Estimating the cost of illness and burden of disease associated with the 2014–2015 chikungunya outbreak in the U.S. Virgin Islands

Leora R. Feldstein1,2,*, Esther M. Ellis3, Ali Rowhani-Rahbar1, Morgan J. Hennessey4, J. Erin Staples4, M. Elizabeth Halloran2,5,6, Marcia R. Weaver7

1 Department of Epidemiology, University of Washington School of Public Health, Seattle, Washington, United States of America, 2 Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States of America, 3 U.S. Virgin Islands Department of Health, Saint Croix, United States Virgin Islands, United States of America, 4 Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado, United States of America, 5 Center for Inference and Dynamics of Infectious Diseases, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States of America, 6 Department of Biostatistics, University of Washington School of Public Health, Seattle, Washington, United States of America, 7 Departments of Health Metrics Sciences and Global Health, Institute for Health Metrics and Evaluation, University of Washington, Seattle, Washington, United States of America

* lrfeldst@uw.edu

Abstract

Chikungunya virus (CHIKV), an alphavirus that causes fever and severe polyarthralgia, swept through the Americas in 2014 with almost 2 million suspected or confirmed cases reported by April 2016. In this study, we estimate the direct medical costs, cost of lost wages due to absenteeism, and years lived with disability (YLD) associated with the 2014–2015 CHIKV outbreak in the U.S. Virgin Islands. For this analysis, we used surveillance data from the USVI Department of Health, medical cost data from three public hospitals in USVI, and data from two studies of laboratory-positive cases up to 12 months post illness. On average, employed case-patients missed 9 days of work in the 12 months following their disease onset, which resulted in an estimated cost of $15.5 million. Estimated direct healthcare costs were $2.9 million for the first 2 months and $0.6 million for 3–12 months following the outbreak. The total estimated cost associated with the outbreak ranged from $14.8 to $33.4 million (approximately 1% of gross domestic product), depending on the proportion of the population infected with symptomatic disease, degree of underreporting, and proportion of cases who were employed. The estimated YLDs associated with long-term sequelae from the CHIKV outbreak in the USVI ranged from 599–1,322. These findings highlight the significant economic burden of the recent CHIKV outbreak in the USVI and will aid policymakers in making informed decisions about prevention and control measures for inevitable, future CHIKV outbreaks.
Author summary

Chikungunya, a virus carried and transmitted by mosquitoes, causes fever, headache, and severe joint pain in humans that often resolves within 7–10 days. However, a proportion of cases, up to 79% in some outbreaks, report persistent joint pain and chronic inflammatory rheumatism, resulting in decreased quality of life for months to years following initial infection. In 2014, chikungunya virus swept through the Americas, resulting in almost 2 million suspected or confirmed cases reported by April 2016. Previous studies have noted the large resource burden from chikungunya outbreaks, including high healthcare costs, lost wages due to absenteeism, and decreased quality of life for months following infection. Our work aimed to estimate the direct medical costs, cost of lost productivity due to absenteeism, and years lived with disability associated with the chikungunya outbreak in the U.S. Virgin Islands. This information may aid policy-makers in making informed decisions about prevention and control measures for inevitable, future chikungunya outbreaks.

Introduction

Chikungunya virus (CHIKV), an alphavirus transmitted by Aedes (Stegomyia) species mosquitoes, was introduced into the Americas in December of 2013 [1]. By April 2016, almost 2 million suspected or confirmed cases were reported in 45 countries and territories in the Caribbean, Central, South, and North America [2,3]. Acute symptoms, including high fever, severe polyarthralgia, headache and myalgia, often resolve within 7–10 days [4–6]. However, a proportion of cases, up to 79% in some outbreaks, report persistent arthralgia and chronic inflammatory rheumatism, resulting in decreased quality of life for months to years following initial infection [5–16]. Currently, there is no antiviral treatment or vaccine for the infection, there are no specific therapeutics for chronic symptoms, and public health prevention measures, such as mosquito reduction, have thus far proven to be insufficient [4,17].

CHIKV was first identified to be locally transmitted in the U.S. Virgin Islands (USVI) in June 2014. By February 2015, almost 2,000 suspected cases had been reported in a population of 103,574 people [18,19]. The epidemiology of the CHIKV outbreak in the USVI has been previously described [20]. Previous studies from CHIKV outbreaks in La Réunion, Colombia, and India have noted the large resource burden from these outbreaks including high healthcare costs, lost wages due to absenteeism, and decreased quality of life for months following infection [21–26]. To our knowledge, the economic impact of the recent CHIKV epidemic in the Caribbean and years lived with disability (YLDs) associated with long-term sequelae of CHIKV illness have not been quantified. This information would inform decisions about prevention and control measures for inevitable, future CHIKV outbreaks. Using a societal perspective, we aim to estimate the cost of illness and burden of disease associated with the 2014–2015 CHIKV outbreak in the USVI by estimating direct medical costs, indirect cost of lost productivity due to absenteeism, and YLDs associated with long-term sequelae of the outbreak.

Methods

Ethics statement

Verbal informed consent was obtained from all participants before interviewing them. Parental/guardian consent was acquired on behalf of all child participants and parents/guardians responded for children under the age of 12. Verbal informed consent was documented on the
questionnaire by the interviewer and entered into the database. Oral consent was used because almost half of the interviews took place over the phone. Ethics approval for this study, as well as the use of verbal consent was obtained from the University of the Virgin Islands and the University of Washington.

**Study populations and data inputs**

Estimates of the direct and indirect cost of the outbreak were based on suspected cases reported to USVI Department of Health (DOH). All costs were expressed in 2014 U.S. dollars (USD). A suspected case was defined as a resident of the USVI who visited a hospital or healthcare clinic on St. John, St. Thomas, or St. Croix with acute onset of fever (≥38˚C) and severe arthralgia or arthritis not explained by another medical condition. A laboratory-positive case was defined as a suspected case whose blood sample tested positive for either CHIKV RNA or IgM antibodies. Of all reported suspected CHIKV cases who were tested, 30% tested negative for CHIKV. Therefore, when we used surveillance data to estimate potential costs, we used 0.70 as the proportion of non-tested reported suspected CHIKV cases who would have been positive had they been tested.

Laboratory-positive cases were contacted by telephone and invited to participate in a follow-up investigation at 1–2, 6 and 12 months after the acute phase of illness, as previously defined (S1 Table) [27]. The 1 to 2-month questionnaire asked about hospitalization and healthcare utilization during the first months after initial infection. The 12-month questionnaire asked additional questions about use of prescription medication and healthcare utilization between the first and last interview.

Estimates of YLDs were based on reports of persistent arthralgia. Similar to a previous study [21], we defined persistent arthralgia as joint pain at least once per week that occurred more than 15 days after the acute phase of illness. We used data from two previous studies to determine YLDs. The first study assessed the proportion of persons with laboratory-positive CHIKV infection who reported persistent arthralgia compared to a non-symptomatic control group of individuals who visited an emergency room of a hospital or a health care clinic in the USVI and were interviewed regarding presence of persistent arthralgia [27]. The control group was defined as USVI residents who did not report experiencing sudden onset of fever and joint pain in June 2014-June 2015. The second study was a population-based study of seroprevalence that assessed the frequency of persistent arthralgia approximately 12 months following the introduction of the CHIKV and determined the proportion of persistent arthralgia attributable to CHIKV infection [28].

**Estimating indirect costs**

Productivity lost per CHIKV case was estimated assuming a standard 40-hour work week, and using the average hourly wage for each island [29]. Average hourly wages from the USVI were not available by gender or age. The following formula was used to estimate value of time lost due to CHIKV disease:

\[
\text{Value of time lost} = \frac{\text{Mean # of work days missed at each time point} \times \ 8 \ \text{hours per day} \times \ \text{average hourly wage} \times \ \left( \frac{\text{total # of reported laboratory-positive CHIKV cases}}{\text{total # of reported laboratory-negative CHIKV cases} + 0.70 \times \text{# of non-tested reported suspected CHIKV cases}} \right)}
\]

where mean of work days missed include both market and non-market productivity. To obtain an estimate of the total wages lost for cases who were not reported, we used data from a 2015 seroprevalence study in the USVI that found an infection rate of 31%, (95% CI: 26%–36%), with 72% of those infected reporting symptomatic infection [28]. Based on this information, we estimated the fraction of the population with symptomatic infection to be
22% (0.31 \times 0.72). The estimated number of symptomatic CHIKV infections in the USVI population was multiplied by productivity lost per person to obtain an overall cost estimate of absenteeism due to the outbreak. This estimate assumes that absenteeism from school and other non-market activities has the same monetary value as formal employment. In reviewing both CHIKV and dengue cost-of-illness methodologies, some studies included all individuals with the disease or condition regardless of employment status (to capture overall loss of productivity), while others included only those who were officially employed [22,23,25,30–38]. As a sensitivity analysis, we calculated absenteeism associated with CHIKV illness for only those who were employed (52.2% of the USVI population as of 2010) [39]. Because the 2015 serosurvey estimated that 70% of symptoms (acute fever and joint pain) among CHIKV infected individuals were attributable to their infection, we also conducted a sensitivity analysis to estimate the cost of absenteeism when including only the proportion of individuals with symptoms directly attributable to CHIKV infection (0.31 \times 0.72 \times 0.70 = 0.16) [26].

**Estimating direct medical costs**

The medical costs for two phases of the illness (acute and long-term) were estimated with two different sources of data. For the acute phase of illness, inpatient and outpatient charges of all suspected CHIKV cases from Governor Juan F. Luis Hospital and Medical Center (JFLHMC), the public hospital in St. Croix, were obtained from the finance department of the hospital. Mean costs of inpatient and outpatient visits among reported cases were calculated separately and multiplied by the total number of inpatient and outpatient visits captured by the USVI DOH surveillance system. Calculation assumes standard of care was the same across hospitals. These costs were applied to patients on all three islands, because cost data for suspected CHIKV cases were unavailable from Schneider Regional Medical Center (SRMC) in St. Thomas and Myra Keating Community Health Center (MKCHC) in St. John, the other two public healthcare facilities in the USVI. A sensitivity analysis was conducted for the missing cost data from SRMC and MKCHC based on the mean cost of standard outpatient and inpatient visits from those two healthcare facilities (S2 Table). Data on diagnosis codes and length of inpatient stay were not collected.

For the cost of subsequent outpatient visits up to 12 months after illness onset, the mean cost of standard outpatient visit was obtained from the finance departments of JFLHMC, SRMC and MKCHC. The mean number of additional healthcare visits reported by cases for treatment of CHIKV after acute illness from the interview sample was calculated from the 1–2 and 12-month questionnaires. The mean number of visits was multiplied by the total number of reported laboratory-positive cases and 70% of suspected but not tested cases by island to obtain an overall estimate of additional healthcare costs up to 12 months after acute illness. Note that these calculations are limited to reported cases, assuming that only people who sought healthcare at 1–2 months after the outbreak would seek follow-up care.

Current literature indicates that a recall period of 1–2 months provides reliable estimates for outpatient visits [40–43]; however, previous studies have shown that 5%–47% of visits were not reported when individuals were interviewed about healthcare utilization of physician visits during a 12 month recall period [44,45], while other studies have shown no underreporting [46]. Due to potential underreporting of healthcare utilization 12 months after illness onset, a sensitivity analysis was performed using a range of underreporting from 5–47% (S3 Table).

**Estimating YLDs**

Prior studies estimating YLDs for CHIKV have used disability weights for osteoarthritis and rheumatoid arthritis since a disability weight has not been assigned to CHIKV disease.
However, these weights are from the 1990 Global Burden of Disease [48]. Here, we use the disability weight for post-acute effects from infectious diseases from the 2013 Global Burden of Disease study [49], and use the weights for osteoarthritis and rheumatoid arthritis as a sensitivity analysis to maintain consistency with previous studies.

We calculated YLDs to estimate the amount of time, ability, and activity lost due to persistent arthralgia from CHIKV illness using the following equation [50]:

\[
YLD = (\text{Disability weight} \times \text{Number of symptomatic CHIKV infections in the USVI} \times \text{Prevalence of persistent arthralgia 6 months after acute illness onset} + \frac{182.625}{365.25}) + (\text{Disability weight} \times \text{Number of symptomatic CHIKV infections in the USVI} \times \text{Prevalence of persistent arthralgia 12 months after acute illness onset} + \frac{182.625}{365.25})
\]

The number of symptomatic CHIKV infections in the USVI is based on an estimate from the 2015 serosurvey in the USVI [28]. To ensure that reported persistent arthralgia among cases was due to CHIKV and not from other causes, we used a 32% prevalence estimate of persistent arthralgia among CHIKV cases interviewed at 6 months and a 21% prevalence estimate of persistent arthralgia among CHIKV cases interviewed at 12 months: 44% at 6 months and 33% at 12 months net of the 12% prevalence of persistent arthralgia in the non-symptomatic control group [27]. This latter estimate is consistent with the prevalence of reported arthritis in the USVI population from the Behavioral Risk Factor Surveillance System Report (15%) [39]. We also used a more conservative 12-month estimate of persistent arthralgia attributable to CHIKV from the 2015 serosurvey in the USVI of 12% (95% CI: 7–17%) [28]. The serosurvey did not assess persistent arthralgia at 6 months. Years of life lost were not calculated because cause of death could not be determined for the three deceased suspected CHIKV cases.

Results

Impact of CHIKV outbreak in USVI

One to two months after acute disease onset, 86 laboratory-positive CHIKV cases were interviewed. Of the cases who were employed (33%), 89% reported missing work due to CHIKV illness (Table 1). On average, employed cases reported missing 6 days of work within 1–2 months after onset of CHIKV symptoms. One to two months after their initial healthcare visit, 33% of cases reported seeking additional healthcare at a clinic after initial infection and 9% reported being hospitalized due to CHIKV illness.

Six months after acute disease onset, 165 laboratory-positive CHIKV cases were interviewed. Of the cases who were employed (41%), 88% reported missing work due to CHIKV illness, 4–5 months after their 1–2 month interview (Table 1). On average, employed cases reported missing two additional days of work 4–5 months after the 1–2 month interview.

Twelve months after acute disease onset, 128 of the 165 laboratory-positive CHIKV cases were interviewed. Of the cases who were employed (34%), 9% reported missing work due to CHIKV illness during the six months after their 6-month interview (Table 1). On average, employed cases reported missing one additional day of work during that time period. Of the interviewed cases, 25% reported seeking additional healthcare 10–11 months after the 1–2 month interview and 24% reported taking prescription medication in the last 12 months for CHIKV-related symptoms. Forty percent (n = 12) of those who reported taking prescription medication indicated that they were prescribed prednisone for joint pain and 47% (n = 14) reported taking prescribed opioids for joint pain.
Indirect cost estimate

The average cost of absenteeism related to CHIKV disease 1–2 months after illness onset ranged from $713–$825 per person, depending on island of residence (Table 2). Six months after illness onset, the average cost of absenteeism ranged from $275–$318 per person and 12 months after illness onset, the average cost per person ranged from $148-$172. The total estimated cost of absenteeism associated with acute and long-term CHIKV illness up to 12 months after CHIKV disease onset was $1.76 million for all reported laboratory-positive cases and 70% of all suspected but not tested CHIKV cases. However, when using the estimated proportion of symptomatic CHIKV infection in the USVI (0.22), almost 12 times the number of individuals were infected with CHIKV than were captured by surveillance data. When including these additional cases, the total estimated cost of absenteeism for acute and long-term CHIKV illness up to 12 months after CHIKV disease onset was $29.7 million (Table 2 & Fig 1). The total estimated cost of absenteeism associated with acute and long-term CHIKV illness up to 12 months after CHIKV disease onset for only the USVI population that was employed (52%) was $15.5 million but this figure does not account for absenteeism from school and other non-market activities. Among infected individuals with symptoms attributable to CHIKV (0.16), the estimated cost of absenteeism associated with acute and long-term CHIKV illness up to 12 months after CHIKV disease onset was $21.6 million, and $11.3 million when including only the proportion of the USVI population who was employed (S4 Table).

Direct cost estimate: Acute phase of illness

The average cost of an outpatient visit for a suspected CHIKV case during the acute phase of illness was $1,526 and the average cost of an inpatient visit was $16,982 (Table 3). These costs include laboratory testing and prescription medication. Of the 1,929 reported suspected cases, 1,850 had outpatient visits and 79 suspected cases were hospitalized. Assuming that 70% of these suspected cases were laboratory-positive, the total estimated cost of outpatient and inpatient healthcare visits associated with suspected CHIKV cases during the acute phase of the outbreak was $2.9 million, with the hospitalized cases comprising 48% of the total cost. As shown from the sensitivity analysis in S2 Table, adjusting the direct costs by the relative average outpatient cost reduces the total estimated direct cost by 27%.

*Many of the students interviewed at the 1 to 2-month follow-up were on summer vacation when they became ill with CHIKV and therefore the number of school days missed is lower than what might be expected if the outbreak occurred during the school year.

https://doi.org/10.1371/journal.pntd.0007563.t001

### Table 1. Percentage of laboratory-positive cases 1–2, 6, and 12 months after disease onset who missed work, daily activities/chores, sought additional healthcare, were hospitalized due to chikungunya (CHIKV) illness and prescribed medication for CHIKV, U.S. Virgin Islands.

| Interview date | 1–2 Month (n = 86) | 3–6 Month (n = 165) | 7–12 Month (n = 128) |
|----------------|-------------------|-------------------|-------------------|
| Employment Status | % (n) | Median (range) | Mean | % (n) | Median (range) | Mean | % (n) | Median (range) | Mean |
| Working | 33 (28) | - | - | 41 (67) | - | - | 34 (43) | - | - |
| Child/Student | 24 (21) | - | - | 16 (26) | - | - | 23 (30) | - | - |
| Missed work/school | 89 (25) | 4.5 (0–21) | 5.6 | 88 (58) | 0.5 (0–60) | 2.2 | 9 (4) | 0 (0–40) | 1.2 |
| Working (days) | 1.0 (0–7) | 1.6 | 62 (16) | 2.3 (0–20) | 3.4 | 7 (2) | 0 (0–60) | 2.1 |
| Child/Student (days) | 86 (61) | 5 (0–62) | 11.7 | 86 (135) | 5.0 (0–140) | 13.0 | 15 (19) | 0 (0–168) | 6.4 |
| Missed daily activities/chores (days) | 33 (28) | 0 (0–6) | 0.5 | - | - | - | 25 (34) | 0 (0–17) | 0.6 |
| Additional healthcare (visits) | 9 (8) | 0 (0–14) | 0.4 | - | - | - | - | - |
| Hospitalization | - | - | - | - | - | - | 24.19 (30) | - | - |

*Many of the students interviewed at the 1 to 2-month follow-up were on summer vacation when they became ill with CHIKV and therefore the number of school days missed is lower than what might be expected if the outbreak occurred during the school year.
Direct cost estimate: Up to 12 months after acute phase of illness

The 86 CHIKV cases interviewed 1–2 months after acute illness reported, on average, having 0.5 additional healthcare visits related to CHIKV disease (Table 4). The average cost of a standard outpatient visit varied by healthcare facility and island but ranged from $234-$600. The 128 CHIKV cases interviewed 12 months after acute illness reported having on average 0.62 additional healthcare visits related to CHIKV disease 10–11 months after their 1–2 month interview. Therefore, the total estimated cost of additional outpatient healthcare visits related to CHIKV disease up to one year after illness onset was $620,400 (Table 4 & Fig 1).

The sensitivity analysis for the potential underreporting of healthcare utilization 12 months after illness onset provided the following range of total estimated costs of additional outpatient healthcare visits related to CHIKV disease up to one year after illness onset: $620,400 for zero underreporting to $781,100 for 47% underreporting (S3 Table). As a result, the total estimated direct cost associated with the CHIKV outbreak in the USVI ranges from $3,536,000-$3,696,700.

Total cost estimate of the 2014–2015 CHIKV outbreak

The total direct and indirect estimated cost associated with the 2014–2015 CHIKV outbreak in the USVI ranges from $14,827,500–$33,424,600 depending on the proportion of the
population infected with symptomatic CHIKV, the degree of underreporting of healthcare utilization, and the proportion of cases who were employed at the time of the outbreak.

**Years lived with disability.** In addition to the indirect cost calculation, the estimated number of YLDs associated with long-term sequelae from the 2014–2015 CHIKV outbreak in the USVI was 599–1,322 when using the disability weight for post-acute effects of infectious diseases and ranged from 427–1,407 when using disability weights consistent with prior studies (Table 5).

Table 3. Direct cost estimate (2014 USD) of the chikungunya outbreak in the U.S. Virgin Islands up to 2 months after illness onset, based on cost estimates from St. Croix.

|                      | Outpatient | Inpatient |
|----------------------|------------|-----------|
| Median cost of an outpatient healthcare visit ($) | 1,365      | 14,551    |
| Mean cost of an outpatient healthcare visit ($)   | 1,526      | 16,983    |
| Total number of outpatient reported suspected cases * 70% of suspected not-tested cases | 1,295      | 55        |
| Total cost of outpatient visits related to CHIKV ($) | 1,976,442  | 939,145   |
| Total cost of outpatient and inpatient visits related to CHIKV ($) | 2,915,600  |           |

Note: Total cost estimate was rounded to the nearest hundred.
Discussion

This study estimated the total direct and indirect cost and burden of disease associated with the 2014–2015 CHIKV outbreak in the USVI. The total estimated cost associated with the outbreak ranged from $14.8–$33.4 million, of which 12–24% was direct costs and 76–88% was indirect costs. Up to 1% of gross domestic product (GDP) in the USVI was estimated to be lost due to the CHIKV outbreak (GDP in 2014 = $3.67 billion USD [51]).

Our direct cost estimate of the outbreak in the USVI was comparable to the cost estimate of the 2005–2006 outbreak in La Réunion, ($3.5 million for 22,786 cases in the USVI [$155 per case] compared to $50.4 million for 266,000 cases in La Réunion [$189 per case]) [23,52]. Our indirect cost estimates, were also comparable when including only the proportion of the population who was employed [23]. The seroprevalence estimate of symptomatic CHIKV cases suggests that between 16–22% of the USVI population had symptomatic infection [26]. The surveillance data may not have captured many of these cases because during the height of the outbreak, hospitals and healthcare clinics reached capacity and had to turn residents away who were seeking care. Additionally, due to public health announcements in the media during the outbreak, many residents were aware of symptoms associated with infection and knew

### Table 4. Direct cost estimate (2014 USD) of the chikungunya outbreak in the U.S. Virgin Islands up to 12 months after illness onset.

| Island       | St. Croix | St. Thomas | St. John |
|--------------|-----------|------------|----------|
| Mean cost of a healthcare visit* ($)| 600 | 300 | 234 |
| Number of reported laboratory-positive cases + 70% of suspected not-tested cases | 508 | 804 | 34 |
| Mean number of additional healthcare visits at 1–2 months | 0.5 | 0.5 | 0.5 |
| Total cost of healthcare visits at 1–2 months ($) | 152,400 | 120,600 | 3,978 |
| Mean number of additional healthcare visits at 12 months | 0.62 | 0.62 | 0.62 |
| Total cost of healthcare visits 3–12 months ($) | 188,976 | 149,544 | 4,933 |
| Cost of outpatient visits related to CHIKV up to 12 months ($) | 620,400 |
| **Cost of acute (1–2 months) outpatient and inpatient visits related to CHIKV ($)** | 2,915,600 |
| **Total direct cost estimate of the CHIKV outbreak up to 12 months ($)** | 3,536,000 |

*The mean cost of an outpatient visit associated with a suspected CHIKV cases is higher than the mean cost of a standard outpatient visit due to additional serological testing for both chikungunya and dengue fever virus.

Note: Total cost estimates were rounded to the nearest hundred.

https://doi.org/10.1371/journal.pntd.0007563.t004

### Table 5. Years lived with disability due to persistent arthralgia following the chikungunya outbreak, (total U.S. Virgin Islands population = 103,574).

| Disability weight | Osteo-arthritis | Post-acute effects | Rheumatoid arthritis |
|-------------------|----------------|--------------------|---------------------|
| Proportion of USVI population with symptomatic infection = 0.22 [28] | 0.156 | 0.219 | 0.233 |
| Prevalence of persistent arthralgia attributable to CHIKV 6 months after illness onset* [27] | 0.32 (95% CI: 0.23–0.41) | 22,786 |
| Prevalence of persistent arthralgia attributable to CHIKV 12 months after illness onset* [27] | 0.21 (95% CI: 0.11–0.31) |
| **Years lived with Disability** | 942 | 1,322 | 1,407 |
| Prevalence of persistent arthralgia attributable to CHIKV 12 months after illness onset [28] | 0.12 (95% CI: 0.07–0.17) |
| **Years lived with Disability** | 427 | 599 | 637 |

*Unadjusted for sex, age, history of arthritis.
*Using a persistent arthralgia estimate of 32% at 6 months and 21% at 12 months.
*Using a persistent arthralgia estimate of 12%.

Note: Total YLDs were rounded to the nearest whole number.

https://doi.org/10.1371/journal.pntd.0007563.t005
treatment for CHIKV did not exist, so they may have opted to stay home instead of seeking healthcare.

We estimated that the number of years lived with disability associated with chronic symptoms of CHIKV ranges from 427–1,407. Our YLD estimates are more conservative than the disability-adjusted life year estimates from Latin America, due to the fact that we provided a lower estimate of persistent arthralgia attributable to CHIKV illness at 12 months (21% and 12% compared to ~50% in Latin America) [24,53]. This difference is present because both studies in the USVI [27,28] subtracted the prevalence of persistent arthralgia among non-diseased individuals from the prevalence of persistent arthralgia among CHIKV cases 12 months after acute illness, whereas the study in Latin America did not [53]. The Second United States Panel on Cost-Effectiveness in Health and Medicine recommends counting both productivity costs and YLDs for an analysis from the societal perspective, based on evidence that disability weights reflect health rather than productivity [[54]]. Although their recommendation does not necessarily apply to cost-of-illness studies, two of five published CHIKV cost-of-illness studies presented both indirect costs and YLDs, while the other three studies only presented YLDs [22–24,26,47].

Certain limitations should be considered when interpreting the results of this study. The total direct and indirect estimated costs of the 2014–2015 CHIKV outbreak in the USVI may lack precision. Ambulatory service charges, absenteeism of caretakers for those who were ill due to CHIKV and additional hospitalization costs after the acute phase of illness could not be measured and were therefore not included in analysis. The analysis also does not account for the cost of individuals with symptomatic CHIKV who did not seek acute care but did seek follow-up care. The mean cost of outpatient and inpatient visits was based solely on data from JFLHMC, and does not account for varying costs from SMRC, MKCHC and private healthcare clinics. We addressed this issue by conducting a sensitivity analysis of direct costs based on the standard cost of healthcare visits at SMRC and MKCHC. Although another sensitivity analysis was conducted to account for underreporting of healthcare utilization, the true magnitude of underreporting up to 12 months after illness onset remains unknown. Additionally, there are three potential sources of bias in the estimates of disability: 1) if cases with persistent arthralgia were more likely to participate in the follow-up study, disability would be over-estimated, 2) if the cause of death among the three cases who died was primarily CHIKV, disability would be underestimated by excluding their years of life lost, and 3) there are other documented long-term sequelae associated with CHIKV disease that we did not account for, such as mental health diagnoses, that would result in an underestimation of disability [55,56]. As a result, our YLD estimates are either consistent or more conservative than previous CHIKV studies [24,26,48,56]. Lastly, although using means, instead of medians to estimate costs is standard practice in economic analysis, the estimates presented might be elevated by certain individuals who incurred higher costs than others.

Despite these limitations, this is one of the initial cost-of-illness studies that quantifies the number of years lived with disability due to long-term sequelae of CHIKV illness in the Caribbean. The results from this study highlight the substantial economic and long-term health burden of a CHIKV outbreak and provide evidence to inform policy decisions about prevention and control measures for inevitable future CHIKV outbreaks.

Supporting information

S1 Table. Eligibility and enrollment numbers of laboratory-positive cases at 1–2, 6 and 12 months after illness onset.

(DOCX)
S2 Table. Sensitivity analysis of direct cost estimate (2014 USD) of the acute phase of the CHIKV outbreak in the USVI where acute phase costs on St. Croix are adjusted by the relative costs of an average outpatient visits on St. Thomas and St. John. (DOCX)

S3 Table. Sensitivity analysis of reporting of healthcare utilization 12 months after acute onset of CHIKV illness and associated cost estimates (2014 USD). (DOCX)

S4 Table. Sensitivity analysis of indirect cost estimates (2014 USD) due to absenteeism from the chikungunya outbreak in the U.S. Virgin Islands up to 12 months after disease onset. (DOCX)

S1 Surveillance questionnaire data. USVI chikungunya surveillance data from Governor Juan F. Luis Hospital and Medical Center, including cost per suspected, probable, and confirmed chikungunya case by date of symptom onset, and 1 to 2-month, 6-month, and 12 month questionnaire data. (XLSX)

S1 STROBE Checklist. (DOC)

Acknowledgments
Diagnostic expertise and assistance was generously provided by the Centers for Disease Control and Prevention.

Author Contributions
Conceptualization: Leora R. Feldstein, Esther M. Ellis, M. Elizabeth Halloran, Marcia R. Weaver.
Data curation: Leora R. Feldstein, Morgan J. Hennessey.
Formal analysis: Leora R. Feldstein, J. Erin Staples, Marcia R. Weaver.
Funding acquisition: Esther M. Ellis, M. Elizabeth Halloran.
Investigation: Leora R. Feldstein, Morgan J. Hennessey.
Methodology: Leora R. Feldstein, Ali Rowhani-Rahbar, J. Erin Staples, Marcia R. Weaver.
Resources: Esther M. Ellis, M. Elizabeth Halloran.
Supervision: Ali Rowhani-Rahbar, J. Erin Staples, M. Elizabeth Halloran, Marcia R. Weaver.
Validation: Marcia R. Weaver.
Visualization: Leora R. Feldstein.
Writing – original draft: Leora R. Feldstein.
Writing – review & editing: Leora R. Feldstein, Esther M. Ellis, Ali Rowhani-Rahbar, J. Erin Staples, M. Elizabeth Halloran, Marcia R. Weaver.

References
1. Pan American Health Organization. Number of Reported Cases of Chikungunya Fever in the Americas, by Country or Territory. 2014.
2. Pan American Health Organization. Number of Reported Cases of Chikungunya Fever in the Americas, by Country or Territory 2013–2015. 2015.

3. Pan American Health Organization. Number of Reported Cases of Chikungunya Fever in the Americas, by Country or Territory: April, 2016. 2016.

4. Brighton SW, Prozesky OW, de la Harpe AL. Chikungunya virus infection. A retrospective study of 107 cases. S Afr Med J. 1983; 63: 313–5. PMID: 6298956

5. Calabrese LH. Emerging viral infections and arthritis: the role of the rheumatologist. Nat Clin Pract Rheumatol. 2008; 4: 2–3. https://doi.org/10.1038/nrclinrheum0679 PMID: 18403599

6. Schilte C, Staikovsky F, Couderc T, Madec Y, Carpentier F, Kassab S, et al. Chikungunya Virus-associated Long-term Arthralgia: A 36-month Prospective Longitudinal Study, Singh SK, editor. PLoS Negl Trop Dis. 2013; 7: e2137. https://doi.org/10.1371/journal.pntd.0002137 PMID: 23556021

7. Mohd Zim MA, Sam I-C, Omar SFS, Chan YF, AbuBakar S, Kamarulzaman A. Chikungunya infection in Malaysia: comparison with dengue infection in adults and predictors of persistent arthralgia. J Clin Virol. 2013; 56: 141–5. https://doi.org/10.1016/j.jcv.2012.10.019 PMID: 23201456

8. Economopoulou A, Dominguez M, Helynck B, Sissoko D, Wichmann O, Quenet P, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005–2006 outbreak on Réunion. Epidemiol Infect. 2009; 137: 534–41. https://doi.org/10.1017/S0950268808001167 PMID: 18694529

9. Dupuis-Maguiraga L, Noret M, Brun S, Le Grand R, Gras G, Roques P, Chikungunya disease: infection-associated markers from the acute to the chronic phase of arbovirus-induced arthralgia. PLoS Negl Trop Dis. 2012; 6: e1446. https://doi.org/10.1371/journal.pntd.0001446 PMID: 22479654

10. Gérardin P, Fianu A, Malvy D, Mussard C, Boussaïd K, Rollot O, et al. Perceived morbidity and community burden after a Chikungunya outbreak: the TELECHIK survey, a population-based cohort study. BMC Med. 2011; 9: 5. https://doi.org/10.1186/1741-7015-9-5 PMID: 21235760

11. Hoarau J-J, Jaffar Bandjee M-C, Krejbich Trotot P, Das T, Li-Pat-Yuen G, Dassa B, et al. Persistent chronic inflammation and infection by Chikungunya arthritogenic alphavirus in spite of a robust host immune response. J Immunol. American Association of Immunologists; 2010; 184: 5914–27. https://doi.org/10.4049/jimmunol.0900255 PMID: 20404278

12. Weaver SC, Osorio JE, Livengood JA, Chen R, Stinchcomb DT. Chikungunya fever in Singapore: acute clinical and laboratory features, and factors associated with persistent arthralgia. J Clin Virol. 2010; 49: 111–4. https://doi.org/10.1016/j.jcv.2010.07.004 PMID: 20674479

13. Queyriaux B, Simon F, Grandadam M, Michel R, Tolou H, Boutin J-P. Clinical burden of chikungunya virus infection. Lancet Infect Dis. 2008; 8: 2–3. https://doi.org/10.1016/S1473-3099(07)70294-3 PMID: 18156079

14. Weaver SC, Osorio JE, Livengood JA, Chen R, Stinchcomb DT. Chikungunya virus and prospects for a vaccine. Expert Rev Vaccines. 2012; 11: 1087–101. https://doi.org/10.1586/erv.12.84 PMID: 23151166

15. The CIA World Factbook: U.S. Virgin Islands [Internet]. 2014.

16. Ellis E. Chikungunya Surveillance Weekly Report: US Virgin Islands Department of Health. 2015.

17. The CIA World Factbook: U.S. Virgin Islands [Internet]. 2014.

18. Ellis E. Chikungunya Surveillance Weekly Report: US Virgin Islands Department of Health. 2015.

19. Feldstein LR, Ellis EM, Rowhani-Rahbar A, Halloran ME, Ellis BR. The First Reported Outbreak of Chikungunya in the U.S. Virgin Islands, 2014–2015. Am J Trop Med Hyg. The American Society of Tropical Medicine and Hygiene; 2016; 95: 885–889. https://doi.org/10.4269/ajtmh.16-0288 PMID: 27402523

20. Morrison TE. Reemergence of chikungunya virus. J Virol. 2014; 88: 11644–7. https://doi.org/10.1128/JVI.01432-14 PMID: 25078691

21. Seyer T, Hutin Y, Ramanchandran V, Ramakrishnan R, Manickam P, Murhekar M. Estimating the burden of disease and the economic cost attributable to chikungunya, Andhra Pradesh, India, 2005–2006. Trans R Soc Trop Med Hyg. 2010; 104: 133–8. https://doi.org/10.1016/j.trstmh.2009.07.014 PMID: 19709705
23. Soumahoro M-K, Boelle P-YY, Gaüzere B-AA, Atsou K, Pelat C, Lambert B, et al. The Chikungunya epidemic on La Réunion Island in 2005–2006: a cost-of-illness study. PLoS Negl Trop Dis. 2011; 5: e1197. https://doi.org/10.1371/journal.pntd.0001197 PMID: 21695162

24. Cardona-Ospina JA, Diaz-Quijano FA, Rodríguez-Morales AJ. Burden of chikungunya in Latin American countries: estimates of disability-adjusted life-years (DALY) lost in the 2014 epidemic. Int J Infect Dis. 2015; 38: 60–61. https://doi.org/10.1016/j.ijid.2015.07.015 PMID: 26216764

25. Cardona-Ospina JA, Villamil-Gómez WE, Jimenez-Canizales CE, Cañastafeda-Hernández DM, Rodríguez-Morales AJ. Estimating the burden of disease and the economic cost attributable to chikungunya, Colombia, 2014. Trans R Soc Trop Med Hyg. Oxford University Press; 2015; 109: 793–802. https://doi.org/10.1093/trstmh/trv094 PMID: 26626342

26. Krishnamoorthy K, Harichandrakumar KT, Krishna Kumari A, Das LK. Burden of chikungunya in India: estimates of disability adjusted life years (DALY) lost in 2006 epidemic. J Vector Borne Dis. 2009; 46: 26–35. PMID: 19326705

27. Feldstein LR, Rowhani-Rahbar A, Staples JE, Weaver MR, Halloran ME, Ellis EM. Persistent Arthralgia Associated with Chikungunya Virus Outbreak, US Virgin Islands, December 2014–February 2016. Emerg Infect Dis. 2017; 23: 673–676. https://doi.org/10.3201/eid2304.161562 PMID: 28322703

28. Hennessy M, Ellis EM, Delorey M, Panella A, Kosoy O, Kirking H, et al. Seroprevalence and Symptomatic Attack Rate of Chikungunya Virus infection, United States Virgin Islands, 2014–2015. Am J Trop Med Hyg. 2017; 99(5):1321–6. https://doi.org/10.4269/ajtmh.18-0437

29. Annual Average Gross Pay & Employment by County / Industry 2013–2014 Virgin Islands, Quarterly Census of Employment & Wages Program. 2014.

30. Gopalan SS, Das A. Household economic impact of an emerging disease in terms of catastrophic out-of-pocket health care expenditure and loss of productivity: investigation of an outbreak of chikungunya in Orissa, India. J Vector Borne Dis. 2009; 46: 57–64. PMID: 19326709

31. Suaya JA, Shepard DS, Siqueira JB, Martelli CT, Lum LCS, Tan LH, et al. Cost of Dengue Cases in Eight Countries in the Americas and Asia: A Prospective Study. Am J Trop Med Hyg. 2009; 80: 846–855. PMID: 19407136

32. Carrasso LR, Lee LK, Lee VJ, Ooi EE, Shepard DS, Thein TL, et al. Economic impact of dengue illness and the cost-effectiveness of future vaccination programs in Singapore. PLoS Negl Trop Dis. Public Library of Science; 2011; 5: e1426. https://doi.org/10.1371/journal.pntd.0001426 PMID: 22206028

33. Rafique I, Nadeem Saqib MA, Munir MA, Qureshi H, Siddiqui S, Habibullah S, et al. Economic burden of dengue in four major cities of Pakistan during 2011. J Pak Med Assoc. 2015; 65: 256–9. PMID: 25933566

34. Salomon-Mulanovitch G, Blazes DL, Lescano AG, Bausch DG, Montgomery JM, Pan WK. Economic Burden of Dengue Virus Infection at the Household Level Among Residents of Puerto Maldonado, Peru. Am J Trop Med Hyg. 2015; 93: 684–90. https://doi.org/10.4269/ajtmh.14-0755 PMID: 26217040

35. Halasa YA, Shepard DS, Zeng W. Economic cost of dengue in Puerto Rico. Am J Trop Med Hyg. 2012; 86: 745–52. https://doi.org/10.4269/ajtmh.2012.11-0784 PMID: 22556069

36. Wettstein MS, Fleming M, Chang AY, Copenhagen DJ, Wateska AR, Bartsch SM, et al. Total economic cost and burden of dengue in Nicaragua: 1996–2010. Am J Trop Med Hyg. The American Society of Tropical Medicine and Hygiene; 2012; 87: 616–22. https://doi.org/10.4269/ajtmh.2012.12-0146

37. Shepard DS, Halasa YA, Tyagi BK, Adhish SV, Nandan D, Karthiga KS, et al. Economic and disease burden of dengue illness in India. Am J Trop Med Hyg. The American Society of Tropical Medicine and Hygiene; 2014; 91: 1235–42. https://doi.org/10.4269/ajtmh.14-0002 PMID: 25294616

38. Shepard DS, Undurraga EA, Halasa YA, Stanaway JD. The global economic burden of dengue: a systematic analysis. Lancet Infect Dis. Elsevier; 2016; https://doi.org/10.1016/S1473-3099(16)00146-8

39. Centers for Disease and Prevention. Behavioral Risk Factor Surveillance System 2011 Summary Data Quality Report. 2011.

40. Lavado RF, Brooks BPC, Hanlon M. Estimating health expenditure shares from household surveys. Bull World Health Organ. 2013; 91: 519–24C. https://doi.org/10.2471/BLT.11.115535 PMID: 23825879

41. Lu C, Chinn B, Li G, Murray CJL. Limitations of methods for measuring out-of-pocket and catastrophic private health expenditures. Bull World Health Organ. 2009; 87: 238–244. https://doi.org/10.2471/BLT.08.054379 PMID: 19377721

42. Machlin SR. A methodological comparison of ambulatory health care data collected in two national surveys. Agency for Healthcare Research and Quality.; 2007.

43. White E, Armstrong BK, Saracci R. Principles of Exposure Measurement in Epidemiology. Oxford University Press. 2008. https://doi.org/10.1033/a4e/kwq035

44. Yaffe R, Shapiro S, Fuchsberg RR, Rohde CA, Corperio HC. Medical Economics Survey- Methods Study: Cost-Effectiveness of Alternative Survey Strategies on JSTOR. Med Care. 1978; 16: 641–659. PMID: 97474
45. Cleary PD, Jette AM. The Validity of Self-Reported Physician Utilization Measures. Med Care. 1984; 22: 796–803. PMID: 6492908

46. Marquis KH, Marquis SM, Newhouse JP. The Measurement of Expenditures for Outpatient Physician and Dental Services: Methodological Findings from the Health Insurance Study. Med Care. 1976; 14: 913–931. PMID: 824510

47. Labeaud AD, Bashir F, King CH. Measuring the burden of arboviral diseases: the spectrum of morbidity and mortality from four prevalent infections. Popul Health Metr. 2011; 9: 1. https://doi.org/10.1186/1478-7954-9-1 PMID: 21219615

48. Murray C, Lopez A. The Global Burden of Disease. Boston, MA: Harvard University Press 1996.

49. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Heal. Elsevier; 2015; 3: e712–23. https://doi.org/10.1016/S2214-109X(15)00069-8

50. Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bull World Health Organ. 1994; 72: 429–45. PMID: 8062401

51. Hamano A, Joshua TH. The Bureau of Economic Analysis Releases 2014 Estimates of Gross Domestic Product for the U.S. Virgin Islands. 2015.

52. UNdata | Country Profile | Réunion. In: United Nations Statistics Division. 2016.

53. Rodriguez-Morales AJ, Cardona-Ospina JA, Villamil-Gómez W, Paniz-Mondolfi AE. How many patients with post-chikungunya chronic inflammatory rheumatism can we expect in the new endemic areas of Latin America? Rheumatol Int. 2015; 35: 2091–4. https://doi.org/10.1007/s00296-015-3302-5 PMID: 26045218

54. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-effectiveness in Health and MedicineRecommendations From the Second Panel on Cost-effectiveness in Health and MedicineRecommendations. JAMA. 2016; 316: 1093–1103. https://doi.org/10.1001/jama.2016.12195 PMID: 27623463

55. Soumahoro M-K, Gérardin P, Boëlle P-Y, Perrau J, Fianu A, Pouchot J, et al. Impact of Chikungunya virus infection on health status and quality of life: a retrospective cohort study. PLoS One. 2009; 4: e7800. https://doi.org/10.1371/journal.pone.0007800 PMID: 19911058

56. Bhatia MS, Gautam P, Jhanjee A. Psychiatric Morbidity in Patients with Chikungunya Fever: First Report from India. J Clin Diagn Res. 2015/10/01. JCDR Research and Publications (P) Limited; 2015; 9: VC01–VC03. https://doi.org/10.7860/JCDR/2015/14569.6586 PMID: 26557595