

Short Report: Increasing Access to Treatment for Chagas Disease: The Case of Morelos, Mexico

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Abstract. Chagas disease is a neglected vector-borne disease with an estimated prevalence of 1.1 million cases in Mexico. Recent research showed that access to treatment of Chagas disease is limited in Mexico, with < 0.5% of infected cases treated. This brief report used quantitative data from the Morelos Program on Chagas disease and qualitative analysis of key informant interviews to examine strategies to increase treatment access for infected patients in Morelos, Mexico. From 2007 to 2011, 263 (9.2%) of the registered cases of Chagas disease in Mexico occurred in Morelos. Among these, 152 (57.8%) were treated and 97.3% of those treated received benznidazole. The assessment finds that state officials decided to directly purchase benznidazole from the distributor to increase access and improve clinical quality of treatment of patients in their state. They also faced significant barriers, especially in regulation and health system organization, which limited efforts to make high quality treatment available.

Chagas disease is a neglected vector-borne disease with a prevalence of 8–10 million cases globally, with an estimated 1.1 million cases in Mexico.^{1,2} Recent research conducted in Mexico showed that access to treatment of Chagas disease is limited, with < 0.5% of those who are infected having received treatment in recent years, despite evidence of cost-savings with early diagnosis and treatment.^{3,4} The research found multiple regulatory, organizational, and political barriers to treatment access at the national level in Mexico. This brief report uses both quantitative and qualitative analysis to show how the state of Morelos overcame these barriers in Mexico to increase access to treatment of Chagas disease in that state.

Morelos has a population of just over 1.7 million inhabitants or about 1.6% of the Mexican total. Economically, Morelos ranked 21 out of 31 states by gross domestic product (GDP) in 2007. Geographically, it is located south of Mexico City, and is bordered by the states of Mexico, Puebla, and Guerrero. The national Program on Onchocerciasis, Leishmaniasis, and Chagas Disease, within the Mexican Secretary of Health's National Center for the Prevention and Control of Diseases (CENAPRECE), is the unit responsible for establishing guidelines and coordinating national activities for Chagas disease control, including facilitating the donation and distribution of nifurtimox, often considered the second line therapeutic agent for Chagas disease.⁴ Within the state's Secretary of Health, the state program on Chagas disease has the operational responsibility for prevention and control activities for this illness, and coordination with healthcare providers for procurement of medication, treatment, and follow-up of those who are infected. Neither benznidazole nor nifurtimox has received market authorization in Mexico from the national medicine regulatory body, called the Federal Commission for Protection against Health Risks (COFEPRIS). As such, they have historically not been included in the national formulary or the formulary of the *Seguro Popular* health insurance program. It is likely that the

absence of a market authorization is one major reason for their exclusion from the formulary, though another possible reason is that the importance of treatment has only recently been acknowledged by the wider medical community.^{5,6}

This report about the state of Morelos is part of a larger national study of Chagas disease in Mexico that consisted of 18 semi-structured in-depth interviews, among which eight interviews involved discussions of Morelos.⁴ The Morelos state program provided data on the number of cases diagnosed and treated. Contact with initial interviewees was established through in-country key informants and subsequent interviews were obtained through a snowball sampling method. For all processes described in the interviews, official reports and supporting documentation were requested. These documents, along with the published literature and other interview responses, were used in triangulating interview responses. The institutional review board (IRB) exemption was obtained from Harvard School of Public Health (Protocol no. 21514-101) and the National Institute for Public Health (INSP) located in Cuernavaca, Mexico. Oral informed consent was obtained from all interviewees. The data were analyzed according to the Flagship Framework for Pharmaceutical Policy Reform's control knobs: regulation, payment, financing, organization, and persuasion.⁷ Here, we assess the approaches used in Morelos to procure and distribute benznidazole, organized according to the Flagship Framework for Pharmaceutical Policy Reform.

NUMBER OF REGISTERED AND TREATED CASES BETWEEN 2007 AND 2011

Between 2007 and 2011, 263 of the 2,847 cases (9.2%) registered by Mexico's national Program on Onchocerciasis, Leishmaniasis, and Chagas Disease (hereafter national program) were located in the state of Morelos. The Morelos program further reported that 152 of these 263 (57.8%) cases received treatment of *Trypanosoma cruzi* infection over the same time period. Moreover, 148 (97.3%) of the treated cases in Morelos received 30 days of benznidazole, whereas all other cases treated in Mexico during this period received nifurtimox. Among the remaining 111 registered cases in Morelos who went untreated during this period,

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TABLE 1

Prevalence estimates and case registration at the state and national level in Mexico

	State of Morelos	National level
Population	1,780,000	112,340,000
Prevalence estimate - blood bank estimate ^{8,9}	0.652%	0.652%
Expected cases - blood bank estimate ^{8,9}	11,605	733,333
Prevalence estimate - PAHO estimate ²	1.03%	1.03%
Expected cases - PAHO estimate ²	18,300	1,157,000
Cases registered (2007–2011)	263	2,847
% of target (2007–2011)	N/A	80.48%
% of expected cases - blood bank estimate	2.26%	0.39%
% of expected cases - PAHO estimate	1.42%	0.25%

PAHO = Pan American Health Organization.

the largest group were those pending diagnostic validation by the national level ($N = 40$, 36%), followed by those who could not be reached ($N = 22$, 19.8%), or refused treatment ($N = 22$, 19.8%). Only 2 (1.8%) registered cases died. Table 1 provides a summary table of case registration for Chagas disease in Morelos and blood bank estimates or World Health Organization (WHO) estimates for national prevalence.¹⁰

HEALTH SYSTEM BARRIERS

In 2010–2011, Morelos sought to procure benznidazole for treatment of infected patients. Table 2 summarizes the obstacles to access benznidazole that we identified from the interviews and the strategies that the Morelos program used to overcome them.

Regulation. Given the lack of market authorization in Mexico for benznidazole, the Morelos Program on Chagas Disease must request a permit each time it seeks to import the medicine. For benznidazole, the permit was provided in the category of “medicines that do not have a sanitary license” based on the justification that it was a “special treatment for a low incidence disease with a social impact.”¹¹

The state requested the one-time importation permit for benznidazole in April 2010 and was able to secure a permit in 2011. Key informants reported that the process of obtaining this permit was complex and required multiple applications.

Payment. The costs of purchasing benznidazole, including the price of the medication, transportation, and distribution, fell entirely to the state of Morelos. The direct cost for purchasing the medicine in 2011 totaled ~\$30,000 US dollars (USD).¹² This included the cost of delivering the medicine to Mexico, but excluded any costs associated with distribution within the state to providers and patients, such as employee time, fuel costs, etc.

Financing. To purchase benznidazole, Morelos officials decided to use a state discretionary fund called “Ramo 33” (Budget Line 33) with the support of senior officials in the state Secretary of Health.

Organization. State officials were able to purchase benznidazole directly from the distributor, Masters Pharmaceuticals Ltd., in the United Kingdom.¹² However, the procurement process for the medicines took over 1 year from initial application to receipt of the medication.

Persuasion. Officials in Morelos, with support from collaborators at the INSP, Mexico’s major academic public health research institute, which is located within the state, established a program to provide training on Chagas disease to health workers in Morelos. The training program began as local workshops for physicians and later became an annual health education program offered to all health workers. Despite these efforts, Morelos officials reported that there were still many physicians in the state who had limited understanding of Chagas disease or were reluctant to diagnose or supervise treatment of patients, as a result of a lack of familiarity with the disease, a lack of experience using the medications, or fears about adverse effects of the medications. As a result, the Morelos program has now begun working with physicians in each of its three health regions to provide on-site training to physicians once a case is registered and a decision is made to treat, so that physicians feel more comfortable monitoring treatment.

TABLE 2

Morelos - state strategy for providing benznidazole and remaining state obstacles

Policy intervention ⁷	State strategy during 2007–2011	Remaining state obstacles
Regulation	<ul style="list-style-type: none"> Applied for one-time COFEPRIS permit for importation of benznidazole in 2011 using justification that benznidazole was a treatment of a “disease of low prevalence, but high social impact.” 	<ul style="list-style-type: none"> Complex and time-consuming application process for one-time COFEPRIS importation permit
Financing	<ul style="list-style-type: none"> Mobilized funds for benznidazole from the state discretionary fund “Ramo 33” 	<ul style="list-style-type: none"> Unsustainable source of financing because availability of funds in Ramo 33 may vary
Payment	<ul style="list-style-type: none"> State of Morelos paid for one time purchase and distribution of benznidazole (~\$30,000 USD) in 2010–2011 	<ul style="list-style-type: none"> No institutionally secured payment strategy
Organization	<ul style="list-style-type: none"> No explicit strategy 	<ul style="list-style-type: none"> Procurement process took over 1 year Lack of integration with those working on epidemiology and prevention programs and those responsible for medicine procurement and treatment programming
Persuasion	<ul style="list-style-type: none"> Officials at the Morelos State Program on Chagas disease focused efforts on diagnosing cases; showing burden of disease and justifying need for purchase of benznidazole Presence of the INSP provides both political champion and technical support for state efforts Establishment of educational program for healthcare workers to increase consideration of Chagas disease as a diagnosis and familiarity with approaches to diagnosis and treatment 	<ul style="list-style-type: none"> Limited awareness of the disease among both physicians and patients Concerns about using the medicines among physicians

COFEPRIS = Federal Commission for Protection against Health Risks; INSP = National Institute for Public Health.

State prioritization. The Morelos Program on Chagas Disease is unique in that it is located in close proximity to the National Institute of Public Health. The role of this institute and several of its researchers was mentioned as an important factor in terms of championing the disease among state officials and collaborating with the state program to provide technical support for their activities.

This case study of the Morelos Program on Chagas Disease shows some of the strengths and challenges of providing treatment of Chagas disease in Mexico today. The analysis shows that Morelos officials made a concerted effort to directly purchase benznidazole, often considered the first-line treatment of *T. cruzi* infection, from the distributor, to both increase access to treatment of infected patients and improve the clinical quality of treatment of infected persons in this state.¹³ However, the procurement process was complex and confronted multiple obstacles to access. In particular, this analysis found substantial regulatory challenges, including the lack of COFEPRIS approval of benznidazole, which has important implications at the state level, such as complicating the importation process, and increasing waiting times in the procurement period and thus delaying treatment initiation for patients.¹⁴ In addition, the exclusion of benznidazole from the national formulary has reduced access to treatment by limiting possible sources of financing for medicine procurement.⁶

One limitation of this case study analysis is the difficulty of generalizing the results from Morelos to other states in Mexico or other countries. However, this examination of the Morelos case may increase understanding of the barriers to treatment access that exist in Mexico, and the avenues that may exist for other states in Mexico to overcome similar barriers that they confront. Given that the national regulations, policies, and laws that govern the activities of Morelos are the same as those that govern other states in Mexico, it should be possible for other states to learn from the activities in Morelos to improve access to treatment of Chagas disease patients within their state borders.

This study offers several useful lessons for state and national policymakers in Mexico. First, it highlights that the state maintains a key role in the provision of health services and substantial power to respond to specific issues of local concern that may not be sufficiently addressed by national policies or programs. In addition, it shows that regulatory barriers to treatment of Chagas remain an important concern for states in Mexico and that the addition of benznidazole and nifurtimox to the national and insurance program formularies in particular could advance treatment efforts. Finally, it shows that capacity building in Chagas disease for physicians and health workers, especially in collaboration with academic or policymaking institutions, can advance efforts to increase access.¹⁵

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