



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

Andrés Felipe Mora-Salamanca ^{a, R, B}, Alexandra Porras-Ramírez ^{b, c, d, 1 B}, Fernando Pío De la Hoz Restrepo ^{b, 2 B}

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Highlights

- During 2013–2016, Colombia experienced dengue, chikungunya and Zika epidemics.
- These arboviruses have been associated to several chronic complications.
- Almost 500,000 DALYs were lost due to arboviruses and their complications.
- In 2015, arboviruses exceeded the burden of HIV/AIDS and tuberculosis combined.
- Public health efforts must be made to mitigate new epidemics.

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 (SIVIGILA) 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 Bolívar) contributed 50.5% 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.

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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 Chikungunya and Zika viruses were introduced into the Americas in 2013 and 2015, respectively (Fischer and Erin Staples, 2014, Gatherer and Kohl, 2016). As a consequence, more than 11 million cases of arboviruses were reported throughout the region during the 2013–2016 period (Pan American Health Organization (PAHO) and World Health Organization (WHO), 2018, Pan American Health Organization (PAHO) and World Health Organization (WHO), 2019a, Pan American Health Organization (PAHO) and World Health Organization (WHO), 2019b).

Colombia was one of the most affected countries by these viruses. According to the number of cases reported in the 2013–2016 period, Colombia was the third most affected country by the Dengue virus, just behind Brazil and Mexico (Pan American Health Organization (PAHO) and World Health Organization (WHO), 2019a). Similarly, it ranked the second and third country in the region in terms of the number of Chikungunya (2014–2016), and Zika (2015–2016) cases reported, respectively (Pan American Health Organization (PAHO) and World Health Organization (WHO), 2018, Pan American Health Organization (PAHO) and World Health Organization (WHO), 2019b). In total Colombia reported more than one million acute cases of arboviruses during the 2013–2016 period.

Arboviruses, apart from acute disease, have been associated with chronic complications. Dengue associated with a wide variety of chronic symptoms (depression, insomnia, fatigue, headache, arthralgias, among others) which have been grouped and named—without reaching any consensus—as: post-infectious fatigue syndrome in Dengue, post-Dengue chronic fatigue, persistent or chronic Dengue (Seet et al., 2007, Stanaway et al., 2016, Zeng et al., 2018). Chikungunya has been associated with inflammatory joint diseases such as chronic arthritis (Rodríguez-Morales et al., 2016) while Zika has associated with congenital syndromes and Guillain-Barré syndrome (GBS) (Parra et al., 2016, Rasmussen et al., 2016). Consequently, these disorders generate costs, deaths, and disability both in the short and long term.

Currently, research priorities on Dengue (which should extrapolate to Chikungunya and Zika) should aim at reducing severe Dengue rates and mortality, reducing virus transmission, preventing disease, and the application of public policies (World Health Organization (WHO), 2006, Farrar et al., 2007). According to the WHO, “There is a contradiction between the high priority afforded to Dengue at political level and the low level of resources allocated to Dengue prevention and control program activities” (World Health Organization (WHO), 2006). Likewise, in 2012, the WHO set three

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main objectives: 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 ([Beatty 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](#), [Instituto Nacional de Salud \(INS\), 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, 53% (222,915 cases) of Dengue cases (with or without warning signs) were compatible with the probable case definition and 47% (200,022 cases) were confirmed cases (either by laboratory or epidemiological contact). Concerning severe cases, 25% (2041 cases) were probable cases, and the remaining 75% (6011 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), 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 \(INS\), 2017a](#)). In the 2014–2016 period, 98.6% (480,524 cases) of Chikungunya cases were confirmed by clinical diagnosis, 1% (4984 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, Pinilla 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 2100 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 ([Bennett and Horiuchi, 1981](#)) and expansion factors ([Shepard et al., 2011](#)).

Once the number of deaths for each arbovirus was adjusted, 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 [Beatty 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 SIVIGILA 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 ([Rodríguez-Morales et al., 2016](#), [Zeng et al., 2018](#)) to approximate to the number of cases of these conditions 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 YLLs, 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

estimating YLLs are as follows: standard discount rate (value is 0.03), β standard age-weighting function (value is 0.04) and C standard age-weighting correction constant (value is 0.1658).

The parameters for the calculation of YLDs correspond to values defined in previous studies (Table 1). (Alfaro-Murillo et al., 2016, van den Berg et al., 2013, Chang et al., 2018, Cross et al., 2014, Honeycutt et al., 2003, Meltzer et al., 1998, Nembhard et al., 2001, Rodríguez-Morales et al., 2016, Rodríguez-Morales et al., 2015, Salomon et al., 2015, Sharp et al., 2016, Shepard 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.

Arboviruses	Parameter	Conservative value	Medium value	Extreme value	Reference
All	Expansion factor 1	1.4	2.3	3.3	Shepard et al. (2011)
	Central value – Rank				
	Expansion factor 2	4.5	9	18	Shepard et al. (2011)
	Central value – Rank				
	Duration – Outpatient Dengue (days)	9.5	13.1	20	Zeng et al. (2018)
	Mean-Rank				
	Duration – Hospitalized Dengue (days)	9	12.3	14.2	Zeng et al. (2018)
	Mean-Rank				
	Duration – Severe Dengue (days)	10	14	18	Shepard et al. (2011)
	Mean-Rank				
Dengue	Duration – Post-Dengue chronic fatigue (days)	15	32	131	Zeng et al. (2018)
	Median-CI 95%				
	Disability weight –Outpatient Dengue Mean-Rank	0.24	0.62	0.85	Zeng et al. (2018)
	Disability weight –Hospitalized Dengue Mean-Rank	0.49	0.71	0.9	Zeng et al. (2018)
	Disability weight – Severe Dengue Base value-Rank	0.6	0.81	0.92	Meltzer et al. (1998)
	Disability weight – Post-Dengue chronic fatigue Estimate UI 95%	0.148	0.219	0.308	Salomon et al. (2015); Zeng et al. (2018)
	Incidence – Post-Dengue chronic fatigue (%) Median-CI 95%	27	34	41	Zeng et al. (2018)
	Duration – Outpatient Chikungunya (days) Median-Range	2	6	21	Sharp et al. (2016)
	Duration - Hospitalized Chikungunya (days) Median-Rank	3	7	15	Sharp et al. (2016)
	Duration – Post-Chikungunya chronic arthritis (months) Median-Rank	3	20.12	72	Rodríguez-Morales et al. (2015)
Chikungunya	Disability weight – Outpatient Chikungunya	0.49	0.71	0.9	^a
	Disability weight – Hospitalized Chikungunya	0.6	0.81	0.92	^b
	Disability weight – Post-Chikungunya chronic arthritis in women Mean-CI 95%	0.194	0.275	0.366	Cross et al. (2014)
	Disability weight – Post-Chikungunya chronic arthritis in men Mean-CI 95%	0.149	0.213	0.286	Cross et al. (2014)
	Incidence – Post-Chikungunya chronic arthritis (%) CE-CI 95%	9.31	13.66	18	Rodríguez-Morales et al. (2016)
	Duration – Outpatient Zika (days)	2	5	7	World Health Organization (WHO), 2018b
	Duration – Hospitalized Zika (days)	9	12.3	14.2	^c
	Disability weight – Outpatient Zika	0.24	0.62	0.85	^d
	Disability weight – Hospitalized Zika	0.49	0.71	0.9	^a
	The first-year survival rate (%)	0.797	0.797	0.797	Nembhard et al. (2001)
Microcephaly	Mortality rate after the first year (%)	8	36.4	10.7	Honeycutt et al. (2003)
	Duration of the disease (years)	25	65	35	Honeycutt et al. (2003)
	Disability weight	0.16	0.16	0.16	Salomon et al. (2015)
	Mortality rate (%)	3	3.9	5	van den Berg et al. (2013)
	Duration of the first phase of the disease (months)	6	6	6	Chang et al. (2018)
	Duration of the second phase of the disease (months)	0.75	6	18	Chang et al. (2018)
	Disability weight first phase	0.402	0.402	0.402	Alfaro-Murillo et al. (2016)
SGB	Disability weight second phase	0.317	0.317	0.317	Alfaro-Murillo et al. (2016)

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.

Results

After adjusting the number of cases, a total of 9,284,326 cases of arboviruses and their complications were estimated nationwide for the 2013–2016 period. The most affected year was 2015, with 4,484,386 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% ($n = 4,835,052$) by Chikungunya and its complications, and the remaining 6.9% ($n = 642,757$) by Zika and its complications.

For mortality, a total of 1439 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 ($n = 1326$) were caused by Dengue, 6.5% ($n = 94$) by Chikungunya, and the remaining 1.3% ($n = 19$) by Zika.

In the 2013–2016 period, 491,629.2 DALYs were estimated for arboviruses nationwide (Table 2). In terms of YLLs and YLDs, 6.5% of the total DALYs (31,760.3 YLLs) were years of life lost and 93.5% (459,868.9 YLDs) 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 total DALYs were caused by the acute phase of the diseases and 68.2% (313,409.6 DALYs) by chronic complications. In 2013, 1068 DALYs per million inhabitants were lost, 3131.2 DALYs per million inhabitants in 2014, 8255.6 DALYs per million inhabitants in 2015, and 1579.1 DALYs per million inhabitants in 2016.

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.

Period										
2013		2014		2015		2016				
Age	Male	Female	Male	Female	Male	Female	Microcephaly	Male	Female	Microcephaly
0–4	1704.21	1614.92	2225.19	2236.81	2638.64	3801.39	112.60	1060.89	952.60	2960.60
5–14	6213.62	5833.15	10,634.50	10,043.90	18,521.57	22,164.70	–	4073.43	4085.10	–
15–29	6763.04	4978.91	15,639.57	21,707.03	39,055.99	61,122.07	–	8654.10	10,476.86	–
30–44	3201.42	2465.20	10,606.31	16,744.91	31,115.42	51,469.16	–	5579.19	8015.63	–
45–59	1472.24	1280.00	5158.22	8783.58	16,279.44	27,313.25	–	2839.91	4626.46	–
60–69	391.55	360.30	1308.25	2044.38	3877.64	6893.61	–	774.86	1025.44	–
70–79	179.37	138.41	536.74	722.75	1720.95	2540.58	–	316.85	405.56	–
≥ 80	57.86	52.84	182.00	233.05	599.50	807.20	–	103.30	130.48	–
Total	19,983.29	16,723.72	46,290.78	62,516.41	113,809.16	176,111.96	112.60	23,402.53	29,718.11	2960.60

The year with the highest number of DALYs lost at the national level was 2015 (290,033.7 DALYs), when Colombia reached the peak of the Chikungunya epidemic, while the lowest was 2013 (36,707 DALYs), when only cases of Dengue were reported. Regarding DALYs and different age groups, the age range between 15 and 29 years contributed the most DALYs among all age groups, followed by the age group between 30 and 44 years, being women more affected than men (except in 2013) (Table 2).

At the departmental level, Valle del Cauca contributed 24.2% of the total DALYs for the 2013–2016 period, being the most affected department by arboviruses in Colombia. Five out of 32 deparments (Valle del Cauca, Tolima, Norte de Santander, Huila, and Bolívar) contributed 50.5% of the total DALYs. Twelve other departments, they each accounted for less than 1% of the total DALYs. In total, these departments (Cauca, Caldas, Putumayo, Nariño, Boyacá, Guaviare, San Andrés, Chocó, Amazonas, Vichada, Guainía, and Vaupés) contributed only 4.4% of the total DALYs (Table 3 and Fig 1).

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.

Department	DALYs conservative scenario	DALYs medium scenario	DALYs extreme scenario	Departmental contribution to the total DALYs (%)
Amazonas	310.53	666.32	3000.08	0.14
Antioquia	4454.36	27,055.02	219,625.9	5.50
Arauca	658.05	5399.6	53,663.43	1.10
Atlántico	3035.83	17,211.65	143,035.9	3.50
Bolívar	3541.94	27,606.93	277,876	5.62
Boyacá	421.66	2344.3	17,927.65	0.48
Caldas	632.26	3442.4	30,491.03	0.70
Caquetá	816.86	6621.97	66,789.22	1.35
Casanare	1131.56	14,567.13	150,559.3	2.96
Cauca	592.68	4019.16	38,785.42	0.82
Cesar	2472.83	7002.33	46,106.75	1.42
Chocó	210.4	1024.76	8894.13	0.21
Córdoba	2678.58	16,990.36	162,166.3	3.46
Cundinamarca	3945.35	24,326.19	221,142.2	4.95
Guainía	163.86	394.52	2246.42	0.08
Guajira	1554.57	9750.27	95,820.52	1.98
Guaviare	179.4	2157.1	21,744.15	0.44
Huila	3232.21	28,255.59	276,440.9	5.75
Magdalena	1769.37	11,565.99	111,334.9	2.35
Meta	3812.12	22,677.46	195,433.4	4.61
Nariño	642.78	2808.76	23,881.56	0.57
Norte de Santander	3990.99	30,564.07	291,290.1	6.22
Putumayo	588.76	3152.92	24,291.65	0.64
Quindío	1188.94	8020.83	70,639.19	1.63
Risaralda	906.89	6616.9	62,436.04	1.35
San Andres	74.12	1193.17	12,318.2	0.24
Santander	4442.56	25,582.02	199,435.8	5.20
Sucre	2547.71	18,390.29	180,260.6	3.74

Tolima	6358.01	42,606.45	403,012.3	8.67
Valle del Cauca	11,787.99	119,041.2	1,175,249	24.21
Vaupés	5.85	28.52	337.78	0.01
Vichada	101.17	539.43	4428.19	0.11
Colombia	68,264.73	491,629.2	4,598,006	100

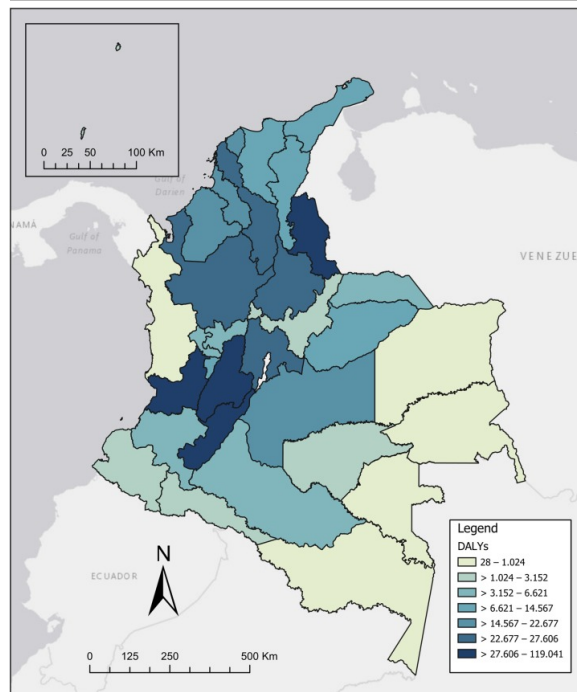


Fig. 1. Total disability-adjusted life years (DALYs) due to arboviruses and its complications at the departmental level in the 2013–2016 period in Colombia. Valle del Cauca, Tolima, Norte de Santander, Huila, and Bolívar contributed 50.5% of the total DALYs.

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 hospitalizations 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: 6,200 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.

Reference	Arbovirus	Study period; location; total cases estimated	Results	Parameters used for the estimation of disability-adjusted life years (DALYs)
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Castro Rodríguez et al. (2016)	Dengue	2010–2012; 2010: 153,165, 2011: 32,639, 2012: 57,238	2010: 1.198,73 DALYs per million inhabitants; 2011–2012: 83.88 DALYs per million inhabitants	Disability weight = 0.81 (0.6–0.92); duration: 15 days (10–21)
World Health Organization (WHO), 2018a	Dengue	2000–2016; World and country level; Colombia 2006–2016 Cases: 648,300 (448,100– 892,200)	Colombia 2000: 9000 DALYs; 2010: 25,900 DALYs; 2015 and 2016 25,600 DALYs	Disability weight: Dengue = 0.053; severe dengue = 0.210; moderate post-Dengue chronic fatigue = 0.051, severe = 0.133D uration: dengue = 6 days; severe dengue = 14 days; post-Dengue chronic fatigue = 6 months
Cardona Ospina et al. (2015b)	Chikungunya	2014; Colombia; 106,592	427.96 DALYs per million inhabitants	Disability weight: acute phase = 0.172; post-Chikungunya chronic arthritis = 0.233; duration: post-Chikungunya chronic arthritis = 20.12 months
Cardona Ospina et al. (2015a)	Chikungunya	2014; Sucre, Colombia; 14,741	3084.74 DALYs per million inhabitants	Disability weight post-Chikungunya chronic arthritis = 0.233; duration post-Chikungunya chronic arthritis = 20.12 months
Teich et al. (2017)	Zika	2016; Brazil; 215,319	0.005 DALYs; 1076.6 DALYs	Disability weight acute phase = 0.16; duration acute phase = 8 days
Alfaro-Murillo et al. (2016)	Zika	2016; Latin America and the Caribbean	Microcephaly: 29.95 DALYs per case; GBS: 1.25 DALYs per case.	Microcephaly: 79.7% probability of survival through the first year of life; disability weight = 0.16; duration = 35 years; GBS: 5% probability of death; 9% probability of severe motor impairment; disability weight = 0.402; duration = 6 months; 84% probability of moderate generalized musculoskeletal problems; disability weight = 0.344; duration = three weeks

In comparison with [Alfaro-Murillo et al. \(2016\)](#), their results are higher than those estimated here (2.75 DALYs per microcephaly case and 0.41 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](#)). 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](#)).

Table 5. The 10 leading causes of disability-adjusted life years (DALYs) in Colombia in 2015.

Health Conditions & Diseases	DALYs (1000) ^a
Interpersonal violence	1311.5
Ischemic heart disease	1047.2
Road injuries	602.6
Stroke	438.9
Diabetes mellitus	398.0
Low respiratory infections	337.5
Arboviruses	290.0 ^b
Other causes of hearing loss	283.3
Cervical and lumbar pain	266.3
Complications of premature birth	260.6

^a Values estimated by the WHO. Source: Global Health Estimates 2016: Disease burden by Cause, Age, Sex, by Country and by Region, 2000–2016. Geneva, World Health Organization; 2018.

^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 databases present underreporting. This was minimized using expansion factors ([Shepard et al., 2011](#)); however, this method cannot guarantee that the study lacks 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 arised from a study published in 2004, but whose data are older, dating back to 1995 and 1997 ([Camacho et al., 2004](#)). 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 ([Rodríguez-Morales et al., 2016](#)). Furthermore, congenital and neurological alterations have been associated with Chikungunya virus ([Gérardin et al., 2008](#), [Barrios-Corrales et al., 2015](#), [Solomon et al., 2018](#)). Similarly, GBS and microcephaly only represent a fraction of the entire spectrum of clinical manifestations associated with Zika ([Moore et al., 2017](#), [Muñoz 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 ([Costa Monteiro et al., 2018](#), [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.

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 (Cross 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 (Hotez and Murray, 2017, Rodríguez-Morales et al., 2017, Romero-Alvarez and Escobar, 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 Porras-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.

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Conflict of interest

The authors declare no conflicts of interest

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Appendix A. Supplementary data

The following are Supplementary data to this article:

 [Download : Download Acrobat PDF file \(33MB\)](#)

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¹ Address: Universidad El Bosque, Edificio Fundadores, Piso 5, Oficina de Epidemiología, Carrera 9 No. 131 A 02, Bogotá, Colombia.

² Address: Universidad Nacional de Colombia – Sede Bogotá, Edificio 471, Departamento de Salud Pública, Carrera 30 No. 45 03, Bogotá, Colombia.

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