

Chagas Disease Transmission in Periurban Communities of Arequipa, Peru

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Background. Chagas disease, caused by *Trypanosoma cruzi* infection, is an urban problem in Arequipa, Peru, and the epidemiology of Chagas disease is likely to be quite different in this area, compared with in rural zones.

Methods. We conducted a serosurvey of 1615 children <18 years old in periurban districts that included hillside shantytowns and slightly more affluent low-lying communities. In addition, 639 adult residents of 1 shantytown were surveyed to provide data across the age spectrum for this community.

Results. Of 1615 children, 75 (4.7%) were infected with *Trypanosoma cruzi*. Infection risk increased by 12% per year of age, and children living in hillside shantytowns were 2.5 times as likely to be infected as were those living in lower-lying communities. However, age-prevalence data from 1 shantytown demonstrated that adults were no more likely to be seropositive than were teenagers; the results of maximum likelihood modeling suggest that *T. cruzi* transmission began in this community <20 years ago.

Conclusions. The problem of Chagas disease in periurban settings, such as those around Arequipa, must be addressed to achieve elimination of vector-borne *T. cruzi* transmission. Identification of infected children, vector-control efforts, and education to avoid modifiable risk factors are necessary to decrease the burden of Chagas disease.

Chagas disease is a major cause of morbidity and mortality in South and Central America, where an estimated 8–10 million people are infected with *Trypanosoma cruzi* [1, 2]. Up to 30% of *T. cruzi*-infected individuals develop potentially life-threatening cardiac disease over the course of their lifetimes. In placebo-controlled trials, antitrypanosomal drug treatment was efficacious in a large proportion of infected children [3, 4], and etiologic treatment appears to decrease the risk of disease progression, even in adults [5]. Accordingly, the standard of care in countries in which the disease is endemic includes identification and treatment of all infected children.

As is common with other tropical diseases, Chagas disease disproportionately affects the poor. Historically, Chagas disease has been considered to be largely a rural disease, associated with poor housing conditions and the proximity of domestic animals [6–11]. However, recent reports document the emergence of Chagas disease in cities, where its epidemiology and ecology may be quite different [12]. In Arequipa, a city of 860,000 people in southern Peru, widespread infestation with the vector *Triatoma infestans* and active transmission of Chagas disease to humans have been documented over the past 10 years [13].

Although small studies in communities in and around Arequipa have reported seroprevalence in children of 0.7%–12.9% [13], no large surveys have been conducted. Thus, the epidemiology of Chagas disease in urban Arequipa remains largely unknown. We conducted a cross-sectional serosurvey in periurban districts of Arequipa to determine the prevalence, spatial patterns, and risk factors of *T. cruzi* infection and to use these data to characterize the urban epidemiology of Chagas disease. The survey focused predominantly

Received 7 December 2007; accepted 11 February 2008; electronically published 5 May 2008.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Clinical Infectious Diseases 2008;46:1822–8

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1058-4838/2008/4612-0003\$15.00

DOI: 10.1086/588299

on school-aged children, the main target group for treatment, but also included a complete population survey in 1 community, allowing us to examine age-specific prevalence patterns and to make inferences about how long *T. cruzi* transmission has been occurring in periurban Arequipa.

METHODS

Study site and population. Arequipa (altitude, 2300 m) is situated in the arid highlands of southern Peru. The city's population has grown rapidly since the 1960s, predominantly through immigration from high Andean villages, which have no triatomine infestation or Chagas disease transmission, to periurban shantytowns or *pueblos jóvenes* ("young towns"). This study was conducted in the districts of Tiabaya and Sachaca, located in the southwestern outskirts of Arequipa (figure 1). Most residents are poor, work in agricultural or informal service industries, and live in substandard housing constructed of brick or *sillar*, a volcanic rock [14]. Because of documented triatomine infestation and cases of Chagas disease, these districts were treated with residual insecticide by the Ministry of Health (MOH) in 2004 and 2005. Most study participants were recruited in the public schools that serve the populations of the 2 districts. In addition, the entire population of 1 hillside *pueblo joven* (Guadalupe, consisting of Santa Maria de Guadalupe and Alto Guadalupe, Sachaca) was invited to enroll in a community-based study [14]. School-aged children living in

Guadalupe were recruited either during the house-to-house survey or in school.

Before the initiation of recruitment, meetings with parents were convened at schools and in the local communities to explain the survey and to answer questions. During specific times designated by school administrators, trained study nurses explained the survey to children in each classroom and distributed consent forms to be signed by parents and returned. Similar meetings were held in Guadalupe, and consent was solicited during home visits by the study nurses. The only inclusion criteria were attendance at 1 of the targeted schools or residence in Guadalupe, age <18 years (for the school surveys), and informed consent (as documented by the consent form signed by adult participants or by the parent or legal guardian for children and by the signed assent form for children 7–18 years old). The protocol was approved by the Institutional Review Boards of Johns Hopkins School of Public Health (Baltimore, MD), the Centers for Disease Control and Prevention (Atlanta, GA), the Peruvian National Institute of Health (Lima, Peru), and Asociación Benéfica Proyectos en Informática, Salud, Medicina y Agricultura (Lima, Peru).

Serosurvey data collection. Age, sex, and place of residence were recorded, and a 5-mL peripheral blood specimen (3 mL for children <5 years of age) was collected from each participant. Specimens were stored at 4°C and were transported the same day to the laboratory of the Universidad Nacional de San

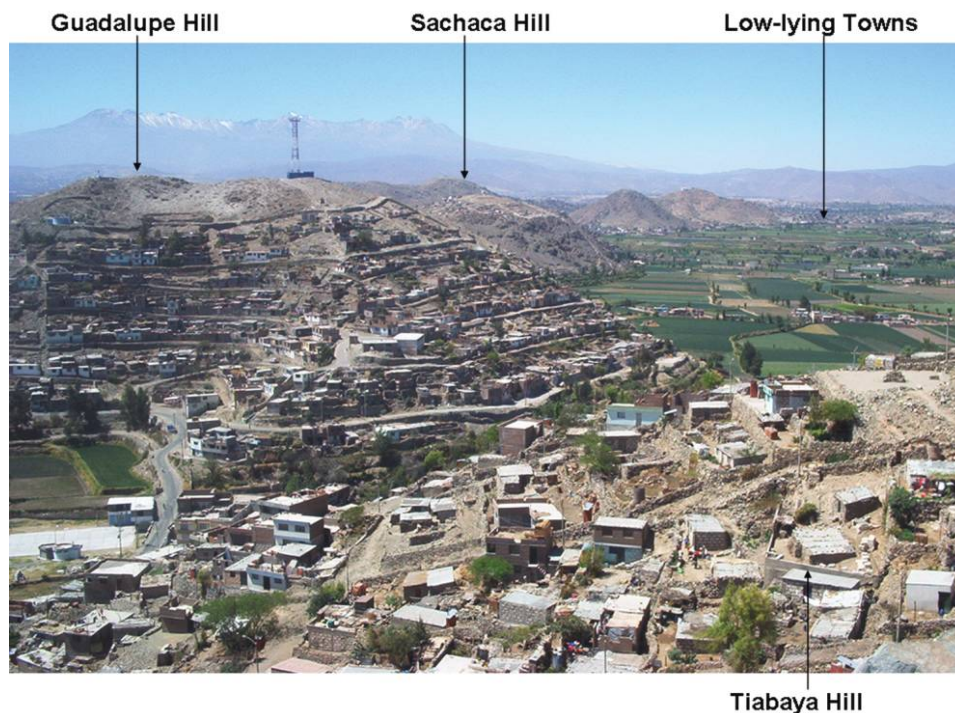


Figure 1. Photo of a portion of the study zone showing hillside shantytowns and low-lying communities. The shantytowns are more densely populated and poorer than most of the low-lying communities.

Augustín (Arequipa, Peru). Blood was separated by centrifugation; serum and cellular portions were stored at -20°C in aliquots. Serum samples were screened for antibodies to *T. cruzi* with use of a commercial ELISA (Chagatek; bioMérieux), in accordance with the manufacturer’s instructions. The threshold for positive results was calculated to be 0.100 optical density units above the mean absorbance of 2 negative control specimens included on each plate. All positive samples and 12% of negative samples were tested by the indirect immunofluorescent antibody test (IFA) at the Centers for Disease Control and Prevention, with use of a titer of 1:32 as the positive cutoff [15]. Specimens with both positive ELISA and positive IFA results were considered to indicate confirmed *T. cruzi* infection [16]. Specimens with positive ELISA results but negative IFA results were considered to have inconclusive results; the participants with inconclusive results were excluded from the epidemiological analyses.

Entomological and spatial data collection. The Arequipa MOH vector control program recorded the presence of *T. infestans* by household in Tiabaya and Sachaca at the time of the first insecticide applications in 2004 and 2005. We used these data to calculate the proportion of infested houses in each community. More-detailed household-level vector data were collected in Guadalupe [14]. Community boundaries were defined using maps made as part of the MOH vector-control program; when these were unavailable, community boundaries were determined with use of municipal maps. Communities were classified as “hillside shantytowns” or “low-lying towns” on the basis of geographic and demographic features (figure 1). Hillside shantytowns are densely populated communities located on dry, rocky hills rising above surrounding farmland. For some analyses, hillside shantytowns were grouped by the hill on which they were located. Low-lying towns are more sparsely populated communities in flat areas, often contiguous with agricultural fields. The low-lying towns were grouped for analysis. For the spatial analysis, the few surveyed children who lived outside the boundaries of the districts of Sachaca and Tiabaya were excluded, because their numbers were too small to provide stable estimates of seroprevalence. Spatial data were mapped using ArcMap 9.1 (ESRI), Google Earth 4.0, and locality-level maps from the MOH.

Statistical analysis. Crude ORs were calculated using the χ^2 test for binary variables and univariate logistic regression or Kruskal-Wallis test for continuous or ordinal data, respectively. Multivariate logistic regression models were constructed, including variables significant at $P \leq .2$ in univariate analyses. As variables were added, the resulting models were tested against sparser models by the likelihood ratio test. Statistical analyses were performed using STATA, version 8.0 (StataCorp), and SAS, version 9.0 (SAS).

We constructed one age-prevalence curve for all children

≤ 18 years of age and a second age-prevalence curve for individuals of all ages living in the community of Guadalupe. On the basis of the relationship between age and *T. cruzi* seroprevalence, we then compared 2 alternative models of transmission. The first model (“constant incidence”) assumed that probability of infection increases linearly with the log of an individual’s age rounded to the nearest year. The model has only 1 parameter, the yearly incidence of infection (λ), which is assumed to be constant [17]. The second model (“recent introduction”) assumed that the probability of infection increases linearly with the log of an individual’s age only if age is greater than the (unknown) time since the initiation of transmission. The recent introduction model has 2 parameters—the time since the initiation of transmission (t) and the yearly incidence of infection each year since that time (λ), which is assumed to be constant. The equation for probability of infection for the constant incidence model is

$$1 - e^{-\lambda \text{age}},$$

and the equations for probability of infection for the recent introduction model are

$$1 - e^{-\lambda \text{age}} \text{age} < t$$

and

$$1 - e^{-\lambda t} \text{age} \geq t.$$

We used the likelihood ratio statistic (1) to compare the fit of the 2 alternative models and (2) to approximate 95% CIs for the estimates of λ and t for the recent introduction model [18]. (All analyses were done in the R statistical programming environment (R, version 2.5 [19]).

RESULTS

Of 3671 children <18 years of age registered in the 11 study schools, 1469 (40.0%) participated in the study. Compared with participating school children, children whose consent forms were not returned were more likely to be male (57.7% vs. 45.4%; $P < .001$) and were older than participants (mean age, 11.7 vs. 10.5 years; $P < .001$). The participation rate was significantly higher in primary than in secondary schools (50.1% vs. 26.6%; $P < .001$). Of the participating children from the study schools, 268 (18.2%) lived in Guadalupe.

During house-to-house recruitment, 785 residents of Guadalupe consented to participate, including 146 additional children <18 years of age who were not included in the school-based surveys. In total, 1053 (54.8%) of the 1921 residents of Guadalupe participated in either the community- or school-based survey. The mean age, sex distribution, and rate of positive serological test results did not differ significantly between

children recruited at home in Guadalupe and all school participants. In subsequent analyses, data from children living in Guadalupe and those recruited in schools were analyzed together.

The 1615 children in the serosurvey included 747 (46.2%) males and 868 (53.7%) females; their median age was 10.3 years (range, 0.9–17.9 years). Specimens from 87 children had positive ELISA results for antibodies to *T. cruzi*; 12 of these specimens had negative IFA results and were excluded from further analysis. The remaining 75 ELISA-positive samples were confirmed to be positive by IFA, yielding a seroprevalence of 4.7% (95% CI, 3.64%–5.71%).

In univariate analysis, males and females were equally likely to be infected (5.3% vs. 4.2%, $P = .31$). The prevalence of infection increased with age (figure 2; $P = .004$, by Kruskal-Wallis test); none of the 36 children <4 years of age was seropositive. There was a positive association between the likelihood of infection and the proportion of infested houses in the child's community ($P = .018$), and hillside shantytowns had higher infestation rates than did other communities ($P < .001$). Residence in a hillside shantytown was associated with an OR of 2.5 (95% CI, 1.1–7.2) compared with low-lying towns; most low-lying towns had no seropositive children.

In a multivariate analysis, *T. cruzi* infection risk increased by 12% per year of age (table 1). Children living on any of the 3 hills in the study area were more likely to be seropositive than were children living in low-lying towns, but the difference reached significance only for Tiabaya Hill. The seroprevalence

was higher on hills farther from the city center, increasing from 3.4% on the Sachaca hillside to 7.3% on the Tiabaya hillside (table 1 and figure 1).

To address the question of transmission risk over time, we used data from the entire population of the community of Guadalupe to compare 2 alternative models; the first model assumed that infection risk was constant over time, whereas the second model tested the hypothesis that transmission began relatively recently. The recent introduction model fit the data much better than did the constant incidence model (likelihood ratio statistic, $\chi^2 = 22.94$; $P < .001$) (figure 3). On the basis of the maximum likelihood estimate, active transmission was estimated to have begun in Guadalupe around 1993, with an estimated annual incidence rate of 0.417%. The 95% confidence region for transmission ranged from 1.5% annual incidence over a 3-year period to 0.291% annual incidence over a 19-year period.

DISCUSSION

Our data confirm that residents of periurban Arequipa are at high risk of *T. cruzi* infection. Nearly 5% of surveyed children were seropositive; these children should receive antitrypanosomal treatment under Peruvian national guidelines. In addition, this serosurvey provides evidence that *T. cruzi* introduction into this periurban setting was relatively recent and that the hillside shantytowns contain the most important foci of ongoing transmission. Other cities in southern Peru may have

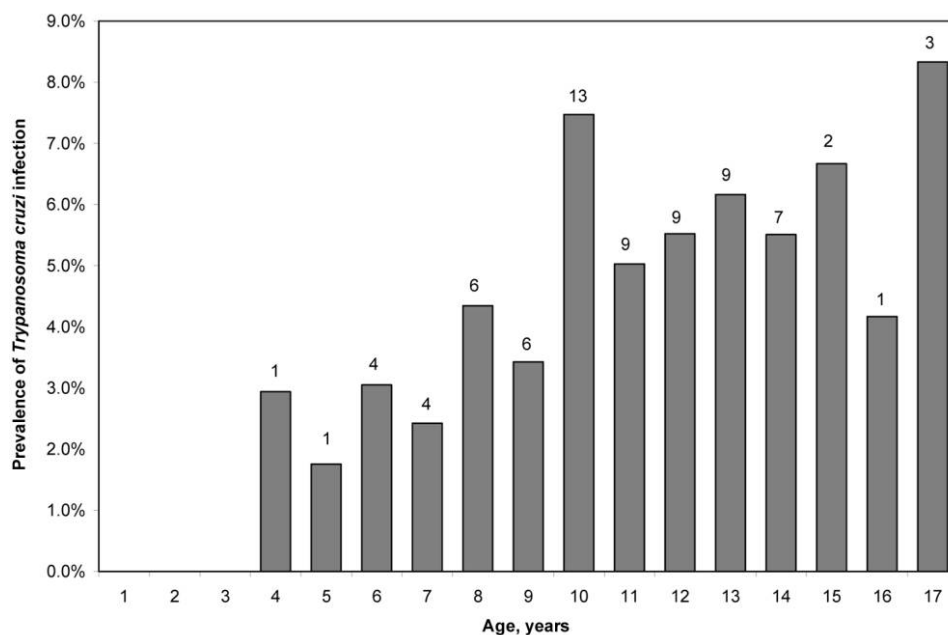


Figure 2. Age-prevalence curve for children in the pediatric survey population. The number of seropositive individuals is shown above the bar for each age group.

similar periurban Chagas disease foci [20]. Large urban populations of triatomines, although not *T. cruzi* transmission, have also been described in Argentina [21, 22]. Our survey findings, together with data from local vector ecology studies [14], suggest ways in which the strategy for Chagas disease control should be tailored for Arequipa and similar periurban areas.

In our data, children living in hillside shantytowns were more than twice as likely to be infected as were children living in low-lying towns. The immediate cause of the difference in infection rates is clear. In MOH data, infestation rates on hillsides were 17%–21% of houses, compared with 3%–9% of houses for low-lying communities (J.G.C.d.C., unpublished data). There are many factors, however, that might contribute to the relative protection of low-lying communities from *T. infestans*. Recent immigrants to Arequipa have constructed houses mainly in hillside communities, whereas low-lying communities are more established. Most houses built by recent immigrants are made of loose *sillar* stone and other materials known to be conducive to infestation by *T. infestans* [14]. In both hillside and low-lying communities, homeowners apply insecticide to their households, but the practice may be more common in the low-lying areas. Ecological factors may also explain the difference in vector infestation rates. Lower household density within low-lying communities and the relative isolation of these communities may slow spread of *T. infestans*. Data on these and other factors affecting vector densities may serve to develop a more efficient strategy to target serologic screening of children living in high-risk communities and even in high-risk foci within these communities [23].

Within our pediatric survey population, seroprevalence increased by 12% per year of age, consistent with reports from other countries in which the disease is endemic [9–11, 24–26]. Nevertheless, the overall age-prevalence curves from Guadalupe, with rates among adults similar to those among teenagers, and the results of our maximum likelihood testing strongly suggest that the onset of Chagas disease transmission was fairly recent in periurban Arequipa. We were not able to assess whether there might be differences in the timing of the onset

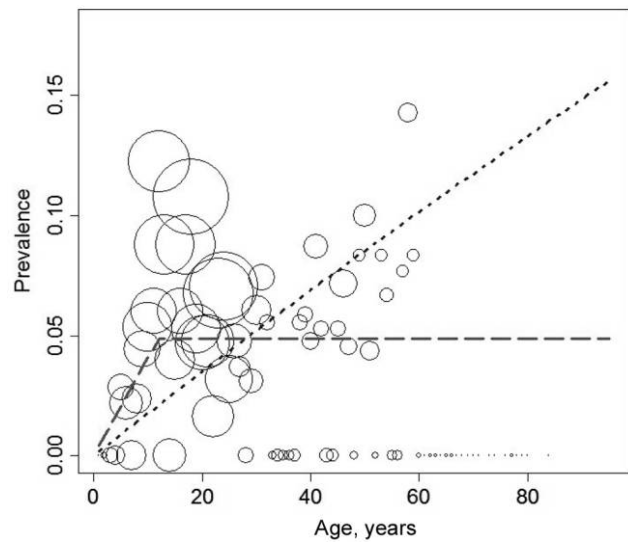


Figure 3. Graph of Chagas disease prevalence by age in the hillside shantytown of Guadalupe. The dashed line represents the best-fit model with the assumption of recent transmission; the dotted line represents the best-fit model with the assumption of constant incidence. The points are scaled to represent the number of individuals at each age (range, 1–90 years).

of transmission in other communities because of the limited age range of the school-based population. In our modeling, we were also unable to control for finer scale heterogeneities in risk within the community, which is an evaluation that may require more-complicated transmission models. Nevertheless, the pattern in Guadalupe clearly contrasts with data from rural sites with long-standing transmission, in which seroprevalence continues to increase with age until fairly late in life [9, 10, 27, 28].

Our analysis thus supports the hypothesis that *T. cruzi* was introduced into periurban Arequipa some time in the past 2 decades. The growth of these hillside shantytowns began in the 1960s and accelerated during the 1970s and 1980s, as thousands of people fled rural areas to escape terrorism and to seek eco-

Table 1. Multivariable logistic regression model of seroprevalence, by age and location.

Variable	No. of children		Percentage seropositive (95% CI)	Adjusted OR (95% CI)
	Tested ^a	Seropositive		
Age	1.12 ^b (1.04–1.21)
Location of residence				
Low-lying town	263	6	2.3 (0.5–4.1)	1 (referent)
Sachaca Hill	319	11	3.4 (1.4–5.5)	1.6 (0.6–4.5)
Guadalupe Hill	509	26	5.1 (3.2–7.0)	2.1 (0.8–5.1)
Tiabaya Hill	423	31	7.3 (4.8–9.9)	3.3 (1.3–8.0)

^a A total of 101 children living outside the districts of Sachaca and Tiabaya (including 1 seropositive child) were excluded from the model.

^b Per 1-year increase in age.

conomic opportunities in cities [13, 29]. Immigrants brought their livestock and animal husbandry practices from the countryside, which created an environment in which sheep, cows, chickens, and guinea pigs live in close proximity to human habitations in densely populated periurban zones. Long-time residents of Guadalupe report that there were few triatomines until the 1980s, coinciding with the increasing density of houses and domestic animals. In addition, many shantytown inhabitants perform seasonal agricultural labor in the rural valleys several hundred kilometers from the cities, which were the historic foci of Chagas disease [30, 31]. These migrant workers may have become infected themselves or may have transported infected animals or triatomines to the city. The combination of a favorable climate, poor housing, proximity to domestic animals, and overcrowding has produced a hospitable periurban environment for triatomines and *T. cruzi* transmission.

Our survey concentrated on an area known to have active transmission and on students at public schools, who are poorer and probably have higher risk of *T. cruzi* infection than do those at private schools. In addition, our study was limited by the relatively low participation rate, especially in secondary schools, which was most likely the result of sending the parental consent form home with the student. Thus, we cannot claim that our results represent the precise risk for the pediatric population of Arequipa as a whole. Nevertheless, there are tens of thousands of children living in shantytowns in southern Peru whose risk is likely to be similar to that of children living on the hillsides of Tiabaya and Sachaca. Increasing rural-to-urban migration in Arequipa and throughout Latin America is undoubtedly bringing many infected persons into urban health care systems that have little previous experience with Chagas disease. In cities with ecological conditions suitable to triatomines, these migrants may inadvertently set up new cycles of vectorial transmission. Our study demonstrates that vectorial transmission of *T. cruzi* occurs in urban as well as in rural areas, placing millions of people at potential risk of infection in rapidly growing Latin American cities.

Acknowledgments

We thank Jenica Pastor of the Arequipa MOH; Paula Maguiña, Phabiola Herrera, and Marjori Meza of Asociación Benéfica Proyectos en Informática, Salud, Medicina y Agricultura; and Cristina Salazar at Johns Hopkins Bloomberg School of Public Health. Additionally, we thank the nurses, sprayers, and biologists who helped with data collection—in particular, Jose Ylla, Victor Quispe, Vander Ticona, Angela Saman, Elizabeth Ramos, Nedy Figueroa, Jessica Calderon, Paola Smith, Carmen Mendoza Gleny, Guiliana Arce, Roberto Meier, Alfonso Parillo, Jaquelin, Marly, Rocsana Villazante, Kati del Carpio, Sofia Quispe, Edgar Manzaneda, Crisithian Velasquez, Juan Mendivil, Emiliano Marco, Alfredo Valdivia, and Guiliana Arroyo. We thank David Smith, for his advice on mathematical modeling of age-prevalence curves; and Jeff Stancil, Lucy Rubio, and Greg Martin (of Naval Medical Research Center Detachment, Lima, Peru) and Gena Lawrence and Bob Wirtz (of the Centers for Disease Control and Prevention, Atlanta, GA), for logistical support. We also appreciate the assistance of the teachers and administrators of Arequipa's public school system. Most

importantly, we thank the participating children and their families and the entire communities of Santa Maria de Guadalupe and Alto Guadalupe, Arequipa.

Financial support. The Small Grants Program of the International Society for Infectious Diseases (to V.K.), the National Institutes of Health International Collaborations in Infectious Disease Opportunity Grant U19-AI-33061 (to R.H.G.), Fogarty-Ellison Fellowship in Global Health and Clinical Research (to N.M.B.), the Centers for Disease Control and Prevention Foundation O. C. Hubert Fellowship (to N.M.B.), the National Institutes of Health Training Grant 5T35-AI-007646-03 (to N.M.B.), and a Howard Hughes predoctoral fellowship (to M.Z.L.).

Potential conflicts of interest. All authors: no conflicts.

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