Estimating the burden of arboviral diseases in Colombia between 2013 and 2016

Andrés Felipe Mora-Galán,*1,2,3, A. Alexandra Parra-García,4,5,6,7,8, Fernando Ruiz De La Hoz Restrepo,9,10

Keywords
- Chikungunya fever
- Colombia
- Dengue
- Disability-adjusted life years
- Zika virus

Introduction

Arboviruses are the leading group of vector-borne diseases in Latin America. Dengue, the main arbovirus in the continent, has caused severe epidemics in recent years, and at the same time, Zika virus, Chikungunya, and other arboviruses, have been associated with several chronic complications. Dengue has been associated with a wide variety of chronic symptoms and syndromes, among others, which have been grouped and named—without reaching any consensus—such as: post-infectious fatigue syndrome in Dengue, post-Dengue chronic fatigue, persistent or chronic arthralgias, among others. As a consequence, more than 11 million people in Colombia were affected by these viruses. According to the number of cases reported in the 2013–2016 period, Colombia was the third most affected country by these arboviruses, just behind Brazil and Mexico. Public health efforts must be made to mitigate new epidemics.

Methods

An exploratory ecological study was carried out using the disability-adjusted life years (DALY) as a unit of measure. The mortality databases of the National Administrative Department of Statistics (DANE) and the morbidity databases of the National Public Health Surveillance System (SEVIGELA) were used. Deaths and cases for each arbovirus were grouped and then adjusted to control biases. Subsequently, we performed a sensitivity analysis.

Results

In the 2013–2016 period, 491,629.2 DALYs were lost due to arboviruses in Colombia. By disease, 26.6% of the total DALYs were caused by Dengue, 71.3% by Chikungunya, and the remaining 2.2% by Zika. The majority of DALYs (68.2%) were caused by chronic complications. Five out of 32 departments (Valle del Cauca, Tolima, Norte de Santander, Huila, and Bolivar) contributed 56.3% of total DALYs.

Conclusion

The burden of disease by arboviruses in the 2013–2016 period exceeded the burden of other infectious diseases such as HIV/AIDS and tuberculosis in Colombia. Public health efforts must be made to mitigate new epidemics of these arboviruses.

Abstract

Objective

During the 2013–2016 period, Dengue, Chikungunya, and Zika affected more than 1 million people in Colombia. These arboviruses and their chronic manifestations pose a public health challenge. Therefore, we estimated the burden of disease by Dengue, Chikungunya, and Zika in Colombia between 2013 and 2016.

Methods

An exploratory ecological study was carried out using the disability-adjusted life years (DALYs) as a unit of measure. The mortality databases of the National Administrative Department of Statistics (DANE) and the morbidity databases of the National Public Health Surveillance System (SEVIGELA) were used. Deaths and cases for each arbovirus were grouped and then adjusted to control biases. Subsequently, we performed a sensitivity analysis.

Results

In the 2013–2016 period, 491,629.2 DALYs were lost due to arboviruses in Colombia. By disease, 26.6% of the total DALYs were caused by Dengue, 71.3% by Chikungunya, and the remaining 2.2% by Zika. The majority of DALYs (68.2%) were caused by chronic complications. Five out of 32 departments (Valle del Cauca, Tolima, Norte de Santander, Huila, and Bolivar) contributed 56.3% of total DALYs.

Conclusion

The burden of disease by arboviruses in the 2013–2016 period exceeded the burden of other infectious diseases such as HIV/AIDS and tuberculosis in Colombia. Public health efforts must be made to mitigate new epidemics of these arboviruses.
main objective: to reduce Dengue mortality by at least 50%, to reduce morbidity by at least 25% and to estimate the true burden of the disease (World Health Organization (WHO), 2012).

Although there have been multiple studies of Dengue burden of disease, the methodologies and parameters used have changed, as knowledge about this disease has increased (Bratty et al., 2011). On the other hand, the literature on the Chikungunya and Zika burden of disease is limited. For these reasons, the objective of this study was to estimate the burden of disease by Dengue, Chikungunya, and Zika in Colombia and its administrative subdivisions between 2013 and 2016.

Methodology

Type of study
Ecological exploratory study aimed at estimating the burden of disease by Dengue, Chikungunya, and Zika in Colombia during the 2013–2016 period.

Sources of information
Dengue, Chikungunya, and Zika mortality information was obtained from the National Administrative Department of Statistics (DANE) (Departamento Administrativo Nacional de Estadística (DANE)), and information from each acute arbovirus case was obtained from the National Public Health Surveillance System (SIVIGILA). Both databases recorded the information of each event (death or case) by sex, age, and department. Additionally, SIVIGILA reports whether the cases required hospitalization or outpatient management.

Dengue, Chikungunya, and Zika case definitions used by SIVIGILA were taken from public health protocols published by the Colombian National Institute of Health (Instituto Nacional de Salud (INS), 2016, 2017a, Instituto Nacional de Salud (INS), 2017b). Dengue case definitions are as follows: probable case, case confirmed by laboratory, and case confirmed by epidemiological contact (Instituto Nacional de Salud (INS), 2017b). In the 2013–2016 period, 55% (222,915 cases) of Dengue cases (with or without warning signs) were compatible with the probable case definition and 47% (201,022 cases) were confirmed cases (either by laboratory or epidemiological contact). Concerning severe cases, 25% (201,022 cases) were probable cases, and the remaining 75% (601,011 cases) were confirmed cases (either by laboratory or epidemiological contact) (Mercado Reyes and Instituto Nacional de Salud (INS), 2014, Mercado Reyes and Instituto Nacional de Salud (INS), 2013, Gómez and Instituto Nacional de Salud (INS), 2015, Gómez and Instituto Nacional de Salud (INS), 2016).

For Chikungunya, the definitions are as follows: suspected case, case confirmed by clinical diagnosis, and case confirmed by laboratory (Instituto Nacional de Salud (INS), 2017b). In the 2014–2016 period, 98.6% (481,534 cases) of Chikungunya cases were confirmed by clinical diagnosis, 1% (4804 cases) were confirmed by laboratory, and the remaining 0.4% (1694 cases) were suspected cases (Salas Botero and Instituto Nacional de Salud (INS), 2014, Salas Botero and Instituto Nacional de Salud (INS), 2015, Puillua Farias and Instituto Nacional de Salud (INS), 2016). For Zika, all cases included in this study were confirmed either by clinical diagnosis or by laboratory.

Population at risk
People living in risk areas for Dengue transmission in Colombia (people living in the urban, peri-urban and rural areas of municipalities with an altitude below 2000 m above sea level with entomological evidence or case reports) were defined as the population at risk for arboviral infection (Instituto Nacional de Salud (INS), 2017). We assumed that the population at risk for Dengue is the same for Chikungunya and Zika since they are transmitted by the same vectors.

Statistic analysis
Mortality
Given that mortality surveillance systems are imperfect because they cannot capture all deaths attributable to a disease, it was necessary to correct the number of deaths for each arbovirus to control biases. The most important bias in burden of disease studies is underreporting. Other biases described are miscoding and “garbage” codes (Murray et al., 1996). These biases were controlled by strategies such as correction for the proportion of deaths with death certificates (Acosta Ramirez et al., 2008, Peñaloza et al., 2014), the Bennet–Horiuchi method (Bennet and Hotzui, 1983) and expansion factors (Shepard et al., 2013).

Once the number of deaths for each arbovirus was corrected, mortality rates were estimated per 1000 and per 100,000 inhabitants per year, by sex, age groups, and by sex and age groups at the national and departmental levels.

Morbidity
The different presentations of Dengue (Dengue without warning signs, Dengue with warning signs, Severe Dengue, and chronic post-Dengue fatigue), Chikungunya (acute phase and post-Chikungunya chronic arthritis) and Zika (acute phase, microcephaly, and GBS) were considered for the morbidity analysis.

Following the recommendations made by Bratty et al. (2011) concerning case counting, Dengue cases were discriminated in 3 groups: Outpatient Dengue, Hospitalized Dengue, and Severe Dengue. In accordance with this approach, we divided the number of acute cases of Chikungunya and Zika into two groups: outpatient and hospitalized.

Morbidity databases, as well as mortality databases, show underreporting. In order to correct underreporting, expansion factors (EF) were used. In the present study, we used the same EFs as Shepard et al. (2011), where they estimated the Dengue burden of disease in the Americas using two EFs. The first EF was used to correct the underreporting of hospitalized cases and the second EF to correct the number of outpatient cases (Table 1). These EFs were multiplied by the number of cases reported to the SIVIGILLA system per year. The two EFs were used to correct the underreporting of cases for the three arboviruses under study.

The resulting Dengue and Chikungunya corrected cases were multiplied by the incidences of post-Dengue chronic fatigue and post-Chikungunya chronic arthritis described in previous studies (Rodriguez-Moreiras et al., 2016, Zeng et al., 2018) to approximate to the number of cases of these disorders in Colombia. We followed this procedure since there is no national database of these disorders.

With the corrected number of cases and the population at risk, incidences were estimated per 1000 and per 100,000 inhabitants by sex and age groups for every year under study, both at the national and departmental levels.

The burden of disease
The burden of disease was expressed in terms of disability-adjusted life years (DALYs). The methodology described by Murray et al. (1996) was used to calculate the DALYs. The DALYs are the result of the sum of the years of life lost (YLL), and the years lived with disability (YLD).

YLLs were calculated from the mortality rates for each arbovirus by year, sex, age group, and department. Among the existing four methods to calculate the YLL, as well as Murray (1994), we chose the standard expected years of life lost method, where the expectation of life at each age is based on an ideal standard. The expectations used by the 2005 and 2010 Colombian burden of disease studies are based on model life-table West Level 26 (Acosta Ramirez et al., 2008, Peñaloza et al., 2014).

In order to achieve comparability of results between studies, we used the same model. This model conforms to the disparity in life expectancy between males and females in Colombia (Departamento Administrativo Nacional de Estadística (DANE), 2007a, 2007b). Other parameter values necessary for
The parameters for the calculation of DALYs correspond to values defined in previous studies (Table 1) [Alflax-Murillo et al., 2016; van den Berg et al., 2013; Chang et al., 2018; Cross et al., 2014; Honeycutt et al., 2003; McInerney et al., 1998; Nembhard et al., 2001; Rodríguez-Morales et al., 2016; Rodriguez-Morales et al., 2015; Salomon et al., 2015; Sharp et al., 2016; Sheperd et al., 2011; Zeng et al., 2018; World Health Organization (WHO), 2018b].

Table 1. Parameters for the estimation of disability-adjusted life years (DALYs) according to each scenario.

<table>
<thead>
<tr>
<th>Arboviruses</th>
<th>Parameter</th>
<th>Conservative value</th>
<th>Median value</th>
<th>Extreme value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Expansion Factor 1</td>
<td>1.4</td>
<td>2.3</td>
<td>3.3</td>
<td>Shepard et al. (2011)</td>
</tr>
<tr>
<td></td>
<td>Central value – Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Expansion Factor 2</td>
<td>4.5</td>
<td>9.0</td>
<td>18.0</td>
<td>Shepard et al. (2011)</td>
</tr>
<tr>
<td></td>
<td>Central value – Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Outpatient Dengue (days)</td>
<td>9.6</td>
<td>13.3</td>
<td>20.0</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Mean-Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Hospitalized Dengue (days)</td>
<td>9.0</td>
<td>12.3</td>
<td>14.3</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Mean-Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Severe Dengue (days)</td>
<td>10.0</td>
<td>14.0</td>
<td>18.0</td>
<td>Sheperd et al. (2011)</td>
</tr>
<tr>
<td></td>
<td>Mean-Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Post-Dengue chronic fatigue (days)</td>
<td>15.0</td>
<td>31.0</td>
<td>63.0</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Median CI 95%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dengue</td>
<td>Disability weight – Outpatient Dengue Mean-Rank</td>
<td>0.26</td>
<td>0.62</td>
<td>0.85</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Disability weight – Hospitalized Dengue Mean-Rank</td>
<td>0.49</td>
<td>0.71</td>
<td>0.90</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Disability weight – Severe Dengue Mean-Rank</td>
<td>0.60</td>
<td>0.81</td>
<td>0.95</td>
<td>McInerney et al. (1998)</td>
</tr>
<tr>
<td></td>
<td>Disability weight – Post-Dengue chronic fatigue Mean-Rank</td>
<td>0.048</td>
<td>0.29</td>
<td>0.39</td>
<td>Salomon et al. (2015); Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Estimate UI 95%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incidence – Post-Dengue chronic fatigue (%) Median CI 95%</td>
<td>37.0</td>
<td>34.0</td>
<td>38.0</td>
<td>Zeng et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Duration – Outpatient Chikungunya (days)</td>
<td>2.0</td>
<td>13.0</td>
<td>21.0</td>
<td>Sharp et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Median-Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Hospitalized Chikungunya (days)</td>
<td>3.0</td>
<td>7.0</td>
<td>15.0</td>
<td>Sharp et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Median-Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Post-Chikungunya chronic arthritis in women (months) Median-Rank</td>
<td>26.12</td>
<td>72.0</td>
<td>72.0</td>
<td>Rodríguez-Morales et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Disability weight – Outpatient Chikungunya</td>
<td>0.49</td>
<td>0.71</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disability weight – Hospitalized Chikungunya</td>
<td>0.64</td>
<td>0.81</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disability weight – Post-Chikungunya chronic arthritis in women</td>
<td>0.299</td>
<td>0.275</td>
<td>0.364</td>
<td>Cross et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Median CI 95%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disability weight – Post-Chikungunya chronic arthritis in men</td>
<td>0.049</td>
<td>0.233</td>
<td>0.266</td>
<td>Cross et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Median CI 95%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incidence – Post-Chikungunya chronic arthritis in men (%) Median CI 95%</td>
<td>9.30</td>
<td>13.66</td>
<td>18.0</td>
<td>Rodríguez-Morales et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Duration – Outpatient Zika (days)</td>
<td>2.0</td>
<td>5.0</td>
<td>7.0</td>
<td>World Health Organization (WHO), 2018b</td>
</tr>
<tr>
<td></td>
<td>Median-Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration – Hospitalized Zika (days)</td>
<td>9.0</td>
<td>12.3</td>
<td>14.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median-Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disability weight – Outpatient Zika</td>
<td>0.26</td>
<td>0.62</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disability weight – Hospitalized Zika</td>
<td>0.49</td>
<td>0.71</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The first-year survival rate (%)</td>
<td>0.790</td>
<td>0.790</td>
<td>0.790</td>
<td>Nembhard et al. (2001)</td>
</tr>
<tr>
<td></td>
<td>Mortality rate after the first year (%)</td>
<td>0.149</td>
<td>0.24</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microcephaly</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration of the disease (years)</td>
<td>3.5</td>
<td>4.5</td>
<td>5.5</td>
<td>Honeycutt et al. (2003)</td>
</tr>
<tr>
<td></td>
<td>Disability weight</td>
<td>0.26</td>
<td>0.36</td>
<td>0.46</td>
<td>Salomon et al. (2015)</td>
</tr>
<tr>
<td></td>
<td>Mortality rate (%)</td>
<td>0.8</td>
<td>1.0</td>
<td>1.2</td>
<td>van den Berg et al. (2013)</td>
</tr>
<tr>
<td></td>
<td>Duration of the first phase of the disease (months)</td>
<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
<td>Chang et al. (2018)</td>
</tr>
<tr>
<td>SGB</td>
<td>Duration of the second phase of the disease (months)</td>
<td>0.75</td>
<td>6.0</td>
<td>18.0</td>
<td>Chang et al. (2018)</td>
</tr>
<tr>
<td></td>
<td>Disability weight second phase</td>
<td>0.462</td>
<td>0.462</td>
<td>0.462</td>
<td>Allans-Murillo et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Disability weight second phase</td>
<td>0.237</td>
<td>0.237</td>
<td>0.237</td>
<td>Allans-Murillo et al. (2016)</td>
</tr>
</tbody>
</table>

UI: uncertainty interval; CI: confidence interval; CE: combined effect.

a Corresponds to the disability weight for hospitalized Dengue.

b Corresponds to the disability weight for severe Dengue.

c Corresponds to the duration of hospitalized Dengue.

d Corresponds to the disability weight for outpatient Dengue.

Sensitivity analysis
DALYs for each disease were calculated under three scenarios: conservative, medium, and extreme. The differences between these scenarios lie in the variability of 5 parameters: (1) EFs with an associated triangular distribution, (2) the incidence of post-Dengue chronic fatigue and post-Chikungunya chronic arthritis, (3) the duration of the diseases, both in their acute phase and in their chronic phase, (4) the disability weight of the acute and chronic phase of each of the diseases under study and (5) the mortality rate of GBS and microcephaly (Table 1).

Some parameters of Chikungunya and Zika are not described in the literature, so Dengue parameters were used to cover these gaps. Dengue was chosen as the model of these parameters since Dengue has similar symptoms to the other two arboviruses and is the principal differential diagnosis.
Table 2. Disability-adjusted life years (DALYs) due to arboviruses and its complications in Colombia by sex and age groups in the 2013–2016 period.

<table>
<thead>
<tr>
<th>Period</th>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
<th>Microcephaly</th>
<th>Male</th>
<th>Female</th>
<th>Microcephaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>0–4</td>
<td>1704.31</td>
<td>164.62</td>
<td>2211.19</td>
<td>22.461</td>
<td>2686.69</td>
<td>3803.39</td>
<td>113.61</td>
<td>1840.09</td>
</tr>
<tr>
<td>2014</td>
<td>5–14</td>
<td>6214.62</td>
<td>5853.15</td>
<td>6561.58</td>
<td>6.1610.88</td>
<td>2151.57</td>
<td>22.646.74</td>
<td>0 –</td>
<td>4873.48</td>
</tr>
<tr>
<td>2015</td>
<td>15–29</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
<td>1570.94</td>
</tr>
<tr>
<td>2016</td>
<td>≥ 30</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
<td>2445.28</td>
</tr>
</tbody>
</table>

The year with the highest number of DALYs lost at the national level was 2015 (3,806,517) were caused by Dengue and its complications, 52.1% (n = 4,831,562) by Chikungunya and its complications, and the remaining 6.9% (n = 442,757) by Zika and its complications.

For mortality, a total of 1,439 deaths were estimated nationwide in the 2013–2016 period. The highest number of deaths occurred in 2015 (427 deaths), while the lowest number occurred in 2014 (310 deaths). By Disease, 92.1% of the deaths (n = 1360) were caused by Dengue, 6.5% (n = 94) by Chikungunya, and the remaining 1.3% (n = 19) by Zika.

Results

After adjusting the number of cases, a total of 3,264,362 cases of arboviruses and their complications were estimated nationwide for the 2013–2016 period. The most affected year was 2015, with 4,831,562 cases, in comparison with 2014, when only 1,064,043 cases were estimated. By disease, 41% of the cases (n = 3,806,517) were caused by Dengue and its complications, 52.1% (n = 4,831,562) by Chikungunya and its complications, and the remaining 6.9% (n = 442,757) by Zika and its complications.

In terms of YLLs and YLDs, 6.5% of the total DALYs (31,760.3 YLLs) were years of life lost and 93.5% (405,56) were years lived with disability. By disease, 26.6% of the DALYs were caused by Dengue and post-Dengue chronic fatigue, 71.3% by Chikungunya and post-Chikungunya chronic arthritis, and the remaining 2.2%, by Zika, microcephaly, and GBS. 31.8% (146,459.3 DALYs) of the DALYs due to arboviruses and its complications at the departmental level in the 2013–2016 period.

For mortality, a total of 1,439 deaths were estimated nationwide in the 2013–2016 period. The highest number of deaths occurred in 2015 (427 deaths), while the lowest number occurred in 2014 (310 deaths). By Disease, 92.1% of the deaths (n = 1360) were caused by Dengue, 6.5% (n = 94) by Chikungunya, and the remaining 1.3% (n = 19) by Zika.

Table 3. Estimation under three scenarios of the disability-adjusted life years (DALYs) due to arboviruses and its complications at the departmental level in the 2013–2016 period.

<table>
<thead>
<tr>
<th>Department</th>
<th>DALYs conservative scenario</th>
<th>DALYs medium scenario</th>
<th>DALYs extreme scenario</th>
<th>Departmental contribution to the total DALYs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amazonas</td>
<td>311.13</td>
<td>60.68</td>
<td>300.68</td>
<td>0.14</td>
</tr>
<tr>
<td>Antioquia</td>
<td>4954.36</td>
<td>27.65</td>
<td>21.09</td>
<td>0.55</td>
</tr>
<tr>
<td>Arauca</td>
<td>608.05</td>
<td>3.89</td>
<td>3.54</td>
<td>0.15</td>
</tr>
<tr>
<td>Atlántico</td>
<td>3013.83</td>
<td>17.23</td>
<td>15.81</td>
<td>0.50</td>
</tr>
<tr>
<td>Bolívar</td>
<td>1541.94</td>
<td>37.80</td>
<td>37.40</td>
<td>0.50</td>
</tr>
<tr>
<td>Boyacá</td>
<td>431.66</td>
<td>2.84</td>
<td>2.70</td>
<td>0.18</td>
</tr>
<tr>
<td>Caldas</td>
<td>632.26</td>
<td>34.94</td>
<td>30.41</td>
<td>0.71</td>
</tr>
<tr>
<td>Caquetá</td>
<td>816.86</td>
<td>6.25</td>
<td>6.79</td>
<td>0.15</td>
</tr>
<tr>
<td>Casanare</td>
<td>1311.16</td>
<td>14.67</td>
<td>13.58</td>
<td>0.20</td>
</tr>
<tr>
<td>Caucar</td>
<td>3036.49</td>
<td>0.39</td>
<td>0.39</td>
<td>0.02</td>
</tr>
<tr>
<td>Cesar</td>
<td>3752.83</td>
<td>76.82</td>
<td>74.66</td>
<td>1.03</td>
</tr>
<tr>
<td>Chocó</td>
<td>251.41</td>
<td>0.63</td>
<td>0.63</td>
<td>0.03</td>
</tr>
<tr>
<td>Córdoba</td>
<td>3078.58</td>
<td>6.58</td>
<td>6.58</td>
<td>1.03</td>
</tr>
<tr>
<td>Cundinamarca</td>
<td>3945.35</td>
<td>42.36</td>
<td>42.36</td>
<td>0.90</td>
</tr>
<tr>
<td>Guainía</td>
<td>363.86</td>
<td>34.64</td>
<td>34.64</td>
<td>0.68</td>
</tr>
<tr>
<td>Guajira</td>
<td>1154.57</td>
<td>75.70</td>
<td>75.70</td>
<td>0.27</td>
</tr>
<tr>
<td>Guaviare</td>
<td>578.4</td>
<td>15.72</td>
<td>15.72</td>
<td>0.33</td>
</tr>
<tr>
<td>Huila</td>
<td>3332.23</td>
<td>252.35</td>
<td>252.35</td>
<td>0.61</td>
</tr>
<tr>
<td>Magdalena</td>
<td>7503.37</td>
<td>13.40</td>
<td>13.40</td>
<td>0.33</td>
</tr>
<tr>
<td>Meta</td>
<td>8310.13</td>
<td>22.77</td>
<td>22.77</td>
<td>0.65</td>
</tr>
<tr>
<td>Nariño</td>
<td>443.78</td>
<td>2.68</td>
<td>2.68</td>
<td>0.07</td>
</tr>
<tr>
<td>Norte de Santander</td>
<td>3909.09</td>
<td>30.64</td>
<td>30.64</td>
<td>0.84</td>
</tr>
<tr>
<td>Putumayo</td>
<td>508.76</td>
<td>312.02</td>
<td>26.16</td>
<td>0.64</td>
</tr>
<tr>
<td>Quindío</td>
<td>1100.94</td>
<td>8.02</td>
<td>7.63</td>
<td>0.20</td>
</tr>
<tr>
<td>Risaralda</td>
<td>906.80</td>
<td>66.15</td>
<td>66.15</td>
<td>0.31</td>
</tr>
<tr>
<td>San Andrés</td>
<td>763.12</td>
<td>2.87</td>
<td>2.87</td>
<td>0.03</td>
</tr>
<tr>
<td>Santander</td>
<td>4642.16</td>
<td>35.30</td>
<td>35.30</td>
<td>0.83</td>
</tr>
<tr>
<td>Sucre</td>
<td>2597.71</td>
<td>12.90</td>
<td>12.90</td>
<td>0.34</td>
</tr>
</tbody>
</table>
The departmental trends are different for each virus, taking into account that Dengue has been present in Colombia for decades, while the Chikungunya virus was introduced in 2014 and the Zika virus in 2015. We added supplementary material to explain the departmental trends for each virus – annual variations in terms of DALYs for each arbovirus at the departmental level [Supplemental Figs. S1–S9].

In 2013 and 2014, Valle del Cauca was the leading department in terms of DALYs for Dengue. During 2014 and 2016, it was the second, preceded by Santander and Antioquia, respectively. After Valle del Cauca, DALYs for Dengue were distributed among the departments located in the Andean region, Meta, and to a lesser extent, the Caribbean region. The rest of the Orinoquia region (without Meta), the Amazon region, and San Andrés were the ones with fewer DALYs due to Dengue (Supplementary Figs. S1–S4).

During 2014, the region most affected by the Chikungunya epidemic was the Caribbean region along with Norte de Santander (Supplementary Fig. S5). In 2015, when the epidemic reached its peak, most DALYs were lost in Valle del Cauca, the Andean region, and Meta (Supplementary Fig. S6). Finally, during 2016, the end of the epidemic phase and the beginning of the endemic phase, once again, most DALYs were lost in Valle del Cauca and the Andean region (Supplementary Fig. S7).

Regarding the Zika virus, during 2015, there were two spotlights: the Caribbean region plus Norte de Santander, and, on the other hand, Valle del Cauca, Meta, Tolima, Huila, and Cundinamarca (Supplementary Fig. S8). In 2016, when the Zika epidemic reached its peak, most DALYs were lost in Valle del Cauca and the Andean region. In general, the DALYs lost in the Orinoquia and Amazon region were scarce (Supplementary Fig. S9).

In the conservative scenario was estimated that a minimum of 68,264.73 DALYs were lost in the 2013–2016 period at the national level, while in the extreme scenario was estimated that a maximum of 4,598,006 DALYs were lost in the same period (Table 3).

Discussion

The results presented here reiterate the importance in public health that arboviruses represent in Colombia. Since the highest number of DALYs were lost in the age group between 15 and 29 years, this translates into productivity lost (due to hospitalisations and complications such as post-Chikungunya chronic arthritis [Bloch, 2016] and GBS [Peixoto et al., 2019]) and school absenteeism (peaks of school absenteeism have been related to peaks of Dengue cases) (Lawpoolsri et al., 2014).

When comparing the estimated DALYs with those reported in the literature, our results should be compared against estimates from epidemic years, given that the period studied (2013-2016) was epidemic for the three arboviruses. For each arbovirus we compared our results against two previously published articles (Table 4). In general, the differences observed between previous studies and ours are explained by the heterogeneity of disability weights and the duration of the diseases used, both in their acute and chronic phases. Likewise, previous studies did not use weights by age, nor discount rate, chose the total population instead of the population at risk, and the number of deaths and cases was not adjusted (Cardona-Ospina et al., 2015a, Cardona-Ospina et al., 2015b).

Particularly, Castro Rodríguez et al. (2016) underestimated the burden of disease for Dengue since they did not include the cases of post-Dengue chronic fatigue. Similarly, according to the WHO estimates, most DALYs are lost within the age range of 5 to 14 years (2015: 6,300 DALYs; 2016: 6,700 DALYs) (World Health Organization (WHO), 2018a), while we determined that the most affected age group were people from 15 to 29 years of age. The WHO used a discount rate value of 0%, and did not use age weights and, as a consequence, their results had an increase in absolute DALYs at younger ages.

Table 4. Summary of arboviral burden of disease studies.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Arbovirus</th>
<th>Study period; location; total cases estimated</th>
<th>Results Parameters used for the estimation of disability-adjusted life years (DALYs)</th>
</tr>
</thead>
</table>
In comparison with Alfaro-Munilla et al. (2016), their results are higher than those estimated here (2,738,000 DALYs per microscopy case and 6,411 DALYs per GBS case). The differences are primarily explained by different values of the parameters used in the calculation of YLDs (Table 4). Also, we did not include deaths from microcephaly and GBS.

In the same way that it is possible to compare our results against previous periods or international studies, DALYs can be compared against other infectious diseases. When combining the DALYs lost by the three arboviruses and comparing them against the WHO estimates, we found that, in 2015, the arboviral burden exceeded the sum of the DALYs lost by tuberculosis, HIV/AIDS, and other sexually transmitted diseases (290,000 DALYs compared with 285,500 DALYs). In 2016, arboviral burden was 56,081 DALYs, being slightly higher than tuberculosis burden (55,300 DALYs) (World Health Organization (WHO), 2018a). In the same way that it is possible to compare our results against previous periods or international studies, DALYs can be compared against other infectious diseases. When combining the DALYs lost by the three arboviruses and comparing them against the WHO estimates, we found that, in 2015, the arboviral burden exceeded the sum of the DALYs lost by tuberculosis, HIV/AIDS, and other sexually transmitted diseases (290,000 DALYs compared with 285,500 DALYs). In 2016, arboviral burden was 56,081 DALYs, being slightly higher than tuberculosis burden (55,300 DALYs) (World Health Organization (WHO), 2018a). Therefore, arboviruses were the leading cause of DALYs among infectious diseases during 2015 and the third cause during 2016 in Colombia. Such was the arboviral burden of disease in Colombia that it was the seventh leading cause of DALYs lost among all health conditions and diseases in 2015 (Table 5).

The limitations of this study can be summarized in 4 points. First, the database present underreporting. This was minimized using expansion factors (Shepard et al., 2011); however, this method cannot guarantee that the study is underreporting. In addition, different EFs have been published to correct the underreporting of Dengue in Colombia (Shepard et al., 2011, Sarti et al., 2016). We used Shepard et al. (2011) EFs, which were published in 2011. Nonetheless, those EFs arise from a study published in 2004, but whose data are older, dating back to 1995 and 1997 (Camacho et al., 2006). Despite Shepard et al. (2011) EFs are outdated, it is necessary to implement correction factors, since surveillance systems are unable to detect all cases.

Second, the entire spectrum of chronic manifestations of Chikungunya and Zika was not taken into account. Chronic post-Chikungunya arthritis accounts for about 50% of all post-Chikungunya chronic inflammatory rheumatism (Rodriguez-Murillo et al., 2016). Furthermore, congenital and neurological alterations have been associated with Chikungunya virus (Gérardin et al., 2018, Barros-Correa et al., 2015, Solomou et al., 2015). Similarly, GBS and microcephaly only represent a fraction of the entire spectrum of clinical manifestations associated with Zika (Moure et al., 2017, Moure et al., 2017). As a result, the burden of disease due to chronic manifestations caused by Chikungunya and Zika is being underestimated. There are no databases of chronic manifestations of these diseases in Colombia, and new clinical manifestations of both diseases are still documented (Gómez Montenegro et al., 2016, Merle et al., 2018).

Third, hospitalized cases and deaths associated with each virus are not necessarily a consequence of the infection, but may be related to pre-existing medical conditions of each patient. However, one cannot ignore that the infection contributed to a patient's hospitalization or death. Therefore, this limitation can lead to a possible overestimation of the burden of disease.

Fourth, microcephaly deaths and GBS deaths were not included in the DALYs calculation. The exclusion of these deaths underestimate Zika’s total DALYs. They were not included because there is no a reliable database of deaths from these causes. Similarly, the number of cases of microcephaly and GBS were not corrected by underreporting, resulting in underestimation of the burden of disease. They were not corrected by underreporting since there are no expansion factors reported previously for these two clinical conditions.

### Table 4. The 10 leading causes of disability-adjusted life years (DALYs) in Colombia in 2015.

<table>
<thead>
<tr>
<th>Health Condition &amp; Disease</th>
<th>DALYs (1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interpersonal violence</td>
<td>1311.5</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1647.2</td>
</tr>
<tr>
<td>Road injuries</td>
<td>655.6</td>
</tr>
<tr>
<td>Stroke</td>
<td>436.9</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>386.0</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>337.5</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>296.0a</td>
</tr>
<tr>
<td>Other causes of hearing loss</td>
<td>283.3</td>
</tr>
<tr>
<td>Cervical and lumbar pain</td>
<td>266.3</td>
</tr>
<tr>
<td>Complications of prematurity birth</td>
<td>280.6</td>
</tr>
</tbody>
</table>


b Combined burden of Dengue, Chikungunya and Zika in Colombia in 2015.

The limitations of this study can be summarized in 4 points. First, the database present underreporting. This was minimized using expansion factors (Shepard et al., 2011); however, this method cannot guarantee that the study is underreporting. In addition, different EFs have been published to correct the underreporting of Dengue in Colombia (Shepard et al., 2011, Sarti et al., 2016). We used Shepard et al. (2011) EFs, which were published in 2011. Nonetheless, those EFs arise from a study published in 2004, but whose data are older, dating back to 1995 and 1997 (Camacho et al., 2006). Despite Shepard et al. (2011) EFs are outdated, it is necessary to implement correction factors, since surveillance systems are unable to detect all cases.
The main strength of this study was to present the total and per arbovirus burden of disease at the national and departmental levels, by sex and age group, following the recommendations of previous studies (Beatty et al., 2011) and including the chronic manifestations associated with the three arboviruses. Moreover, the disability weight of post-Chikungunya chronic arthritis was differentiated by sex since the evidence shows that rheumatoid arthritis is more disabling in women (Ciras et al., 2014). Finally, it is one of the first studies to calculate the Zika burden of disease, taking into account both the acute phase and chronic manifestations of the infection.

This study highlights the importance of the introduction of new viruses in America, especially in Colombia. Other arboviruses, such as mayaro and oropuche, have been proposed as new threats that, if not addressed, could reach the epidemic scale of Chikungunya or Zika (Heijt and Murray, 2017). Rodrigues-Morales et al., 2017, Romero-Alzamán and Escober, 2018. Likewise, there is a great diversity of African arboviruses that could potentially be introduced into the Americas and trigger the next epidemic (Braack et al., 2018). Therefore, public policies established at the national and departmental levels must be improved to detect, prevent, and mitigate the impact of established and emerging arboviruses in Colombia.

Authors contribution
Andrés Felipe Mora-Salamanca, MSc: He did the literature search, designed the study, performed data analysis, and elaborated the discussion.
Alexandra Perna-Ramírez, Ph.D.: she designed the study, performed data analysis, and elaborated the discussion.
Fernando Pío de la Hoz Restrepo, Ph.D.: He performed data analysis, elaborated the discussion, and made corrections.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest
The authors declare no conflicts of interest.

Financial support
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements
The authors thank the Colombian National Institute of Health (Instituto Nacional de Salud) for providing the 2013-2016 Dengue, Chikungunya and Zika virus databases.

Appendix A. Supplementary data
The following are Supplementary data to this article:

References

Acosta Ramirez et al., 2008 N. Acosta Ramirez, R.P. Pehlavan, J. Clarín Rodriguez
Cargo de Enfermedad en Colombia 2005: Resultados Nacionales [Internet]
Available from: http://www.jornetav.edu.co/poliales/CPIs/informes/PresentacionCargo_Informe.pdf
Pontificia Universidad Javeriana (2008)
Google Scholar

A cost-effectiveness tool for informing policies on Zika virus control
Google Scholar

Congenital chikungunya virus infection in Sincelejo, Colombia: a case series
Google Scholar

Health economics of dengue: a systematic literature review and expert panel’s assessment
CrossRef View Record in Scopus Google Scholar

Bennett and Horiuchi, 1981 N.G. Bennett, S. Horiuchi
Estimating the completeness of death registration in a closed population author
Popul Index, 47 (2) (1981), pp. 207-221
CrossRef View Record in Scopus Google Scholar

Camacho et al., 2004 T. Camacho, F. de la Hoz, V. Cardenas, C. Sanchez, L. de Calderon, L. Perez, et al.
Incomplete surveillance of a dengue-2 epidemic in Ibagué, Colombia, 1995-1997
Biomédica, 24 (1) (2004), pp. 174-182
CrossRef View Record in Scopus Google Scholar

The burden of Chikungunya in one coastal department of Colombia (Córdoba): estimates of the disability adjusted life years (DALY) lost in the 2014 epidemic
J Infect Public Health, 8 (9) (2015), pp. 664-666
Article [W] Download PDF View Record in Scopus Google Scholar

Estimating the burden of disease and the economic cost attributable to chikungunya, Colombia, 2014
CrossRef View Record in Scopus Google Scholar

Cassarino et al., 2016 R. Cassarino, D. Bloch, C. Bunschoten, P.A. van Doorn, B.C. Jacobs
Dengue, Chikungunya and Zika virus databases.

Available from:
http://elischolar.library.yale.edu/ysphtdl/1022
http://www.javeriana.edu.co/cendex/GPES/informes/PresentacionCarga_Informe.pdf

van den Berg et al., 2013 B. van den Berg, C. Bunschoten, P.A. van Doorn, B.C. Jacobs
Mortality in Guillain-Barre syndrome
Neurology [Internet], 80 (Apr 28) (2013), pp. 1630-1634, 10.1212/WNL.0b013e318239046c
CrossRef View Record in Scopus Google Scholar

Brock, 2016 D. Brock
The cost and burden of Chikungunya in the Americas [Internet]. Public Health theses
Available from: http://elischolar.library.yale.edu/ysphtdl/1022
Yale University (2016)
Google Scholar

Mosquito-borne arbovirus of African origin review of key viruses and vectors
Parasites Vectors, 11 (3) (2018)
Google Scholar

Incidence and seroprevalence of a dengue-2 epidemic in Ibagué, Colombia, 1995-1997
Biomedica, 24 (1) (2004), pp. 174-182
CrossRef View Record in Scopus Google Scholar

The burden of Chikungunya in one coastal department of Colombia (Córdoba): estimates of the disability adjusted life years (DALY) lost in the 2014 epidemic
J Infect Public Health, 8 (9) (2015), pp. 664-666
Article [W] Download PDF View Record in Scopus Google Scholar

Estimating the burden of disease and the economic cost attributable to chikungunya, Colombia, 2014
CrossRef View Record in Scopus Google Scholar

Salas Botero and Instituto Nacional de Salud (INS), 2015
Informe final del evento Chikunguña, Colombia, 2015. [Internet]
Available from: https://www.ins.gov.co/buscador-eventos/Paginas/Info-Evento.aspx
View Record in Scopus
google Scholar

Solomon et al., 2013
Disability weights for the Global Burden of Disease 2013 study
Lancet Glob Heal, 3 (11) (2015), pp. e712-23
View Record in Scopus
google Scholar

Sarti et al., 2016
A comparative study on active and passive epidemiological surveillance for dengue in five countries of Latin America
Int J Infect Dis, 44 (2016), pp. 44-49
Article
download PDF
google Scholar

Sert et al., 2007
R.C.S. Sert, A.M.I. Querc, E.C.M. Lim
Post-infections fatigue syndrome in dengue infection
Article
download PDF
google Scholar

Sharp et al., 2016
Surveillance for chikungunya and dengue during the first year of chikungunya virus circulation in puerto rico
CrossRef
google Scholar

Shepard et al., 2011
D.S. Shepard, L. Coudreuil, Y.A. Halsea, B. Zambrano, G.H. Dayan
Economic impact of dengue illness in the americas
CrossRef
google Scholar

Solomon et al., 2018
The neurological complications of chikungunya-virus a systematic review
google Scholar

Stanaway et al., 2016
The global burden of dengue: an analysis from the Global Burden of Disease Study 2013
Lancet Infect Dis, 16 (6) (2016), pp. 712-723
Article
download PDF
google Scholar

Teich et al., 2017
V. Teich, H. Antolín, L. Falham
Aedes aegypti e sociedade: o impacto econômico das arboviroses no Brasil
J Bras Econ da Saúde [Internet], 9 (3) (2017), pp. 267-276
CrossRef
google Scholar

World Health Organization (WHO), 2006
Report of the Scientific Working Group meeting on dengue, Geneva, 1–5 October 2006. [Internet]
Available from: https://apps.who.int/iris/handle/10665/69787
(2006)
google Scholar

World Health Organization (WHO), 2012
Global Strategy for Dengue Prevention and Control 2012–2020 [Internet]
Available from: https://www.who.int/denguecontrol/9789241504034/en/
World Health Organization (2012)
google Scholar

World Health Organization (WHO), 2018a
Global health estimates 2016: disease burden by cause, age, sex, by country and by region, 2000–2016. [Internet]
World Health Organization (2018a)
google Scholar

World Health Organization (WHO), 2018b
Zika Virus [Internet]
(2018)
google Scholar

Zeng et al., 2018
W. Zeng, Y.A. Halsea-Rappel, L. Durand, L. Coudreuil, D.S. Shepard
Impact of a nonfatal dengue episode on disability-adjusted life years: a systematic analysis
CrossRef
google Scholar

Address: Universidad El Bosque, Edificio Fundadores, Piso 5, Oficina de Epidemiología, Carrera 9 No. 131 A 02, Bogotá, Colombia.

Address: Universidad Nacional de Colombia – sede Bogotá, Edificio 471, Departamento de Salud Pública, Carrera 30 No. 45 03, Bogotá, Colombia.

View Abstract

© 2018 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.