries. More than half of the publications have at least one author who is affiliated to a Latin American institution, which is the region which most suffers from Chagas. In the whole WoS database, this number is only 3%, indicating that this topic has a relatively high Latin American specialization. It is interesting to note that from these publications with Latin America participation, most (70%) are composed of *only* Latin American authors. This gives the impression that in Chagas research, many Latin American institutions do research autonomously, without depending on northern institutions for publishing.

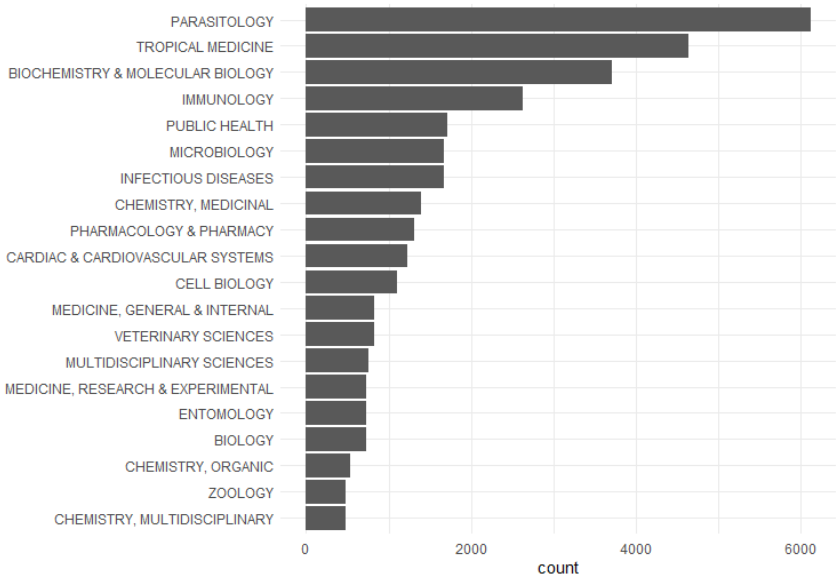
In our dataset 13% of publications count with the participation of at least one Argentine institution. We see a similar pattern to Latin American institutions: most Argentine authors publish *only with Argentine authors*. Interestingly, the participation of Argentine institutions in Chagas research has decreased through time: 11% of publications had solely Argentine authors before 2000 and 16% before 1990. This is likely to be because of two driving factors. On the one hand, as mentioned above, international collaboration has increased. Thus, the proportion of publications with authors from one single country has decreased. On the other hand, in recent decades the problem of Chagas has become a global issue. Thus, research in other countries has increased more than proportionally to Argentine research in the area.

*Scientific categories*

We proceed to analyze the distribution of WoS categories in our database. As can be seen in Figure 2, a great majority belong to Parasitology. The main categories are all in the medical and biological sciences, while, interestingly, public health is in the top categories of the publications, which is principally applied research[12].

*Figure 2: Distribution of WoS categories*

[12] Examples of publications in this field are *"Chagas Disease Control Programme in Brazil: A study of the effectiveness of 13 years of intervention"; "Chagas disease vector control through different intervention modalities in endemic localities of Paraguay"; "Vector-borne infections in the tropics and health policy issues in the twenty-first century"*




However, this classification is very broad and journal based. Thus, we believe it is useful to use a methodology which allows to look deeper into Chagas research and identify the different topics within the corpus. With this aim in mind, we recur to topic modelling method.

### 5.2.2 Topic modeling results

In order to analyze the different areas within Chagas research, we divide our corpus into twelve topics, as this gives a clear idea of the different fields within Chagas research[13].

*Labelling topics*

The following link gives access to an interactive visualization of our topic map with 12 topics: LINK. Each circle in the left panel represents a topic. The size of the circle indicates the relevance of the topic in the corpus, which is also shown in Table A3 in Appendix. The topics are located in the two-dimensional space according to their similarity. Inter-topic distances are projected in two dimensions (Chuang et al., 2012), so that topics with similar keywords of high importance[14] are closer together, and those with more differences are located further apart. The right panel shows a bar chart where the 30 most relevant terms for each topic are selected using the relevance score explained above[15].

This visualization allows to understand the areas within Chagas research corresponding to each topic. In order to improve this understanding, we analyze the relative importance[16] of WoS categories in each topic, the most relevant institutions and the title and abstracts of publications with a high $Gamma_{im}$ for each topic (99$^{th}$ percentile), see Table A4 in Appendix. Table 2 shows the research areas which we assign to each topic, based on their relevant keywords and scientific categories. A table with the main institutions and examples of publications with high Gamma for each topic can be seen in the appendix. We also carry out

[13] We repeated the topic modelling exercise with various numbers of topics: 5, 10, 15 and 20. When selecting more topics, many overlap in our topic map, indicating that they are very similar and can be grouped into one topic. If we choose to few topics (e.g five), the keywords associated to each topic are very general and do not allow for a clear distinction of research areas

[14] We refer to high importance as publications with a relatively high $Gamma_{im}$ for the topic.

[15] $\lambda$ 0.6 is selected for the construction of this score, as this is shown to be the optimal $\lambda$ in Sievert and Shirley (2014).

[16] Frequency of category within cluster / Frequency of category in corpus

an additional check by asking experts in Chagas to label the topics according to the most important keywords, categories, and institutions.

*Table 2: Topic labels*

| Topic | Research area | Relevant keywords | WoS Categories |
|---|---|---|---|
| 1 | Immune response to Chagas | Infection – immune – inflammatory – gamma | Immunology – virology |
| 2 | Drug discovery | Compound – Drugs – Benznidazole – toxicity – Nifurtimox | Chemistry – Pharmacology |
| 3 | Cellular Biology | Cell – membrane – parasite - epimastigotes | Cell Biology - Microscopy |
| 4 | Control of vector transmission | Vector – insect – infestans – triatoma – house – peridomestic – insecticide | Entomology – Ecology - Zoology |
| 5 | Global health | Disease – development – neglected - tropical - health - people | History & Philosophy of Science – General Medicine – Public health |
| 6 | Chronic consequences of Chagas | Patient – heart – cardiac – chronic – megacolon | Gastroenterology & Hepatology – Cardiac & cardiovascular system – respiratory system – clinical neurology |
| 7 | Molecular biology | Enzyme – substrate – trypanothione – protease – reductase | Chemistry – Physics – Computational Biology |
| 8 | Genomics | Protein – Gene – genome – family - encoding | Genetics & Heredity- Evolutionary Biology |
| 9 | Chagas diagnosis tests/methods | Leishmaniasis – visceral – diagnosis – test – sensitivity – elisa – positive | Nanotechnology – medical laboratory technology – veterinary sciences – microbiology |
| 10 | Congenital transmission and blood transmission | Disease – transmission – blood – children – congenital – women | Obstetrics & Gynecology – Pediatrics – Public Health - Hematology |
| 11 | Biodiversity, Ecology & Genetics | Genetic – strains – diversity – lineages - genotype | Biodiversity conservation – Genetics – Evolutionary biology - Ecology |
| 12 | Parasite-host interaction | Sialidase - antibodies – peptide – epitope – surface – receptor | Chemistry – Biochemistry – Molecular Biology |

### 5.3 Demand and supply of research

*Topics and countries*

We start off this section with a descriptive analysis of the research specialization of different countries. This allows for an initial understanding of which demands are met through global research, and which are tackled locally. Although research can be seen as an international public good, understanding each country's research capabilities is very relevant, as these are essential for absorbing international knowledge and applying it in the local context. We evaluate the absolute and relative specialization in each country through two indicators. The absolute specialization indicator for each country ($c$) and topic (m) is given by the average of $Gamma_{im}$ (the probability of document $i$ belonging to topic $m$, see methodology section) for all the documents with authors affiliated to country $c$:

$$ASI_{cm} = \frac{\sum_{i \in c} Gamma_{im}}{\#\ of\ publications\ from\ country\ c}$$

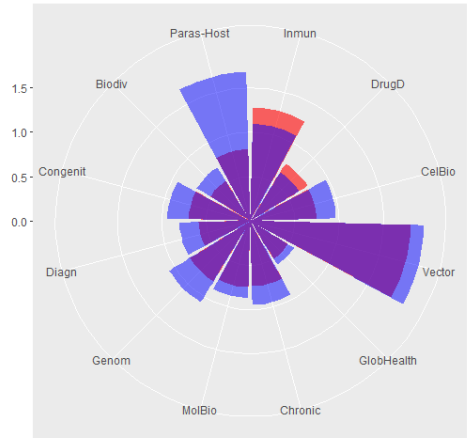
This indicator shows the distribution of research across one country (compares topics within a country). The relative specialization indicator for country *c* and topic *m* compares the index displayed above with the average $Gamma_{im}$ for topic *m* across all documents in the corpus. Thus it is given by the average of $Gamma_{im}$ for all the documents with authors affiliated to country *c*, divided by the average of $Gamma_{im}$ for all documents in the corpus (*I*).

$$RSI_{cm} = \frac{\frac{\sum_{i \in c} Gamma_{im}}{\#\ of\ publications\ from\ country\ c}}{\frac{\sum_{i \in I} Gamma_{im}}{\#\ publications\ in\ corpus}}$$

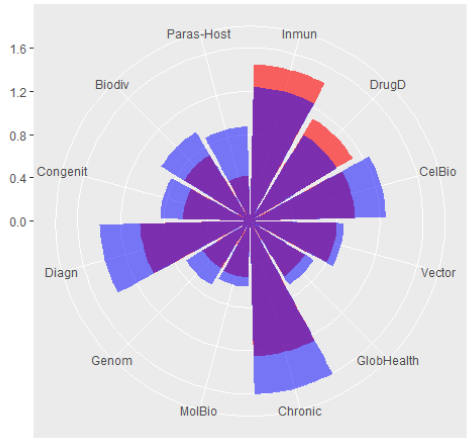
This index compares how relevant each topic is in the subset of publications affiliated to a certain country to the relevance of the topic in the whole corpus. Thus, it allows us to compare the importance of topics across countries. The following images show the distribution of these indicators for four selected countries (two high-income and two low-income) and across the 12 topics. The absolute specialization indicator is displayed in red while the relative specialization is shown in blue:

*Figure 3: Absolute and relative specialization indicators per country*

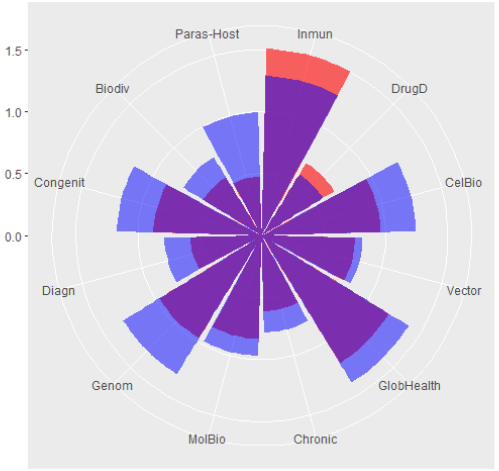
*Argentina*



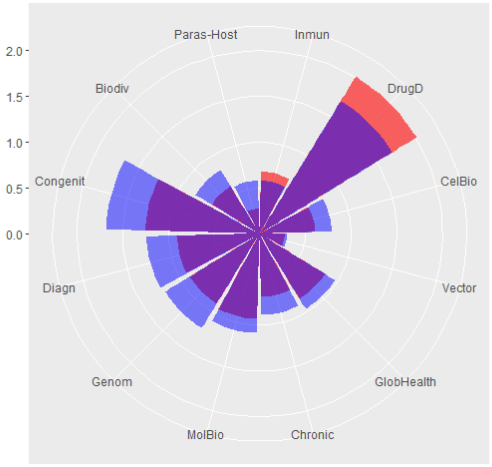

*Brazil*




*USA*




*Spain*



Note: The height of each bar represents the absolute (red bars) and relative specialization (blue bars) indicator for each topic. The number on the left-hand side of the graphs indicate the value of the indicators. The absolute specialization indicator in the graphs is multiplied by 10 for visual purposes

These graphs show a series of interesting results. In first place we can see that Argentina has a high absolute and relative specialization in topic 4, which represents vectoral transmission. This topic is particularly important in this country where there is a higher presence of the kissing bug. Although Brazil also has vectoral transmission, this country does not have much research in topic 4 nor 11 but is stronger in topics 1,6 and 9 which have a more medical focus. This is mainly driven by the research institute Oswaldo Cruz, which is one of the leading institutions in Chagas and has a medical, biochemical orientation rather than and ecological focus.

Topic 10, on congenital transmission is particularly important in Spain and the United States. This is expected as they do not have cases of vectoral transmission, and congenital transmission is the only form of Chagas infection at the moment. In Spain, topic 2 on drug discovery is important in both relative and absolute terms.

A last result to mention is that Global Health (topic 5) is mostly done by USA. Given that Chagas is not a serious problem within this country, it seems that they approach the problem at a more global perspective, with a focus on international health policies which can be done to help solve this problem.

*Accumulation and evolution of scientific knowledge*

In order to simplify association of the topics in research supply with the areas identified in the demand analysis, we divide the topics into five groups according to the research areas they represent. Three of groups represent each of the three research areas demanded. As mentioned in the methodology, this grouping is based on linguistic similarity (i.e the position of the topics in the LDAvis visualization) and citation networks. For the latter, we filter the top 5% of publications with the highest Gamma for each topic. We then select publications which cite or are cited by this group and analyze the distribution of Gammas across topics in this selection. This allows us to see which topics have most citations relations with each topic[20]. Thus, we group together topics which are relatively close in linguistic terms and cite each other frequently. In most cases, both parameters coincided in the grouping of the topics. This exercise produced the following grouping

- Group 1: Ecology, environment, vector transmission (*Ecol – Vector)*, topics 4 and 11
- Group 2: Congenital transmission and early diagnosis,[21] (*Congen – Diagn)*, topics 9 and 10
- Group 3: World Health[22], topic 5
- Group 4: Medicine, topics 1 and 6
- Group 5: Biology and Chemistry (*Biology)*, topics 2, 3,7,8 and 12

We can see in Figure 4 that the biological and chemistry fields are predominant in our corpus, covering five of the twelve topics, while the number of publications mostly belonging to this group (having the highest

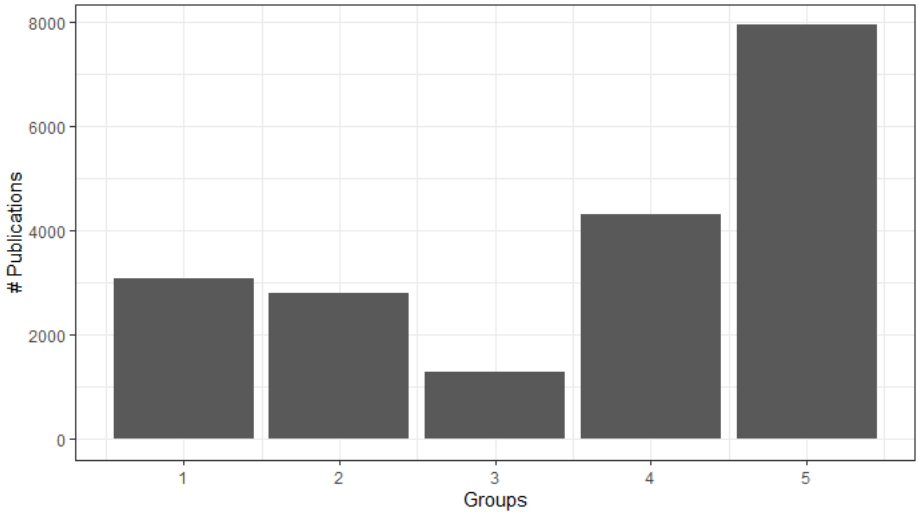
[20] The three topics which most cited each topic were: Topic 1: 6, 5, 3 – Topic 2: 7, 5, 3 – Topic 3: 8, 2, 1 – Topic 4: 11, 10, 5 – Topic 5: 1, 2, 7 – Topic 6: 1, 10, 5 – Topic 7: 2, 5, 3 – Topic 8: 3, 5, 7 – Topic 9: 10, 11, 1 – Topic 10: 6, 4, 9 – Topic 11: 4, 10, 9 – Topic 12: 1, 3, 8

[21] Congenital transmission is closely linked to early diagnosis, as the development of the technologies for diagnosis in newborns allows them to have the opportunity to cure from Chagas if diagnosed on time.

[22] We decide to group this topic individually, as the citation patterns differ significantly from the linguistic proximity to topics and we believe the topic of world health should be evaluated independently.

sum $Gamma_{im}$ for topics in this group[23]) from 1990 to 2019 were almost twice the sum for topics in group 4, the next group in order of importance.

*Figure 4: Publications mostly belonging to each group of topics. 1990-2019*




*Note: Group 1: Ecology and Vector transmission , Group 2: Congenital tranmission and diagnosis, Group 3: World Health, Group 4: Medicine, Group 5: Biology & Chemistry*

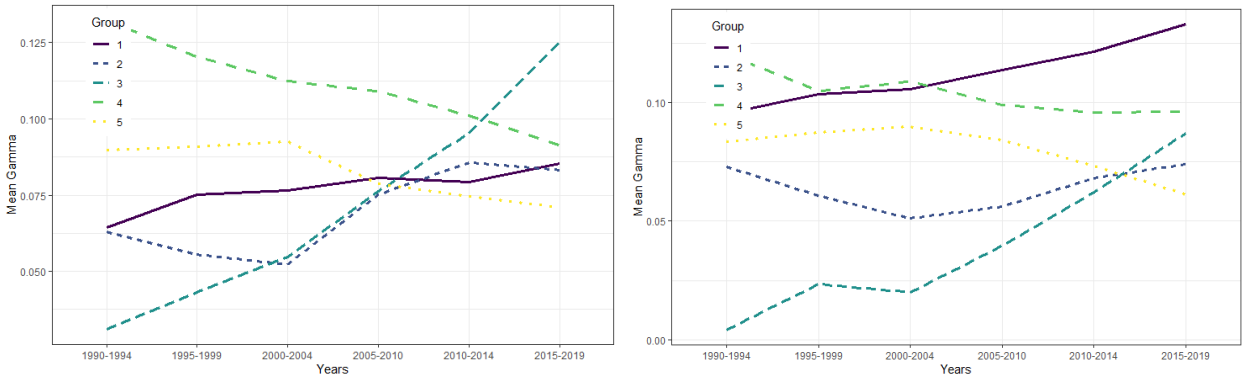
In relation to the demand identified in section 5.1, the topics which seem to be most in demand nowadays are new forms of vector control, studies to control congenital transmission and provide early diagnosis to newborns and studies on the social aspects of Chagas and implementation. While the first two fields in demand are clearly represented by groups 1 *(Ecol – Vector*) and 2 (*Congen – Diagn*) respectively[24], the third area is not directly represented by any group, as there is very little research on Chagas in the social sciences. However, the topic of *World Health* has the most social perspective and includes papers on health policy[25], scientific policy[26] and social sciences[27]. Thus, we consider group 3 to represent this demand.

Given this grouping, we study how the relevance of topics in Chagas research has changed through time both globally and in Argentine research[28]. We do this by analyzing the relevance of the topics in each group for five-year periods between 1990 and 2019. The relevance of topics in each group is measured as the average $Gamma_{im}$ of the topics in the group, for all documents published in each moment of time. The results can be seen below.

*Figure 5: Evolution of topic relevance through time 1990-2019*

[23] For each publication i we compute the sum of $Gamma_{im}$ for all topics belonging to each group. We assign the publication to the group with the highest sum.
[24] Recall group 1 is Ecology and Vector transmission, this includes publications assessing alternatives for vectoral control. Group 2 is on congenital transmission and early diagnosis which is precisely the second demand identified in the qualitative analysis.
[25] E.g. "Ecosystem Approaches to Health for a Global Sustainability Agenda"
[26] E.g. "The Importance of Collaboration between Industry, Academics, and Nonprofits in Tropical Disease Drug Discovery"
[27] E.g. "Chagas disease in non-endemic countries: 'sick immigrant' phobia or a public health concern?"
[28] Publications with the participation of at least one Argentine institution

*Global research* *Argentine Research*




*Note: Group 1: Ecology and vector transmission , Group 2: Congenital tranmission and diagnosis, Group 3: World Health, Group 4: Medicine, Group 5: Biology & Chemistry*

We see that both global and Argentine research show similar trends. Two of the groups identified as having a relevant demand are those with the greatest growth in the past years. The topic which has most increased in relative relevance is topic 5 (group 3, *World Health*). In Argentina, research has also grown, although at a very low rate until recently. This is likely to be because Chagas has turned into an international problem in recent years, and the global health perspective has gained importance. The growing relevance of *World Health* comes in hand with an increasing participation of northern countries, which focus on this issue.

The second group with the most important increase is group 2 (*Congen – Diagn*). These topics had a slight decrease between 1990 and 2000 and increased afterwards. The positive trend is mainly driven by topic 10 on congenital transmission, which has a strong positive trend since the beginning of the century. As above, the increasing focus on this issue comes in hand with a greater participation of northern countries such as Spain and the USA, which do relatively more research in this field. As an example, among the publications with $Gamma_{im}$ for topic 10 above 0.90, more than half were published by USA and Spain in 2019, while before 2007, Spain had no publications in this topic[29].In addition, lower rates of vectoral and blood transmission in Latin America led these countries to focus more on mother-fetus infection. This is the case of research led by Argentine institutions, where this topic also has a positive trend.

The third group which has been identified in the demand analysis, group 1 (*Ecol – Vector*), has been quite stable in the past years, with a slight increase. If we look within this group, both topics 4 (vector control) and 11 (biodiversity, ecology) have been stable through time, with a larger increase in the former. The trend is very similar for Argentine publications. This result is likely to be because the problem of vectoral transmission is not new and has historically received much attention. It was the first form of transmission to be discovered, it used to be the main form of infection, which required much research on the topic and remains an important field due to ecological patterns which imply vector migration and resistance development.

Finally, groups 4 and 5 on Medicine and Biology/Chemistry have decreased in relevance over time, mainly the former. Within these groups, the only topic which has increased in relevance is topic 2 on drug discovery, within group 5. We believe this is because research in these areas was very strong when populations where still discovering what Chagas was, how it attacked people's health systems, how humans reacted to it, and the particularities of the parasite. Nowadays, scientists understand how this parasite acts, and research can then be focused on other areas of the problem.

[29] This result is maintained when looking at publications with $Gamma_{im}$ above 0.5, 0.7, 0.8 and 0.95

*Identifying mismatches between demand and supply:*

From these results, we see that in terms of the internationally accumulated knowledge represented by the total number of publications in each group (Figure 4) the three groups most in demand nowadays (groups 1, 2 and 3) are lagging behind the medical and biological fields (groups 4 and 5). However, when we look at the evolution of knowledge, there seems to be a tendency for research to focus on the topics of *World Health* (group 3) and *Congen - Diagn* (group 2). In the case of *Ecol - Vec*tor (group 1), we do not see an increase, but research has kept stable across years, accumulating more publications than groups 2 and 3.

Argentinean research capabilities have focused on vectoral transmission (topic 4 from Group 1), where research has been constant across time. Argentina has also accumulated capabilities in group 4, *Medicine* and group 5, *Biology* (particularly topics 3, cellular biology, 8, genomics and 12, parasite-host interactions) and research in group 2, *Congen - Diagn* is growing (particularly topic 10 congenital transmission). Group 3 *World Health* also shows a positive tendency but a markedly low accumulation of knowledge.

Thus, when analyzing how research supply could match Argentina demand we could argue:

For group 1 (*Ecol - Vector*), there seems to be substantial locally developed capabilities. The importance of this research area has been stable worldwide and in Argentina this research area remains of primarily importance. Progress in this area may have already reached a plateau. In fact, is we considered that vector infections have been controlled in several Latin American countries (WHO, 2015b p. 35) we may argue that the revealed demand has more to do with policy failures and lack of articulation than lack of relevant research, which nevertheless continues to be important due to vector resistance and changes in ecological systems.

For group 2 (*Congen - Diagn*), there has been an increasing trend in international supply of knowledge. This could be used locally since the country had also accumulated capabilities, especially recently, and this is an area of research where findings worldwide could be adapted to local context, since key knowledge aspects in this area (e.g. diagnosis methods or how to stop congenital transmission) will not be context specific. Thus, in order to improve supply and demand alignment in this case, it may be relevant to further support local participation in international research networks.

There is demand for social sciences that could contribute to policy design and implementation in the areas of health, education, and science policy. In the absent of better candidates on the supply side, we associate this demand very roughly to research in group 3 *World Health*.[30] Although there is growing international research in this area, to meet local demand context-based research is needed. Thus, among the three areas, it is social sciences (proxied by *World Health*), where we identify the clearest mismatches that may justify further support for local research.

### 5.4 Drivers of research supply: Econometric results

To help our understanding on the drivers for pushing Chagas research to certain areas, we use an econometric approach to evaluate how different variables characterizing a publication correlate with a higher gamma for topics in each group. We run five separate regressions where our dependent variable is the sum of $Gamma_{im}$ for the topics included in the each of the five research groups. As the value of $Gamma_{im}$ for one group of topics negatively depends on the value of $Gamma_{im}$ for the other groups, this

[30] Although shortages in social research may be related to disciplinary biases of WoS database which may be further enhanced by the fact that social science research may be published in Spanish in local journal not indexed in WoS, previous studies regarding Argentinean Chagas research reported that most *research was actually published in scientific journals.* Among this, during the period 1995 2005, 72% of publications were from biological fields, 23% medical fields, 4% epidemiology and only 1% from other fields .(Kreimer & Zabala, 2006).

econometric approach represents the relevance of different variables in *relative terms* across research groups. In other words, when interpreting the coefficients for each variable, we are comparing the characteristics of research carried out in each group of topics with the rest of the group areas. Thus, each regression should not be interpreted independently, but in relation to regressions for the other groups of topics.

Table 3 shows the results of our estimations for each of the five groups of topics. The first three columns represent research areas which were identified with a demand, while the other two, although of great importance, were not particularly highlighted as social needs by Chagas experts in Argentina.

We can see from the results that research in *Ecol - Vector* (group 1) tends to have fewer institutions involved, but high international collaboration. In line with previous results, we see that in this research area Argentinean and Latin American institutions have a high participation. We also see that this field tends to have low levels of citations, presumably because it is not a highly relevant area of research for the international community.

In the case of research on *Congen - Diagn* (group 2), there seems to be more institutional collaboration, but institutions working together are concentrated in one or few countries (positive coefficient for concentration index). In line with the results in the figures above, we see that Europe has more research in this field than the rest of the regions in relative terms[31]. This indicates that this knowledge may be absorbed by Latin American institutions, especially considering that the particularities of research on congenital transmission and diagnosis are not as context dependent as research on vectoral transmission. In this area research seems to be interdisciplinary, as authors from the basic sciences (Molecular Biology, Cellular Biology) collaborate with researchers in more applied fields such as public health and pediatrics.

In the area of *World Health* (group 3), as expected international collaboration is relatively high, although there tends to be concentration of collaborating institutions in a few countries. Interdisciplinarity has a negative coefficient in this research area, although this may be explained by the fact that the top WoS categories are quite broadly defined (e.g. tropical medicine, public health). This field presents relatively high citations, possibly due to the high international collaboration and the fact that the USA publishes relatively more in this field, increasing citations (Hugo Confraria et al., 2017; Smith et al., 2014).

In the case of *Medicine* (group 4), we see a lack of international collaboration although research does seem to be interdisciplinary, as researchers from many different medical disciplines and basic sciences collaborate in the same articles in this field. In medicine the most important actor is Latin America, mainly driven by the specialization of Brazil in medical issues.

In the fields of *Biology* (group 5), there is low collaboration both across and within countries and research is mostly intradisciplinary. This suggests that institutions in this field tend to do research independently. In this area Asia, Africa and Oceania have more research relative to other topics. This is likely to be because much research in basic sciences does not exclusively relate to Chagas but also to other infectious diseases with similar biological/chemical bases (e.g. Leishmaniasis, Malaria) which are also present in Asia and Africa.

If we arbitrarily split areas according to Argentinean demand, we could say that international collaboration is important, but collaboration networks are concentrated in few countries. The size of collaborations and interdisciplinarity are only important in *Congen - Diagn* (group 2), while networks in *Ecol - Vector* (group 1) and World Health (group 3) tend to be smaller and more intra-disciplinary. In addition, the regional

[31] The format of the regional categorical variable is such that each region is compared to Europe

source of publications differs according to the research topics, indicating that not all research demanded in Argentina is carried out locally.

.

*Table 3: Regression results*

| | *Dependent variable:* | | | | |
|---|---|---|---|---|---|
| | Ecol - Vector | Congen - Diagn | World Health | Medicine | Biology - Chem |
| | (1) | (2) | (3) | (4) | (5) |
| Number of Institutions | −0.008*** | 0.013*** | −0.006** | 0.002 | −0.001 |
| | (0.001) | (0.003) | (0.002) | (0.002) | (0.003) |
| Number of Countries | 0.017* | 0.007 | 0.029*** | −0.020** | −0.033*** |
| | (0.009) | (0.007) | (0.006) | (0.007) | (0.006) |
| Country concentration index | −0.055 | 0.157*** | 0.058*** | 0.058*** | −0.219*** |
| | (0.032) | (0.024) | (0.020) | (0.020) | (0.023) |
| Interdisciplinarity | −0.0003 | 0.025*** | −0.019*** | 0.018*** | −0.024*** |
| | (0.002) | (0.002) | (0.001) | (0.002) | (0.002) |
| Citations | −0.0004*** | −0.00004 | 0.001*** | 0.00004 | −0.001*** |
| | (0.0001) | (0.0001) | (0.0002) | (0.0002) | (0.0002) |
| Inst Argentina | 0.018*** | −0.001 | −0.011*** | 0.003 | −0.009 |
| | (0.003) | (0.005) | (0.002) | (0.005) | (0.008) |
| Dominant region: Latam | 0.097*** | −0.029** | −0.039*** | 0.062*** | −0.091*** |
| | (0.009) | (0.011) | (0.006) | (0.013) | (0.014) |
| Dominant region: USA | 0.026** | −0.015 | 0.047*** | 0.023** | −0.081*** |
| | (0.011) | (0.016) | (0.010) | (0.010) | (0.017) |
| Dominant Region: Rest | −0.018** | −0.049*** | 0.030*** | −0.007 | 0.043*** |
| | (0.008) | (0.013) | (0.010) | (0.012) | (0.012) |
| Observations | 11,232 | 11,232 | 11,232 | 11,232 | 11,232 |
| $R^2$ | 0.037 | 0.041 | 0.114 | 0.032 | 0.040 |
| Adjusted $R^2$ | 0.034 | 0.038 | 0.112 | 0.030 | 0.037 |
| Residual Std. Error (df = 11203) | 0.303 | 0.291 | 0.190 | 0.324 | 0.402 |
| *Note:* | *p<0.1; **p<0.05; ***p<0.01 - Standard errors clustered at the year level | | | | |

To better understand the relationship of the variables in our regression with each group of topics within research done in Argentina, we run the same econometric analysis with the subsample of publications with at least one Argentine institution.

*Table 4: Regression results for Argentina*

| | *Dependent variable:* | | | | |
|---|---|---|---|---|---|
| | Ecol - Vector | Congen - Diagn | World Health | Medicine | Biology |
| | (1) | (2) | (3) | (4) | (5) |
| Number of Institutions | −0.013 | 0.029*** | −0.005 | 0.004 | −0.015* |
| | (0.008) | (0.008) | (0.003) | (0.008) | (0.007) |
| Number of Countries | 0.011 | −0.013 | 0.013 | −0.045** | 0.033* |
| | (0.016) | (0.019) | (0.010) | (0.019) | (0.019) |
| Country concentration index | −0.074 | 0.132** | 0.001 | 0.003 | −0.062 |
| | (0.055) | (0.054) | (0.028) | (0.069) | (0.079) |
| Interdisciplinarity | −0.002 | 0.029*** | −0.012*** | 0.032*** | −0.047*** |
| | (0.009) | (0.007) | (0.003) | (0.005) | (0.006) |
| Citations | −0.0001 | 0.0001 | 0.001*** | 0.0004 | −0.001*** |
| | (0.0002) | (0.0002) | (0.0002) | (0.0004) | (0.0003) |
| Dominant Region: Latam | 0.019 | −0.013 | −0.096 | 0.049 | 0.042 |
| | (0.071) | (0.064) | (0.073) | (0.071) | (0.087) |
| Observations | 1,413 | 1,413 | 1,413 | 1,413 | 1,413 |
| $R^2$ | 0.015 | 0.122 | 0.070 | 0.041 | 0.090 |
| Adjusted $R^2$ | 0.001 | 0.109 | 0.056 | 0.027 | 0.077 |
| Residual Std. Error (df = 1392) | 0.370 | 0.254 | 0.152 | 0.326 | 0.389 |
| *Note:* | | | | | *p<0.1; **p<0.05; ***p<0.01 - Clustered standard errors at the year level |

In the field of specialization of Argentina (Group 1, *Ecol - Vector*), both collaboration and interdisciplinarity do not seem to drive research. This shows that research in this area in Argentina is fragmented and research groups do not have much interaction, either nationally or internationally.

Argentine institutions tend to publish on *Congen - Diagn* (Group 2) in collaboration with other institutions, including different disciplines, although collaboration with international research groups seems irrelevant. This is a point to highlight, since as seen in the above in Table 3 research in this area is increasing globally.

As seen above, Argentina publishes very little in the area of *World Health* (Group 3), and no driver is particularly relevant in the econometric analysis. Importantly, the variable on international collaboration is not significant, while it is significant for the whole corpus, indicating than Argentine institutions are not well connected to existing international networks in this area.

In the case of *Medicine* (group 4) research is mainly produced within the country in an interdisciplinary manner. In *Biology* (group 5) research done by Argentine institutions has little collaboration within the country, but high cooperation with institutes from other countries in the same disciplines. This is to be highlighted since international collaboration was not significant in Table 3, suggesting that Argentinean researchers in this areas are particularly prone to collaborate internationally but less so nationally. This issue was also expressed by researchers interviewed during the qualitative analysis, and goes in line with Kreimer and Zabala (2006) findings.

To conclude, for most topics international collaboration in Argentine institutions seems to have different patterns from those in global research. In contrast, interdisciplinarity plays similar role in these research areas in Argentina as in the rest of the world.

## 6. Conclusion

The study uses quantitative and qualitative techniques to explore the association between demand and supply of scientific research in the case of Chagas, a neglected tropical disease, with a focus on Argentinean demand. In order to analyze this alignment, we consider both global and local research supply. We assess to what extent relevant knowledge has been produced worldwide and whether Argentina has developed research capabilities to produce useful knowledge or to absorb, use and adapt it from the international research community.

Through interviews and secondary information sources we identified three important areas with perceived demand for research in Chagas nowadays: new forms of controlling vectoral transmission; congenital transmission and early diagnosis; and studies in social sciences to improve educational aspects of Chagas, quality data for research, policy design and implementation. We are aware of the difficulties in distinguishing demand from supply factors: this demand analysis may be affected by expectation formation processes affected by the current state of research supply. We assessed the supply of knowledge through bibliometric analysis and studied the patterns and tendencies of publications in five research areas, three of which could be associated with the perceived demand. Conclusions regarding how to meet demand for research in each area differ.

In first place, the problem of vectoral transmission and ecology seems to be attended by local research. This is the area of specialization of Argentinean research in Chagas. This topic may rely more on national knowledge systems due to its dependence on the local ecosystem and urbanization patterns can which differ across regions. Thus, the fact that Argentina's knowledge base in this area is high and has been constantly increasing across time is a positive result. This research is mostly done independently by Argentina and key needs in this field seem to be currently met in several regions in Latin America, since vector infection rates have dropped. However, due to changes in ecological systems and resistance to pesticides, this is a research area that needs continued support. In addition, current perceived demand needs better coordination in policy making and implementation regarding urbanization and vector control.

The second area is congenital transmission and early diagnosis, which shows quite different characteristics. This phenomenon has global consequences, affecting both southern and northern countries, and does not depend as much on the local context as vectoral studies. In this topic, the international supply of research is high and increasing, while local supply is not high and only slightly increasing. Thus, apart from promoting local research in this area, we believe it is essential to promote Argentine institutions to engage with international networks, where Argentina seems to be lagging behind. This will improve the absorption of international knowledge in this area by local institutions.

Finally, we identify research demanded on social sciences, which is much less present both internationally and locally, although with a positive trend in both cases. Due to the absence of relevant supply, we associate this demand to a research topic we name *World Health*, which may be a subset of potential research production on social science in Chagas. Although the shortage of supply could be partly explained by disciplinary biases in the WoS databases, we believe that our analysis regarding trends and main drivers are still relevant. In this group we see that international collaboration is high, but Argentinean organizations seems not to be particularly involved in those networks. Thus, as a first factor, Argentina could benefit more from international knowledge by international cooperation. However, these issues are also very dependent on the local context. Educational factors, social programs and science policies depend greatly on the local institutional system. Thus, although international cooperation seems to steering research towards these topics, we believe there is also the need to strongly support research locally.

Importantly although groups 3 and 4 on Medicine and Biology/Chemistry were not particularly identified as perceived demands, these are also relevant issues in Chagas research and should not be neglected. However, it is interesting to note that it is precisely on these two issues where most historical research has

been concentrated although both show decreasing trends across time. This can indicate that, on one hand, the current knowledge base for these areas is sufficient to meet current demands, and on the other hand, that this research constitutes a general and basic knowledge base needed to develop research on the other topics. Thus, the growth of these areas in the past may have allowed for the progress of research in the other topics today.

To conclude, when analyzing science policies in relation to societal needs, we see that multiple paths exist to link supply and demand factors. While in some cases fostering local knowledge is beneficial, in others promoting collaboration with international institutes seems the preferred option. However, in all cases there is a need to work closely with the diversity of stakeholders involved in thinking and developing solutions for Chagas multidimensional problems. This will allow to identify the research priorities more effectively and to understand how several Chagas-related issues interact to achieve an integral agenda towards sustainable development. Opening up the policy agenda to bring forward the values and knowledge of multiple stakeholders and engage them in designing solutions may also contribute to develop more integral solution to Chagas., which was the highest priority we identified.

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## Appendix

*Table A1: Summary statistics of independent variables*

| | # Institutions | # Countries | CC Index | # Inst. Argentina | Interdisciplinarity | Citations |
|---|---|---|---|---|---|---|
| **Mean** | 2.65 | 1.46 | 0.84 | 0.22 | 3.4 | 18.2 |
| **Min** | 1 | 1 | 0.08 | 0 | 1 | 1 |
| **Max** | 29 | 15 | 1 | 10 | 18 | 567 |

| Dominant Region | Absolute Frequency | Relative Frequency |
|---|---|---|
| Europe | 1563 | 14% |
| Latin America | 7556 | 67% |
| USA & Canada | 1281 | 11% |
| Rest | 832 | 7.4% |

*Table A2: Correlations between continuous explanatory variables*

| | # Institutions | # Countries | CC Index | # Inst. Argentina | Interdisciplinarity | Citations |
|---|---|---|---|---|---|---|
| **# Institutions** | 1 | | | | | |
| **# Countries** | 0.65 | 1 | | | | |
| **CC index** | -0.48 | -0.88 | 1 | | | |
| **# Inst Argentina** | 0.15 | 0.12 | -0.08 | 1 | | |
| **Interdisciplinarity** | 0.37 | 0.20 | -0.15 | 0.02 | 1 | |
| **Citations** | 0.05 | 0.1 | -0.07 | -0.004 | -0.026 | 1 |

*Table A3: Relevance of each topic in the corpus*

| Topic | Sum of Gamma | # of Publications with Gamma >0.5 |
|---|---|---|
| 1 | 2480.4 | 2346 |
| 2 | 2046.3 | 1145 |
| 4 | 1793.7 | 1378 |
| 3 | 1680.9 | 726 |
| 7 | 1627.7 | 1632 |
| 6 | 1627.1 | 1922 |

| | | |
|---|---|---|
| 5 | 1617.9 | 1126 |
| 9 | 1444.4 | 1390 |
| 10 | 1413.3 | 1213 |
| 8 | 1393.7 | 1388 |
| 11 | 1278.9 | 1197 |
| 12 | 978.9 | 1122 |

*Table A4: Important institutions and examples of publications in each topic*

| Topic | Relevant institutions[32] | Examples of publications with high Gamma for the topic |
|---|---|---|
| 1 | Immunology Dep Univ Fed Mina Gerais, Immunology Dep Univ Sao Paulo, Oswaldo Cruz Institute | Role of Aryl Hydrocarbon Receptor (AhR) in the Regulation o |
| 2 | Swiss Trop & Publ Hlth Inst, Univ Fed Sao Carlos Dep Chemistry, Univ Buenos Aires Dept Organ Chemistry | Antichagasic and trichomonacidal activity of 1-substituted 2-benzyl-5-nitroindazolin-3-ones and 3-alkoxy-2-benzyl-5-nitro-2H-indazoles |
| 3 | Univ Georgia<br>Dept Cellular Biol, Univ Fed Rio De Janeiro Lab Ultraestrutura Celular | Intracellular Ca2(+) Storage In Acidocalcisomes of Trypanosoma-Cruzi |
| 4 | Univ Chile Dept Ecology, Univ Buenos Aires Dept Ecology Genetics & Evolution | Shifting host choices of the vector of Chagas disease, Triatoma infestans, in relation to the availability of hosts in houses in north-west Argentina |
| 5 | Drugs Neglected Dis Initiat, Univ Georgia<br>Ctr Trop & Emerging Global Dis | Quantitative analyses and modelling to support achievement of the 2020 goals for nine neglected tropical diseases -<br>The Importance of Collaboration between Industry, Academics, and Nonprofits in Tropical Disease Drug Discovery |
| 6 | Univ Fed Minas Gerais Medicine Dep,<br>Univ Fed Goias Med school | Left Atrial and Left Ventricular Diastolic Function in Chronic Chagas Disease |
| 7 | Univ Calif San Francisco<br>Dept Pathol, Univ Fed Sao Carlos<br>Dept Chemistry | Molecular docking and molecular dynamics simulation studies of Trypanosoma cruzi triosephosphate isomerase inhibitors. Insights into the inhibition mechanism and selectivity |
| 8 | Seattle Biomed Res Inst,<br>Ctr Trop & Emerging Global Dis Univ Georgia, Biochemistry Department Univ Iowa | Genome-wide analysis of 3 '-untranslated regions supports the existence of post-transcriptional regulons controlling gene expression in trypanosomes |
| 9 | Univ Fed Minas Gerais Dept Parasitol,<br>Intectious Diseases Research Institute | Standardization of micro-enzyme-linked immunosorbent assay (ELISA) and Western blot for detection of Trypanosoma cruzi antibodies using extracts from Mexican strains as antigens |
| 10 | Univ Fed Ceara Dept Community Health,<br>Fundacao Oswaldo Cruz | High prevalence of congenital Trypanosoma cruzi infection and family clustering in Salta, Argentina |
| 11 | Univ Chile<br>Dept Ecology,<br>Univ Republica<br>Dept Genetic Evolution | Holocentric chromosome evolution in kissing bugs (Hemiptera: Reduviidae: Triatominae): diversification of repeated sequences |
| 12 | Univ Buenos Aires<br>Dept Organ Chemistry, Fdn Campomar | Identification of a domain of Trypanosoma cruzi metacyclic trypomastigote surface molecule gp82 required for attachment and invasion of mammalian cells |

[32] Institutions with most publications with Gamma >0.5

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