A decade of arbovirus emergence in the temperate southern cone of South America: dengue, *Aedes aegypti* and climate dynamics in Córdoba, Argentina

Elizabet L. Estallo[1*¶], Rachel Sippy[2,3¶], Anna M. Stewart-Ibarra[2,4¶], Marta G. Grech[5], Elisabet M. Benitez[1], Francisco F. Ludueña-Almeida[1,6], Mariela Ainete[7], María Frias-Cespedes[7], Michael Robert[8], Moory M. Romero[2,9] and Walter R. Almirón[1]

[1] Instituto de Investigaciones Biológicas y Tecnológicas (IIBYT) CONICET- Universidad Nacional de Córdoba. Centro de Investigaciones Entomológicas de Córdoba, Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba. Ciudad Universitaria, Córdoba Capital, Córdoba, Argentina
[2] Institute for Global Health & Translational Sciences, SUNY Upstate Medical University, Syracuse, NY, USA
[3] Department of Medical Geography, University of Florida, Gainesville, FL, USA
[4] InterAmerican Institute for Global Change Research (IAI), Montevideo, Department of Montevideo, Uruguay
[5] Centro de Investigación Esquel de Montaña y Estepa Patagónica (CIEMEP), CONICET and Universidad Nacional de la Patagonia San Juan Bosco. Facultad de Ciencias Naturales y Ciencias de la Salud, Sede Esquel. Esquel, Chubut, Argentina
[6] Cátedra de Matemática (Cs. Biológicas), Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Ciudad Universitaria, Córdoba Capital, Córdoba, Argentina
[7] Ministerio de Salud de la Provincia de Córdoba- Dirección de Epidemiología, Hospital San Roque Viejo, Córdoba Capital, Córdoba, Argentina
[8] Department of Mathematics, Statistics, and Physics, University of the Sciences, Philadelphia, PA, USA
[9] Department of Environmental Studies, State University of New York College of Environmental Science and Forestry (SUNY ESF), Syracuse, NY, USA

*Corresponding author:
Email: eelizabet@gmail.com (ELE)

¶These authors contributed equally to this work.

Abstract

Background: Argentina is located at the southern range of arboviral transmission by *Aedes aegypti* and has experienced a rapid increase in arbovirus transmission in recent years. This study aims to present the study design and findings from the first 9 years of an entomological surveillance work that began in Córdoba following the emergence of dengue one decade ago. We also investigate the temporal dynamics of *Ae. aegypti*, dengue cases, and local climate, and their lagged associations.

Methods: From 2009 to 2017, larval surveys were conducted monthly, from November to May, in 600 randomly selected households distributed across the city. From 2009 to 2013, ovitraps (n=177) were sampled weekly to monitor the oviposition activity of *Ae. aegypti.* Cross correlation analysis was used to identify significant lag periods between climate, entomological and epidemiological variables.

Results: *Aedes aegypti* abundance peaked once annually (from January to March), followed by a peak in autochthonous dengue transmission in April. We identified a notable increase in the proportion of homes with juvenile *Ae. aegypti* (from 5.7% of homes in 2009-10 to 15.4% of homes in 2016-17). The mean number of eggs per ovitrap was positively associated with mean temperature. Monthly juvenile *Ae. aegypti* abundance was not associated with either autochthonous or imported dengue cases. Autochthonous dengue transmission was negatively correlated with lagged temperature and precipitation.

Conclusions: These findings suggest increasing the risk of arbovirus transmission in this temperate region. These results can guide targeted vector control interventions and the development of climate services for the public health sector to reduce the burden of arboviral diseases.

Author summary

There is an increasing risk of arbovirus transmission in temperate regions. Argentina is located at the southern range of dengue virus transmission by the *Aedes aegypti* mosquito, and in the last decade, epidemics of dengue fever have re-emerged. We present the study design and findings from the first 9 years of an entomological surveillance study in Córdoba, Argentina, following the emergence of dengue. We found that *Ae. aegypti* were most abundant from January to March, followed by a peak in local dengue transmission in April. Over the study period, we noted a considerable increase in the proportion of homes with *Ae. aegypti*. We found that vector indices and dengue transmission were associated with local climate conditions (temperature and precipitation). These results highlight the growing risk of arboviral infections and the role of climate in local arbovirus and vector dynamics in the southern cone of South America.

Keywords*: Aedes aegypti,* Argentina, dengue, ovitrap, larval surveys, surveillance, climate

73 ## Introduction

74 Argentina is located at the southern range of arboviral transmission by *Ae. aegypti*
75 and has experienced the emergence of arbovirus transmission in the last decade [1,2].
76 Dengue (DENV serotypes 1-4), Chikungunya (CHIKV) and Zika viruses (ZIKV) cause
77 febrile illnesses and are transmitted principally by the female *Ae. aegypti*, with *Ae.*
78 *albopictus* as a secondary vector. No specific therapeutics or vaccines are yet available for
79 ZIKV [3] or CHIKV [4], and there is limited access to the Dengvaxia© DENV vaccine,
80 which has been licensed in Argentina [5]. During the 2015-2016 epidemic, ZIKV was of
81 great concern to the region, due to potential neurological and congenital complications
82 associated with infections [6]. Vector management remains the primary means of
83 preventing and controlling arboviral disease outbreaks.

84 The earliest outbreaks of dengue fever were recorded in Argentina in 1916, and no
85 cases were reported for 80 years afterwards [7]. *Aedes aegypti* was considered eradicated
86 from Argentina in 1963; nevertheless, in 1986, it was detected in the northeast area [8].
87 Dengue first re-emerged in 1997 and 2000 in the subtropical northern region of Argentina
88 [9]. Within the last decade, dengue has emerged in native populations in central and
89 southern Argentina [10]. In 2009, Argentina suffered its first major dengue outbreak, with
90 more than 26,000 cases, 3 severe dengue cases, and 5 confirmed deaths; 10 jurisdictions
91 registered autochthonous cases for the first time [11]. Outbreaks occurred in 2013, 2014,
92 and 2015 (8,735 total cases). In 2016, the most important dengue outbreak to date occurred,
93 with 41,233 confirmed autochthonous cases, 2,681 imported cases and 11 deaths
94 nationwide [12]. Imported cases by CHIKV were first reported in 2014, and in 2016, the
95 first autochthonous cases by CHIKV were reported [13]. Since 2015, ZIKV has been

96 confirmed in four provinces of Argentina, with a total of 871 cases (last case reported on
97 May 11, 2019) [14].

98 A notable aspect of the emergence of dengue in Argentina has been the expansion
99 of the southern distribution of the vector and virus into temperate latitudes of the Americas.
100 Córdoba (31.4°S, 64.2°W), the second largest city in Argentina (population 1.3 million)
101 has registered 1,429 dengue cases and all four dengue virus serotypes since the first
102 outbreak in 2009 through the end of 2018 [2]. *Aedes aegypti* was first detected in Córdoba
103 14 years prior [15]. Human movement plays a major role in dengue transmission in
104 Córdoba; it is hypothesized that the virus is re-introduced each year to trigger disease
105 transmission. Imported cases have been reported from dengue endemic regions including
106 Brazil, Bolivia, Venezuela, northern Argentina, Colombia, Mexico and Costa Rica [2].
107 Córdoba is an important place to investigate the emergence of arboviruses, as it is among
108 the southernmost cities in the Western Hemisphere to report autochthonous arbovirus
109 cases.

110 *Aedes aegypti* is an urban mosquito vector, living in and around human dwellings,
111 and feeding preferentially on human blood [16]. Arbovirus transmission by the mosquito
112 vector occurs from 18-34°C, due to the constraints of the ambient temperature on vector
113 physiology and life history traits [17]. *Aedes aegypti* juvenile habitat consist of water-
114 bearing containers such as tree holes to man-made cisterns, discarded bottles and tires [18].
115 Rainfall and drought can both potentially increase the availability of larval habitat,
116 depending on local water storage practices and housing characteristics [19,20].

117 Our current understanding of *Ae. aegypti* population dynamics in Argentina is
118 largely derived from prior studies on oviposition activity in the northern and central areas

119 of the country. Prior studies in the subtropical northwest region of Argentina revealed a
120 year-round vector population in areas with an annual mean temperature around 20ºC. A
121 low number of eggs was recorded during the winter season, and peak in oviposition was
122 detected during summer months (December to March in the southern hemisphere) [21–24].
123 Studies from the temperate central areas, like Buenos Aires [25–29] and Córdoba provinces
124 [30–32], found that oviposition discontinued during the winter months due to low
125 temperatures (below 17ºC), with a peak in *Ae. aegypti* during the warm, rainy summer
126 months, from October to April.

127 In response to the first dengue outbreak in Córdoba City in 2009, the province
128 promulgated the 9666 law, which created the "Master Plan to Fight Dengue", and other
129 diseases transmitted by the same vector [33]. Epidemiological and vector surveillance are
130 the responsibilities of the Epidemiology Area of the Zoonosis Program of the Ministry of
131 Health (MoH) of the province. The MoH began the *Ae. aegypti* surveillance and control
132 using larval surveys and ovitraps during the season of vector activity (October to May) in
133 cooperation with local academic partners. Vector surveillance is used to determine changes
134 in the distribution and density of the vector, to evaluate control programs, obtain relative
135 measurements of the vector population over time, and facilitate appropriate and timely
136 decisions regarding interventions [34]. In Córdoba, vector control is mostly focal around
137 homes with dengue cases, and includes control of adult mosquitoes by indoor and outdoor
138 fumigation, control of larval mosquitoes by *Bacillus thuringiensis israelensis* (BTI)
139 larvicide, and eliminating standing water [7].

140 Monitoring vector populations, disease cases, and local climate conditions can
141 provide important information for assessing arbovirus transmission risk [20,35,36,37].

142 However, the linkages between entomological risk, arbovirus risk, and local climate are
143 not always clear when comparing regions with distinct eco-epidemiological contexts (e.g.,
144 tropical endemic region versus temperate emergence region) and when different
145 entomological surveillance methodologies are used (e.g., ovitraps, larval surveys, adult
146 trapping). Studies in Puerto Rico, Vietnam, and Trinidad found that vector density
147 measurements were associated with dengue transmission [38–40]; however, studies in
148 Venezuela and Malaysia found no relation [41,42]. Few studies of this nature have been
149 conducted in temperate zones of arbovirus emergence.

150 To address this gap, this study aims to present the study design and findings from
151 the first 9 years of an entomological surveillance study that began in Córdoba following
152 the dengue emergence one decade ago. We also investigate the temporal dynamics of *Ae.*
153 *aegypti*, dengue cases, and local climate, and their lagged associations. The results of this
154 study can inform surveillance strategies, which are urgently needed to reduce disease risk
155 in settings of arbovirus emergence.

156

157 ## Methods

158 ### Ethics

159 Entomological data were collected from households by the MoH of Córdoba as part
160 of the routine surveillance program, thus no ethical review or informed consent was
161 required. For this analysis, weekly and monthly entomological data were aggregated to the
162 city-level, with no identifying information for households. Dengue case data at the city-
163 level were extracted from National MoH bulletins and aggregated to weekly and monthly
164 case counts; no identifying information was provided.

165 **Study site**

166 This study was conducted in the city of Córdoba (31.4°S, 64.2°W), which is located
167 in the central region of Argentina (elevation: 360-480 m above sea level) [43]. The city has
168 grown outward from the center to the periphery; agricultural fields with patches of forest
169 surround the urban core [44] (Fig 1). The local climate of Córdoba is warm temperate with
170 hot summers and four seasons (Cwa under the Köppen-Geiger classification system) [45].
171 On average, the city center is several degrees warmer than the urban periphery, due to
172 dense construction and location in a topographic depression [46]. Summer is a warm, rainy
173 season from November to March (monthly mean temp: 22.7°C, max temp: 37.6°C, min
174 temp: 11.8°C, monthly total rainfall: 123.2mm), and winter is a cool, dry season from June
175 to September (monthly mean temp: 14.8°C, max temp: 30.9°C, min temp: 2.4°C, monthly
176 total rainfall: 36.1mm). *Aedes aegypti* is the only known vector of dengue in Córdoba. The
177 vector does not reproduce (oviposit) during the winter, presumably due to cool
178 temperatures [31]; it is thought that the vectors persist through the cold season as egg.

179

180 **Fig 1**. **Location of Córdoba in South America** (A)**.** Show the lat/long lines, and the 5
181 sampling quadrants in the city (B).

182

183 Field studies were conducted under the *Ae. aegypti* surveillance program of the
184 Department of Epidemiology of the Córdoba Province Ministry of Health in cooperation
185 with the Córdoba Entomological Research Centre (CIEC) of Córdoba National University
186 (UNC) and the Biological and Technological Research Institute (IIByT) of Córdoba
187 National University (UNC) and the National Research Council (CONICET). No formal

188 ethical review or consent procedure was required for this study, as the field operations were
189 conducted as part of routine surveillance activities by the MoH. Entomological samples
190 were collected from households that verbally agreed to participate in the study and were
191 taken to the CIEC laboratory to be processed.
192
193 **Larval sampling**
194 From 2009 to 2017, the distribution and abundance of *Ae. aegypti* were monitored
195 through monthly larval surveys conducted across the city. Sample periods each year were
196 chosen by the CIEC laboratory team to span the period before, during and after mosquito
197 activity peak in the region [32]. Each month, 600 homes were randomly selected for
198 sampling. The city was divided into 215 quadrants (1.2 km per side), which were
199 distributed across five areas of approximately the same land area: Central, Northeast,
200 Northwest, Southeast, and Southwest (Fig 1). In each quadrant, we randomly selected 6
201 neighborhoods, and the field technicians randomly selected 20 homes to be inspected per
202 neighborhood.
203 At each home, an inspector noted all containers inside and outside the home with
204 standing water. Inspectors noted the presence of juvenile mosquitoes and collected
205 specimens for species identification. Whenever possible, all juvenile mosquitoes were
206 collected; for large containers where it was not possible to collect all specimens, an
207 inspector collected three samples using a white dipper (62 ml volume). Specimens were
208 transported to the CIEC laboratory; pupae were reared to adults, and 3rd and 4th instar larvae
209 were preserved in 80% ethanol and were identified using taxonomic keys [47]. First and
210 2nd instar larvae were reared until reaching the 3rd instar in plastic trays with 500 ml of

211 water from the natural larval habitat or dichlorine water. Each day larvae were fed 0.25 mg
212 of liver powder per larva, and we cleaned the surface of the water using absorbent paper to
213 avoid contamination by fungi and/or bacteria. The juvenile mosquitoes were counted and
214 identified to species. For the purposes of this study, data were aggregated to the city level
215 and we calculated the proportion of households and neighborhoods with juvenile *Ae.*
216 *aegypti* present during each sampling period.
217
218 **Ovitraps**
219 The weekly oviposition activity of *Ae. aegypti* was observed from November to
220 May over four years (2009 – 2013) using ovitraps, a sensitive method of detecting the
221 presence of gravid female of *Ae. aegypti* [48]. Ovitraps were placed in randomly selected
222 households (N=177) that were distributed evenly across the city. To assess oviposition
223 during the winter months, a subset of evenly distributed ovitraps (n=40) were selected to
224 continue sampling during June (late autumn-early austral winter seasons) to September
225 2010 (late winter-early austral spring seasons).
226 Ovitraps consisted of plastic bottles (350 ml volume, 8 cm diameter x 13 cm
227 height) with filter paper as an oviposition substrate. An attractive infusion (250 ml) was
228 prepared by fermenting dry cut grass with tap water [49]. Each week the traps were
229 inspected and replaced. Traps were transferred to the laboratory and the number of *Ae.*
230 *aegypti* eggs per trap were counted using a stereomicroscope. For the purposes of this
231 study, ovitrap data were aggregated to the city level. We calculated the proportion of traps
232 that were positive/negative for *Ae. aegypti* eggs and the mean number of eggs per trap
233 during each sampling period.

234 **Climate information**

235 The Argentinian National Meteorological Service provided daily weather data for
236 the study period (rainfall, min/mean/max temperature, min/mean/max relative humidity)
237 from the Observatory station (31.42°S; 64.20°W). This is one of the oldest weather stations
238 in Latin America (in operation since 1871) and the most reliable in Córdoba [50]. We
239 calculated summary monthly values (mean, standard deviation) over the study period,
240 summary values by epidemiologic week, and summary values corresponding with the
241 timing of ovitrap and larval survey collection periods.

242

243 **Dengue case data**

244 Weekly dengue case reports (January 2009 to December 2017) were extracted from
245 the weekly epidemiological bulletins of the Argentina Health Secretary [51]. Dengue
246 diagnostic procedures and case definitions have been previously described [2]. Data
247 extraction was described in detail previously [2]. Cases include suspected and laboratory
248 confirmed cases aggregated at the city-level and annual incidence was calculated using the
249 total city population for the corresponding year.

250

251 **Statistical analysis**

252 Statistical analyses were conducted at the city-level using R (version 3.3.3) in
253 RStudio (version 1.0.136), using the packages splines, TSA, geepack, MASS, lubridate,
254 TSimpute [52–58]. Missing values in the ovitrap data (n=10) were imputed via seasonally
255 decomposed structural modeling with Kalman smoothing. Missing values in the larval data
256 (n=20) were imputed via seasonally decomposed random selection. For each climate,

257 mosquito abundance, and dengue incidence variable, we performed a spectral analysis and
258 subsequently tested for the presence of inter-annual variability with a restricted cubic spline
259 using model fit to determine the periodic frequency and the number of knots. Models were
260 fit using a generalized linear model with appropriate distributions for each variable using
261 generalized estimating equations (auto-regressive correlation); best fit was determined
262 using quasi-likelihood information criteria (QIC) as compared to a null model. Residual
263 plots and model assumptions were examined to inform final model selection. Data were
264 analyzed in relation to the collection periods of each respective variable; means and
265 frequencies for these collection periods were calculated for reference.

266 We assumed a unidirectional temporal relationship between the variables as
267 follows: climate affecting all other variables, *Ae. aegypti* eggs affecting *Ae. aegypti* larvae
268 and dengue incidence, and *Ae. aegypti* larvae variables affecting dengue incidence. Both
269 local and imported cases were included in the analysis: local cases because they would
270 have been acquired within the local climate and mosquito population imported cases
271 because typical vacation periods (e.g. school vacations, holidays) coincide with specific
272 times of year and the climate conditions of those annual occurrences. To examine the
273 correlations between these variables, cross-correlation functions were calculated between
274 differenced monthly summary data for each variable with lags up to two months. We
275 selected this period as it is a biologically plausible period of time that includes the
276 combined time for *Ae. aegypti* egg hatching and larval development to adult mosquitoes.

277

278 **Results**

279 *Aedes aegypti* were detected over the entire study period, with the exception of the
280 winter months (June to September), where winter was sampled in 2010 only. Time series
281 of *Ae. aegypti* abundance and dengue cases are shown in Fig 2. Monthly mean temperature,
282 total precipitation, and mean daily relative humidity are shown in Fig 3. Annual (over a
283 season) and monthly summary statistics for *Ae. aegypti* eggs and larval abundance and
284 dengue incidence are shown in Figs 4-9. Summary statistics for all variables are in S1
285 Table.
286
287 **Fig 2. Time series of monthly dengue and *Aedes aegypti* abundance.** Top: Dengue cases.
288 Center: proportion of homes with juvenile *Aedes aegypti*. Bottom: proportion of ovitraps
289 (N=177) positive for *Aedes aegypti* and the mean number of eggs per ovitrap.
290
291 **Fig 3. Times series of monthly climate variables.** Mean monthly temperatures (°Celsius)
292 are in the top panel (red) (minimum and maximum in dashed lines), total monthly
293 precipitation (mm) is in the central panel (blue) and mean monthly relative humidity
294 (percentage) is in the bottom panel (green) (minimum and maximum in dashed lines).
295
296 **Fig 4. Seasonality in ovitrap *Aedes aegypti* egg counts and positivity (2009-2013).** Box
297 and whisker plots show the median and quartiles. Top: Number of *Aedes aegypti* eggs
298 collected per ovitrap. Bottom: The percent of ovitraps with *Aedes aegypti* eggs.
299
300 **Fig 5. Annual ovitrap *Aedes aegypti* eggs counts and positivity**. Box and whisker plots
301 show the median and quartiles for annual sampling season (November—May). Top:

302 Number of *Aedes aegypti* eggs collected per ovitrap per annual sampling season. Bottom:
303 The percent of ovitraps with *Aedes aegypti* eggs per annual sampling season.
304
305 **Fig 6. Seasonality in *Aedes aegypti* larval abundance (2009-2017).** Box and whisker
306 plots show the median and quartiles. Top: Percent of homes with water-bearing containers
307 with juvenile *Aedes aegypti*. Bottom: Percent of neighborhoods with water-bearing
308 containers with juvenile *Aedes aegypti*.
309
310 **Fig 7. Annual *Aedes aegypti* larval abundance**. Box and whisker plots show the median
311 and quartiles for annual sampling season (November—May). Top: Percent of homes with
312 water-bearing containers with juvenile *Aedes aegypti*. Bottom: Percent of neighborhoods
313 with water-bearing containers with juvenile *Aedes aegypti*.
314
315 **Fig 8. Total annual dengue cases.** Top: Total annual autochthonous dengue cases (no
316 travel history). Bottom: Total annual imported dengue cases.
317
318 **Fig 9. Seasonality in dengue cases (2009-2017).** Box and whisker plots show the median
319 and quartiles. Top: Counts of autochthonous dengue cases (no travel history). Bottom:
320 Counts of imported dengue cases.
321
322 *Aedes aegypti* egg abundance was highest in January (Fig 4), with a median of 33
323 eggs per trap and 61% of traps positive for eggs during this month. *Aedes aegypti* egg
324 abundance was highest in the 2009-10 and 2011-12 seasons (Fig 5), with a mean of 21 eggs
325 per ovitrap per month for both seasons, and 36.4% and 41.6% of traps positive for *Ae.*

326 *aegypti* eggs in 2009-10 and 2011-12, respectively. Note that ovitraps were used only until
327 2013 (4 collection seasons).

328 *Aedes aegypti* larval abundance was highest in March (residences) and February
329 (neighborhoods) in each year (Fig 6). During these months, 14% of residences and 85% of
330 neighborhoods had containers positive for larvae. There was a notable increase in *Ae.*
331 *aegypti* larval abundance, with the highest infestation levels detected in 2015-16 and 2016-
332 17 (Fig 7), with 14 and 15.8% of residences and 83.1 and 71.3% of neighborhoods having
333 containers positive for *Ae. aegypti* larvae in 2015-16 and 2016-17, respectively.

334 Dengue cases were highest during April across all years, with a local transmission
335 season from March to May (mean 65 autochthonous cases and mean 9 imported cases, Fig
336 8). The number of dengue cases was highest in 2016 (Fig 9), with 689 total autochthonous
337 and 139 total imported cases.

338

339 **Periodicity**

340 The results of the seasonal analysis for climate, mosquito abundance, and dengue
341 incidence variables are presented in Table 1. All climate variables were found to have a
342 12-month periodicity with nonlinear interannual variability, except for minimum relative
343 humidity, which had no interannual variability, and maximum relative humidity, which
344 had no periodicity nor interannual variability (*i.e.* temporal trend).

345

346 **Table 1. Seasonality and Interannual Variability of Data.**

Variable	Frequency of Season	Period Frequency	Mean Timing of Seasonal Peak	Shape of Interannual Variability

Climate	Minimum Temperature	12 months	annual	early June	non-linear
	Mean Temperature	12 months	annual	late May	non-linear
	Maximum Temperature	12 months	annual	early May	non-linear
	Total Precipitation	12 months	annual	early June	non-linear
	Minimum Relative Humidity	12 months	annual	early August	none
	Mean Relative Humidity	12 months	annual	late August	non-linear
	Maximum Relative Humidity	none	na	na	none
Eggs	% Positive Traps	27 periods[A]	~annual	na	none
	Mean Number of Eggs per Trap	27, 53 periods[A]	~annual, every 2 years	na	non-linear
Larvae	Positive Homes	none	na	na	none
	Positive Neighborhoods	5 & 50 periods[B]	~annual, every 10 years	na	non-linear
Dengue Incidence	Autochthonous	24 & 45.5 periods[C]	~twice per year, ~annual	na	non-linear
	Imported	60.2 & 120.7 periods[C]	~every 1.5 years, ~every 3 years	na	non-linear

For each variable, the seasonal frequency and presence of interannual variability for the best-fit model is reported, with period frequency included for those variables with partial-year collection periods. For variables with an annual seasonality, the timing of the seasonal peak is also reported.

na=not applicable

[A]On average, collection periods were every 7 days and occurred 26 times in a collection season (November—May).

[B]On average, collection periods were every 39 days and occurred six times in a collection season (September—May)

[C]On average, surveillance frequency was 8 days and occurred 39 times in a year

359 *Aedes aegypti* eggs were collected from ovitraps every 7 days on average; an
360 average of 26 times within each collection season. Both *Ae. aegypti* egg abundance
361 variables (trap positivity and mean number of eggs) exhibited a peak about once each year
362 on average, and the mean number of eggs had an additional peak occurring every 2 years
363 on average. Trap positivity had no interannual variability while the mean number of eggs
364 had nonlinear interannual variability.

365 Over the study period, on average, *Ae. aegypti* larvae were collected every 39 days,
366 six times per collection season. *Aedes aegypti* larvae abundance variables (proportion of
367 positive homes, proportion of positive neighborhoods) were found to have different
368 seasonal patterns: there was no periodicity nor interannual variability for the proportion of
369 positive homes, but the proportion of positive neighborhoods peaked once per year, as well
370 as every 10 years.

371 Dengue surveillance reports of autochthonous and imported cases occurred every 8
372 days on average; an average of 39 times per year. Autochthonous dengue incidence peaked
373 approximately twice per year and annually. Imported dengue incidence peaked
374 approximately every 1.5 and 3 years. There was no interannual variability in autochthonous
375 or imported dengue incidence.

376

377 **Cross correlation analysis**

378 The results of the cross-correlation between *Ae. aegypti* eggs and larval abundance,
379 climate, and dengue incidence variables are shown in Table 2. *Aedes aegypti* egg
380 abundance (mean number of eggs per ovitrap) was positively correlated with mean
381 temperature in the same month. *Aedes aegypti* larval abundance (percent of neighborhoods

382 with positive larval traps) was positively correlated with minimum temperature in the same
383 month, while the percentage of residences with positive larval traps was not correlated with
384 any climate variable. Autochthonous dengue incidence was negatively correlated with
385 mean and maximum temperature at lag 2, and negatively correlated with total precipitation
386 in the same month, with no correlation to any relative humidity variables. Imported dengue
387 incidence was negatively correlated with mean temperature at lag 2, positively correlated
388 with minimum relative humidity at lag 1, and correlated with total precipitation in the same
389 month (positively) and at lag 1 (negatively). *Aedes aegypti* egg abundance was not
390 correlated with autochthonous nor imported dengue incidence. *Aedes aegypti* egg
391 abundance was positively correlated with the percent of neighborhoods with positive larval
392 traps at lag 1. *Aedes aegypti* larvae abundance (percent of neighborhoods with positive
393 larval traps) was negatively correlated with autochthonous dengue incidence at lag 1; both
394 percent of neighborhoods and percent of residences with positive larval traps were
395 positively correlated with imported dengue incidence in the same month.
396

397 **Table 2. Cross-Correlation Between Climate, Mosquito Abundance, and Dengue**
398 **Cases for 2009—2017.**

Pairing	Variable A	Variable B	Correlated Lags	Direction of Correlation
Climate & Egg Abundance	Min Temp	Mean Number of Eggs	none	
	Mean Temp		0 months	positive
	Max Temp		none	
	Min Rel Humidity		none	
	Mean Rel Humidity		none	
	Max Rel Humidity		none	
	Total Precipitation		none	
Climate & Larvae Abundance	Min Temp	% Positive Homes	none	
	Mean Temp		none	
	Max Temp		none	
	Min Rel Humidity		none	
	Mean Rel Humidity		none	

	Max Rel Humidity		none	
	Total Precipitation		none	
	Min Temp	% Positive Neighborhoods	0 months	positive
	Mean Temp		none	
	Max Temp		none	
	Min Rel Humidity		none	
	Mean Rel Humidity		none	
	Max Rel Humidity		none	
	Total Precipitation		none	
Climate & Dengue Incidence	Min Temp	Autochtonous Dengue Incidence	none	
	Mean Temp		2 months	negative
	Max Temp		2 months	negative
	Min Rel Humidity		none	
	Mean Rel Humidity		none	
	Max Rel Humidity		none	
	Total Precipitation		0 months	negative
	Min Temp	Imported Dengue Incidence	none	
	Mean Temp		2 months	negative
	Max Temp		none	
	Min Rel Humidity		1 months	positive
	Mean Rel Humidity		none	
	Max Rel Humidity		none	
	Total Precipitation		0, 1 months	positive, negative
Mosquito Egg & Dengue Incidence	Mean Eggs/ovitrap	Autochtonous Dengue Incidence	none	
		Imported Dengue Incidence	none	
Mosquito Egg & Larvae Abundance	Mean Eggs/ovitrap	% Positive Homes	none	
		% Positive Neighborhoods	1 months	positive
Mosquito Larvae Abundance & Dengue Incidence	Positive Homes	Autochtonous Dengue Incidence	none	
	Positive Neighborhoods		1 months	negative
	Positive Homes	Imported Dengue Incidence	0 months	positive
	Positive Neighborhoods		0 months	positive

Using the cross-correlation function, we examined the correlation between pairs of variables, with variable A hypothesized to occur 0 to 2 months before variable B.

Discussion

Here we describe the seasonal and interannual patterns of climate, *Ae. aegypti* eggs and larval abundance, and dengue transmission in the temperate city of Córdoba, Argentina, one decade after the first epidemic of dengue. We identified a notable increase in the proportion of homes with juvenile *Ae. aegypti* (from 5.7% of homes in 2009-10 to

407 15.4% of homes in 2016-17), suggesting an increased risk of arbovirus transmission in the
408 region.

409 Climate is a critical driver of *Ae. aegypti* eggs and larval abundance and dengue
410 incidence. Long-term and seasonal patterns of dengue vary around the globe, with some
411 locations experiencing stable transmission throughout the year and other experiencing
412 single or multiple dengue seasons within each year [59–63]. We found that the
413 temperatures of Córdoba were warm enough to support survival and breeding of *Ae.*
414 *aegypti* populations from October to April. We found that *Ae. aegypti* eggs and larval
415 abundance peaked once annually (from January to March), followed by a peak in
416 autochthonous dengue transmission in April. Prior studies from Córdoba found that *Ae.*
417 *aegypti* egg-to-adult survival began at mean minimum ambient temperatures greater than
418 13°C [32], suggesting that *Ae. aegypti* populations in Córdoba are not likely to survive
419 from May to September, when temperatures drop below this threshold. Thus, these findings
420 indicate that the temporal window for a stable *Ae. aegypti* population in Córdoba is very
421 short, limiting the period of potential autochthonous dengue transmission. Indeed, Estallo
422 *et al*. [11] showed that low autumnal temperatures were an important factor limiting the
423 spread of dengue during the first dengue outbreak in 2009.

424 Ambient temperatures were associated with vector abundance, as expected from
425 the thermal biology of ectothermic mosquito vectors [64]. We found that the mean number
426 of eggs per ovitrap was positively associated with mean temperature; the number of eggs
427 laid per female of *Ae. aegypti* is closely linked to temperature [17]. As we would expect
428 from thermal limits of egg-to-adult survival [17], larval abundance (neighborhoods) was
429 correlated with minimum temperature. Whether a particular abundance measure is best

430 correlated to minimum or mean temperature likely has to do with how well these particular
431 measures represent the day-to-day temperature-mosquito dynamics that are occurring
432 within Córdoba. Our data represent monthly summaries that vary in their ability to
433 precisely detect the complex relations between climate and mosquitos. The vector activity
434 in the temperate Córdoba city begins after low winter temperatures. Larvae probably
435 hatched from eggs laid during the previous season. In Córdoba vector activity decreases at
436 low autumnal temperatures until adults die. Grech *et al*. [65] found that, for Córdoba city,
437 once the ambient temperature has become greater than the thermal threshold (11.11ºC),
438 93.7 degree-days are necessary to for larval-pupa development and adult emergence to be
439 completed.

440 While we would not expect imported dengue cases to be affected by local *Ae.*
441 *aegypti* populations, imported cases also peak annually in March. This pattern could be
442 caused by human movement within and outside the country, as this is a significant risk
443 factor for dengue emergence in a non-endemic city like Córdoba [11]. For example, during
444 2009 dengue outbreak in the city, the introduction of DENV was associated with outbreaks
445 in the neighboring countries of Bolivia, Brazil and Paraguay at the end of 2008, and also
446 with dengue transmission in the Northern provinces of Argentina, where 92% of dengue
447 cases occurred [11]. It is likely that human movement into Córdoba from neighboring areas
448 corresponds with summer breaks in school schedules in Argentina (December-February)
449 before university classes begin each year in March. An estimated 60% of the ~132,000
450 university students in the National University of Córdoba originate from other provinces
451 or countries [66,67]. Therefore, cases of dengue could be imported by students who travel
452 between Córdoba and northern provinces and people vacationing in tropical dengue

453 endemic countries. Additionally, cases could be imported by migrant workers traveling to
454 and from endemic countries, like Bolivia and Paraguay.

455 Autochthonous dengue transmission was negatively correlated with several
456 variables such as temperature and precipitation, which was somewhat unexpected. As
457 temperatures declined towards the later part of the season of vector activity (end of
458 summer), dengue transmission increased. As previously indicated, this may be related to
459 the timing of the importation of dengue virus from people traveling from neighboring
460 endemic regions.Transmission peaked in April, when mean daily temperatures were 18ºC
461 (mean min temp = 13.6ºC, mean max temp = 25.5ºC). Prior studies reported that arbovirus
462 transmission by *Ae. aegypti* declined to zero below 17.8ºC (lower thermal limit) [17]. We
463 hypothesize that local *Ae. aegypti* populations have adapted to cooler climate conditions,
464 while at the same time local climate conditions have warmed to permit arbovirus
465 transmission at the lower thermal limit [64].

466 We found that monthly juvenile *Ae. aegypti* abundance was not associated with
467 either autochthonous or imported dengue cases, confirming prior studies in Córdoba [11].
468 Several possible explanations are as follows: (1) surveillance of juvenile vectors did not
469 capture the entomological risk presented by adults of *Ae. aegypti;* (2) spatial variation in
470 entomological risk leads to localized hotspots of transmission risk that are not captured in
471 the aggregated city-level data; and (3) in a zone of emergence, a high proportion of the
472 population is immunologically naive to dengue, thus transmission depends on the timing
473 of the introduction of the virus and may be sustained with low vector densities. Prior studies
474 also found that dengue transmission was not associated with vector densities. In Brazil,

475 dengue transmission was most closely related to the movement of viremic humans rather
476 than vector densities [68].

477 As indicated by the appearance and continued transmission of dengue in Córdoba,
478 the city, along with other parts of temperate Argentina, are actively experiencing the
479 emergence of dengue [1,2]. Emergence of dengue in temperate regions has been occurring
480 with more frequency in the past two decades [69–71] as climate becomes increasingly
481 favorable for *Ae. aegypti* in Argentina, and increase their distribution and active periods of
482 the year. Our study highlighted significant relationships between temperature and
483 mosquito indices, indicating that climate is potentially playing an important role in the
484 emergence of dengue in Córdoba; however, our study was not conclusive on the
485 environmental drivers of vector activity and dengue transmission in the city and highlights
486 the need to conduct further studies investigating emergence. In particular, studies of human
487 movement, including origins, destinations, and timing, throughout South America will be
488 critical to understanding patterns of emergence of dengue and other arboviruses in
489 Córdoba. Further, our study, independently and combined with future studies, will be
490 helpful in understanding dengue emergence on a more global scale. The data presented
491 here is one of the most comprehensive databases describing dengue emergence and drivers
492 thereof that is currently available and our study is among few such studies investigating
493 arbovirus emergence in a temperate climate as it is actively occurring.

494 Our results can be used to guide surveillance and control efforts in this region.
495 Based on *Ae. aegypti* egg abundance variables (trap positivity and mean number of eggs)
496 exhibiting a peak once per collection season, we suggest public health authorities to make
497 vector management and educational campaigns before the occurrence of peaks to prevent

498 the spread of larvae. Juvenile vector surveillance is a useful tool to detect temporal
499 variation, and we recommend the maintenance of surveillance through ovitraps and larval
500 surveys. Alternative surveillance and control strategies, such as novel adult traps, should
501 also be explored [72,73]. Our results also suggest the potential to develop climate services
502 to support the public health sector [74]. For example, if seasonal climate forecasts are
503 shared on a regular basis with the health sector, this information can potentially be used to
504 predict when there will be an increase in vector abundance and disease transmission risk,
505 as done demonstrated in dengue endemic regions [19,75]. Climate services, such as
506 climate driven early warning systems to predict arbovirus transmission risk, can leverage
507 the existing robust entomological and climate surveillance and monitoring systems.

508 Empirical studies such as this, from the lower thermal range of arbovirus
509 transmission, can be used to improve models that investigate arbovirus dynamics in
510 temperate zones of emergence, predict future outbreaks, and explore potential control
511 measures. Understanding seasonal variability in vector populations and dengue
512 transmission that is potentially driven by variability in temperature, precipitation, and/or
513 humidity is crucial to understanding periods of the year in which risk of dengue
514 transmission is highest [59,76,77]. For example, our study indicates that meteorological
515 variables such as mean and maximum temperature and minimum relative humidity are
516 significantly correlated with dengue transmission at one- or two-month lags (Table 2). By
517 combining this information with known mechanistic relationships between meteorological
518 variables and mosquito population and dengue transmission parameters, models can help
519 to predict transmission or windows of risk of transmission utilizing meteorological indices.
520 This, in turn, can help inform mathematical models for studying the potential impacts of

521 vector and disease control measures so that the most appropriate control measures can be
522 implemented at optimal times to have the greatest impact on reducing dengue transmission.
523 Furthermore, well-characterized relationships between vector dynamics and arbovirus
524 transmission and current typical meteorological conditions are important for providing
525 baseline information for mathematical models that can be utilized to better understand how
526 changes in climate, such as increased average temperatures and extreme deviations in
527 precipitation patterns, may alter the potential for arbovirus emergence and spread in the
528 future [64,78,79].

529 It is important to note that we do not expect that the correlations between climate
530 or mosquito abundance and imported dengue case incidence to be causal in any way. Cross-
531 correlation analyses do not adjust for potential confounding and we expect that the
532 correlation found is due to the coincidental timing of Argentina vacation periods and peak
533 larval activity. One limitation of our work is irregular sampling in the surveillance data,
534 creating gaps in some periods, though the sampling design was strong and carefully
535 designed by the team of researchers at the CIEC.

536

537 **Conclusions**

538 This longitudinal study provides insights into the complex dynamics of arbovirus
539 transmission and vector populations in a temperate region of arbovirus emergence. Studies
540 such as this provide critical local-level information to guide public health interventions.
541 Our findings suggest that Córdoba is well suited for arbovirus disease transmission, given
542 the stable and abundant vector populations. It is possible that the region may shift from

epidemic to endemic dengue transmission if measures are not taken to reduce vector populations and disease transmission.

Conflict of interest

The authors report no conflicts of interest.

Acknowledgements

The authors wish to acknowledge the United States Embassy in Argentina and Fulbright Commission as well as the Department of Epidemiology of the Córdoba Province Ministry of Health. AMSI and MAR were support in Córdoba Argentina by the USA Zika program of the United States Embassy in Argentina administrated by Fulbright commission. ELE, MGG, and WRA is a member of the Consejo de Investigaciones Cientificas y Tecnologicas (CONICET) from Argentina, EMB is a PhD Student with scholarship support from CONICET.

558 **References**

559 1. Masuh H. Re-emergence of dengue in Argentina: Historical development and
560 future challenges. Dengue Bull. 2008; 32: 44-54.
561 2. Arbovirus emergence in the temperate city of Córdoba, Argentina, 2009–2018.
562 3. Robert MA, Tinunin DT, Benitez EM, Ludueña-Almeida F, Romero M, Stewart-
563 Ibarra AM, et al. Arbovirus emergence in the temperate city of Córdoba, Argentina,
564 2009-2018. Scientific Data. 2019; 6:276. Available from:
565 https://doi.org/10.1038/s41597-019-0295-z.
566 4. Cohen J. The race for a Zika vaccine is on. Science. 2016; 351: 543–544.
567 5. Smalley C, Erasmus JH, Chesson CB, Beasley DW. Status of research and
568 development of vaccines for chikungunya. Vaccine. 2016; 34: 2976–2981.
569 6. Vannice KS, Durbin A, Hombach J. Status of vaccine research and development of
570 vaccines for dengue. Vaccine. 2016; 34: 2934–2938.
571 7. WHO. Zika virus. World Health Organization [Cited 2016 Feb 24]. Available from:
572 http://www.who.int/mediacentre/factsheets/zika/en/.
573 8. Plan nacional para la prevención y el control del dengue y la fiebre amarilla; 2009
574 [cited 2018 Apr 25]. Available from:
575 http://www.msal.gob.ar/images/stories/cofesa/2009/acta-02-09/anexo-5-resumen-
576 plan-dengue-02-09.pdf.
577 9. Curto S, Boffi R, Carbajo AE, Plastina R, Schweigmann N. Reinfestación del
578 territorio Argentino por *Aedes aegypti*. Distribución geográfica (1994-1999). In:
579 Salomón OD, editor. Actualizaciones en Artropodología Sanitaria Argentina.
580 Buenos Aires: Fundación Mundo Sano; 2002. pp. 127–137.

10. Avilés G, Rangeón G, Vorndam V, Briones A, Baroni P, Enria D, et al. Dengue reemergence in Argentina. Emerg Infect Dis. 1999; 5: 575.
11. Vezzani D, Carbajo AE. *Aedes aegypti*, *Aedes albopictus*, and dengue in Argentina: current knowledge and future directions. Mem Inst Oswaldo Cruz. 2008; 103: 66–74.
12. Estallo EL, Carbajo AE, Grech MG, Frías-Céspedes M, López L, Lanfri MA, et al. Spatio-temporal dynamics of dengue 2009 outbreak in Córdoba City, Argentina. Acta Trop. 2014; 136: 129-136.
13. Dirección nacional de epidemiología y análisis de la situación de salud. Boletín integrado de vigilancia: No. 341, SE 52; 2016 [cited 2019 Apr 17]. Available from: https://www.argentina.gob.ar/sites/default/files/boletin_integrado_vigilancia_n341-se52.pdf.
14. Dirección nacional de epidemiología y análisis de la situación de salud. Boletin Integrado de Vigilancia: No. 327, SE 37; 2016 [cited 2018 Jul 10]. Available from: http://www.msal.gob.ar/images/stories/boletines/Boletin-Integrado-De-Vigilancia-N327-SE37.pdf.
15. PAHO. PLISA Health Information Platform for the Americas. Pan American Health Organization / World Health Organization; 2019 [cited 2019 Oct 8]. Available from: http://www.paho.org/data/index.php/en/?option=com_content&view=article&id=524&Itemid=.
16. Almirón WR, Ludueña-Almeida F. *Aedes aegypti* (Diptera: Culicidae) en Córdoba, Argentina. Rev Soc Entomol Argent. 1998; 57: 27-28.

604 17. WHO. Dengue: guidelines for diagnosis, treatment, prevention and control. World
605 Health Organization; 2009 [cited 2018 Apr 28]. Available from:
606 https://apps.who.int/iris/handle/10665/44188
607 18. Mordecai EA, Cohen JM, Evans MV, Gudapati P, Johnson LR, Lippi CA, et al.
608 Detecting the impact of temperature on transmission of Zika, dengue, and
609 chikungunya using mechanistic models. PLoS Negl Trop Dis. 2017; 11: e0005568.
610 19. Manrique-Saide P, Che-Mendoza A, Rizzo N, Arana B, Pilger D, Lenhart A, et al.
611 Operational guide for assessing the productivity of *Aedes aegypti* breeding sites.
612 Geneva Switz WHO-TDR. 2011; pp. 1–30.
613 20. Lowe R, Gasparrini A, Van Meerbeeck CJ, Lippi CA, Mahon R, Trotman AR, et
614 al. Nonlinear and delayed impacts of climate on dengue risk in Barbados: A
615 modelling study. PLoS Med. 2018; 15: e1002613.
616 21. Stewart Ibarra AM, Ryan SJ, Beltrán E, Mejía R, Silva M, Muñoz Á. Dengue
617 Vector Dynamics (*Aedes aegypti*) Influenced by Climate and Social Factors in
618 Ecuador: Implications for Targeted Control. PLoS One. 2013; 8: e78263.
619 22. Micieli MV, Campos RE. Oviposition activity and seasonal pattern of a population
620 of *Aedes* (*Stegomyia*) *aegypti* (L.) (Diptera: Culicidae) in subtropical Argentina.
621 Mem Inst Oswaldo Cruz. 2003; 98: 659–63.
622 23. Estallo EL, Benitez EM, Lanfri MA, Scavuzzo CM, Almirón WR. MODIS
623 environmental data to assess Chikungunya, Dengue, and Zika diseases through
624 *Aedes* (*Stegomia*) *aegypti* oviposition activity estimation. IEEE J Sel Top Appl
625 Earth Obs Remote Sens. 2016; 9: 5461–5466.

24. Estallo EL, Más G, Vergara-Cid C, Lanfri MA, Ludueña-Almeida F, Scavuzzo CM, et al. Spatial patterns of high *Aedes aegypti* oviposition activity in northwestern Argentina. PLoS One. 2013; 8: e54167.
25. Estallo EL, Ludueña-Almeida FF, Introini MV, Zaidenberg M, Almirón WR. Weather variability associated with *Aedes* (*Stegomyia*) *aegypti* (Dengue vector) Oviposition dynamics in northwestern Argentina. PLoS One. 2015; 10: e0127820.
26. Campos RE, Maciá A. Observaciones biológicas de una población natural de *Aedes aegypti* (Diptera: Culicidae) en la provincia de Buenos Aires, Argentina. Rev Soc Entomol Argent. 1996; 55: 67–72.
27. Carbajo AE, Gómez SM, Curto SI, Schweigmann NJ. Variación espacio-temporal del riesgo de transmisión de dengue en la Ciudad de Buenos Aires. Med B Aires. 2004; 64: 231–234.
28. Carbajo AE, Curto SI, Schweigmann NJ. Spatial distribution pattern of oviposition in the mosquito *Aedes aegypti* in relation to urbanization in Buenos Aires: southern fringe bionomics of an introduced vector. Med Vet Entomol. 2006; 20: 209–218.
29. Vezzani D, Velázquez SM, Schweigmann N. Seasonal pattern of abundance of *Aedes aegypti* (Diptera: Culicidae) in Buenos Aires city, Argentina. Mem Inst Oswaldo Cruz. 2004; 99: 351–356.
30. Micieli MV, García JJ, Achinelly MF, Martí GA. Dinámica poblacional de los estadios inmaduros del vector del dengue *Aedes aegypti* (Diptera: Culicidae): un estudio longitudinal (1996-2000). Rev Biol Trop. 2006; 54: 979–983.

31. Avilés G, Cecchini R, Harrington ME, Cichero J, Asis R, Rios C. *Aedes aegypti* in Córdoba province, Argentina. J Am Mosq Control Assoc Mosq News. 1997; 13: 255–258.

32. Grech MG. Bioecología de culícidos (Diptera) urbanos de importancia sanitaria de la ciudad de Córdoba, Córdoba (Argentina). PhD. Thesis in Biological Sciences, National University of Córdoba. 2013. Available from: https://catalogo.biblio.unc.edu.ar/Record/exactas.25342/Description#tabnav

33. Domínguez MC, Ludueña Almeida FF, Almirón WR. Dinámica poblacional de *Aedes aegypti* (Diptera: Culicidae) en Córdoba capital. Rev Soc Entomol Argent. 2000; 59: 41–50.

34. Constitución de la provincia de Córdoba; 2001 [cited 2018 May 3]. Available from: http://www.infoleg.gob.ar/basehome/ConstituciondeCordoba.htm.

35. Focks DA. A review of entomological sampling methods and indicators for dengue vectors. Geneva World Health Organization; 2003 [cited 2013 May 7]. Available from: http://203.90.70.117/PDS_DOCS/B0219.pdf#page=233.

36. Barrera R, Navarro JC, Mora JD, Dominguez D, Gonzalez J. Public service deficiencies and *Aedes aegypti* breeding sites in Venezuela. Bull Pan Am Health Organ. 1995; 29: 193–205.

37. Arunachalam N, Tana S, Espino F, Kittayapong P, Abeyewickrem W, Wai KT, et al. Eco-bio-social determinants of dengue vector breeding: a multicountry study in urban and periurban Asia. Bull World Health Organ. 2010; 88: 173–184.

38. Benitez EM, Estallo EL, Grech M, Frías-Céspedes M, Almirón WR, Ludueña-Almeida FF. Temporal models using environmental variables to predict *Aedes*

670 *aegypti* oviposition activity in a temperate region of Argentina. BioRxiv [Preprint].
671 2019 bioRxiv 816421[posted 2019 Oct 23; cited 2019 Oct 30]: [29 p.]. Available
672 from: https://www.biorxiv.org/content/10.1101/816421v1 doi: 10.1101/816421
673 39. Chadee DD. Dengue cases and *Aedes aegypti* indices in Trinidad, West Indies. Acta
674 Trop. 2009; 112: 174–180.
675 40. Barrera R, Amador M, MacKay AJ. Population dynamics of *Aedes aegypti* and
676 Dengue as influenced by weather and human behavior in San Juan, Puerto Rico.
677 PLoS Negl Trop Dis. 2011; 5: e1378.
678 41. Pham H, Doan H, Phan T, Minh NT. Ecological factors associated with dengue
679 fever in a central highlands Province, Vietnam. BMC Infect Dis. 2011; 11: 172.
680 42. Sulaiman S, Pawanchee ZA, Arifin Z, Wahab A. Relationship between Breteau and
681 House indices and cases of dengue/dengue hemorrhagic fever in Kuala Lumpur,
682 Malaysia. J Am Mosq Control Assoc. 1996; 12: 494-496.
683 43. Barrera R, Delgado N, Jiménez M, Valero S. Eco-epidemiological factors
684 associated with hyperendemic dengue haemorrhagic fever in Maracay City,
685 Venezuela. Dengue Bull. 2002; 26: 84–95.
686 44. INDEC. Censo Nacional de Población, Hogares y Viviendas 2010; 2010 [cited
687 2019 Apr 18]. Available from:
688 https://www.indec.gob.ar/censos_provinciales.asp?id_tema_1=2&id_tema_2=41
689 &id_tema_3=135&p=14&d=999&t=0&s=0&c=2010.
690 45. Maristany A, Abadía L, Angiolini S, Pacharoni A, Pardina M. Estudio del
691 fenómeno de la isla de calor en la ciudad de Córdoba-Resultados preliminares. Av
692 Energ Renov Medio Ambient. 2008; 12: 11–69.

46. Peel MC, Finlayson BL, McMahon TA. Updated world map of the Köppen-Geiger climate classification. Hydrol Earth Syst Sci Discuss. 2007; 4: 439–473.

47. Asar ML, Estallo EL, Benítez EM, Di Benedetto HM, Ludueña-Almeida FF. Un estudio sobre el efecto Isla de Calor Urbano en la ciudad de Córdoba, Argentina. EIDIPA+UNC 2019. Tercer encuentro interdisciplinario de investigaciones en problemáticas ambientales de la Universidad Nacional de Córdoba.

48. Darsie Jr RF. Mosquitoes of Argentina. I. Keys for identification of adult females and fourth stage larvae in English and Spanish (Diptera, Culicidae). Mosq Syst. 1985; 17: 153-253.

49. Fay RW, Eliason DA. A preferred oviposition site as a surveillance method for *Aedes aegypti*. Mosq News. 1966; 26: 531–535.

50. Reiter P, Amador MA, Colon N. Enhancement of the CDC ovitrap with hay infusions for daily monitoring of *Aedes aegypti* populations. J Am Mosq Control Assoc. 1991; 7: 52-55.

51. de la Casa A, Nasello O. Breakpoints in annual rainfall trends in Córdoba, Argentina. Atmos Res. 2010; 95: 419–427.

52. Ministerio de Salud de Nación. Boletines Epidemiologicos; 2009-2019 [cited 2018 Apr 28]. Available from: https://www.argentina.gob.ar/salud/epidemiologia/boletinesepidemiologicos.

53. RStudio Team (2015). RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/.

54. Moritz S, Bartz-Beielstein T. ImputeTS: time series missing value imputation in R. R J. 2017; 9: 207–218.

716 55. Grolemund G, Wickham H. Dates and times made easy with lubridate. J Stat Softw.
717 2011; 40: 1–25.
718 56. Bates MD, Venables B. Team MRC. Package 'splines.' R Version. 2011.
719 57. Chan K-S, Ripley B. TSA: time series analysis. R package version 1.01; 2012 [cited
720 2018]. Available from: https://CRAN.R-project.org/package=TSA
721 58. Halekoh U, Højsgaard S, Yan J. The R package geepack for generalized estimating
722 equations. J Stat Softw. 2006; 15: 1–11.
723 59. Venables WN, Ripley BD. Modern applied statistics with S-PLUS. 4th ed. New
724 York: Springer Science & Business Media; 2013.
725 60. Sippy R, Herrera D, Gaus D, Gangnon RE, Patz JA, Osorio JE. Seasonal patterns
726 of dengue fever in rural Ecuador: 2009-2016. PLoS Negl Trop Dis. 2019; 13:
727 e0007360.
728 61. Stoddard ST, Wearing HJ, Reiner RC, Morrison AC, Astete H, Vilcarromero S, et
729 al. Long-term and seasonal dynamics of Dengue in Iquitos, Perú. PLoS Negl Trop
730 Dis. 2014; 8: e3003.
731 62. Eastin MD, Delmelle E, Casas I, Wexler J, Self C. Intra-and interseasonal
732 autoregressive prediction of dengue outbreaks using local weather and regional
733 climate for a tropical environment in Colombia. Am J Trop Med Hyg. 2014; 91:
734 598–610.
735 63. Stewart-Ibarra AM, Lowe R. Climate and non-climate drivers of dengue epidemics
736 in southern coastal Ecuador. Am J Trop Med Hyg. 2013; 88: 971–981.
737 64. Stewart Ibarra AM, Munoz AG, Ryan SJ, Borbor MJ, Ayala EB, Finkelstein JL, et
738 al. Spatiotemporal clustering, climate periodicity, and social-ecological risk factors

739 for dengue during an outbreak in Machala, Ecuador, in 2010. BMC Infect Dis.
740 2014; 14: 610.
741 65. Mordecai EA, Caldwell JM, Grossman MK, Lippi CA, Johnson LR, Neira M, et al.
742 Thermal biology of mosquito-borne disease. Ecol Lett. 2019; 22: 1690–708.
743 66. Grech MG, Sartor PD, Almirón WR, Ludueña-Almeida FF. Effect of temperature
744 on life history traits during immature development of *Aedes aegypti* and *Culex*
745 *quinquefasciatus* (Diptera: Culicidae) from Córdoba city, Argentina. Acta Trop.
746 2015; 146: 1-6.
747 67. Centenario de la Reforma Universitaria. La UNC en cifras. [cited 2019 Oct 8].
748 Available from: https://centenariodelareforma.unc.edu.ar/la-unc-en-cifras/.
749 68. Telediario Digital. Población estudiantil: bajo la lupa de la UNC. [cited 2019 Oct
750 8]. Available from: https://www.telediariodigital.net/2014/11/poblacion-
751 estudiantil-bajo-la-lupa-de-la-unc/.
752 69. Honório N, Codeço C, Alves F, Magalhães M, Lourencco-de-Oliveira R. Temporal
753 distribution of *Aedes aegypti* in different districts of Rio de Janeiro, Brazil,
754 measured by two types of traps. J Med Entomol. 2009; 46: 1001–1014.
755 70. Messina JP, Brady OJ, Scott TW, Zou C, Pigott DM, Duda KA, et al. Global spread
756 of dengue virus types: mapping the 70 year history. Trends Microbiol. 2014; 22:
757 138–46.
758 71. Radke EG, Gregory CJ, Kintziger KW, Sauber-Schatz EK, Hunsperger EA,
759 Gallagher GR, et al. Dengue outbreak in key west, Florida, USA, 2009. Emerg
760 Infect Dis. 2012; 18: 135-137.

761 72. Lourenço J, Recker M. The 2012 Madeira Dengue outbreak: epidemiological
762 determinants and future epidemic potential. PLoS Negl Trop Dis. 2014; 8: e3083.
763 73. Ritchie SA, Long S, Smith G, Pyke A, Knox TB. Entomological investigations in
764 a focus of dengue transmission in Cairns, Queensland, Australia, by using the sticky
765 ovitraps. J Med Entomol. 2004; 41: 1–4.
766 74. Barrera R, Amador M, Acevedo V, Caban B, Felix G, Mackay AJ. Use of the CDC
767 autocidal gravid ovitrap to control and prevent outbreaks of *Aedes aegypti* (Diptera:
768 Culicidae). J Med Entomol. 2014; 51: 145–154.
769 75. Global framework for climate services. Health Exemplar to the user interface
770 platform of the Global Framework for Climate Services. Geneva, Switzerland:
771 World Meteorological Association; 2014 [cited 2018 Nov 18]. Available from:
772 http://www.gfcs-climate.org/sites/default/files/Priority-Areas/Health/GFCS-
773 HEALTH-EXEMPLAR-FINAL-14152_en.pdf.
774 76. Lowe R, Stewart-Ibarra AM, Petrova D, García-Díez M, Borbor-Cordova MJ,
775 Mejía R, et al. Climate services for health: predicting the evolution of the 2016
776 dengue season in Machala, Ecuador. Lancet Planet Health. 2017; 1: e142–e151.
777 77. Huber JH, Childs ML, Caldwell JM, Mordecai EA. Seasonal temperature variation
778 influences climate suitability for dengue, chikungunya, and Zika transmission.
779 PLoS Negl Trop Dis. 2018; 12: e0006451.
780 78. Robert MA, Christofferson RC, Silva NJ, Vasquez C, Mores CN, Wearing HJ.
781 Modeling mosquito-borne disease spread in US urbanized areas: The case of
782 Dengue in Miami. PLoS One. 2016; 11: e0161365.

783 79. Butterworth MK, Morin CW, Comrie AC. An analysis of the potential impact of
784 climate change on dengue transmission in the southeastern United States. Environ
785 Health Perspect. 2016; 125: 579–585.
786 80. Ryan SJ, Carlson CJ, Mordecai EA, Johnson LR. Global expansion and
787 redistribution of *Aedes*-borne virus transmission risk with climate change. PLoS
788 Negl Trop Dis. 2019; 13: e0007213.

789

790 **Supplemental Table 1. Summary Statistics of Climate, *Aedes aegypti*, and Dengue**

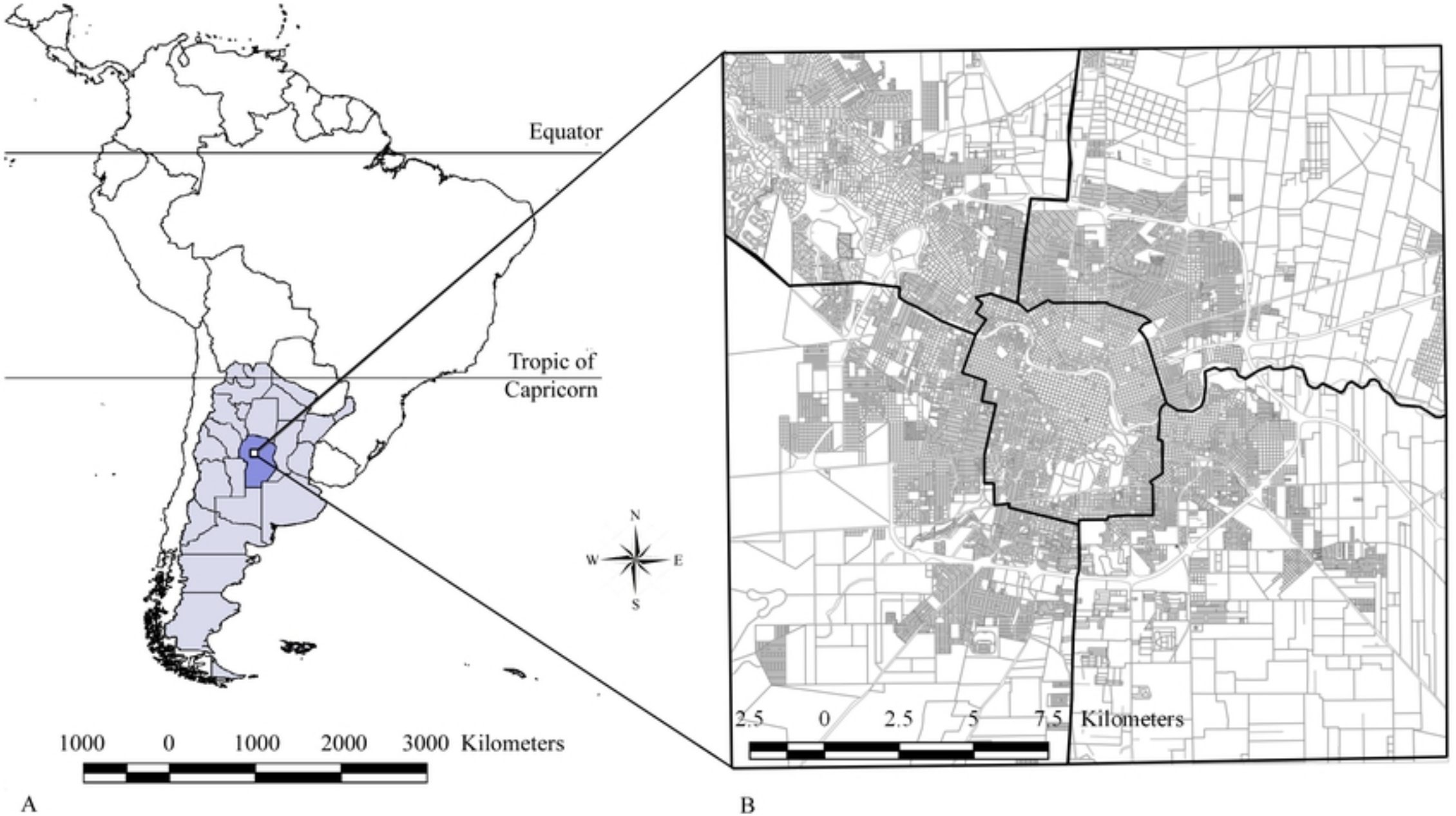
791 **Measures.** Mean and range by year are given for climate, *Aedes aegypti*, and dengue

792 measures used in this study.

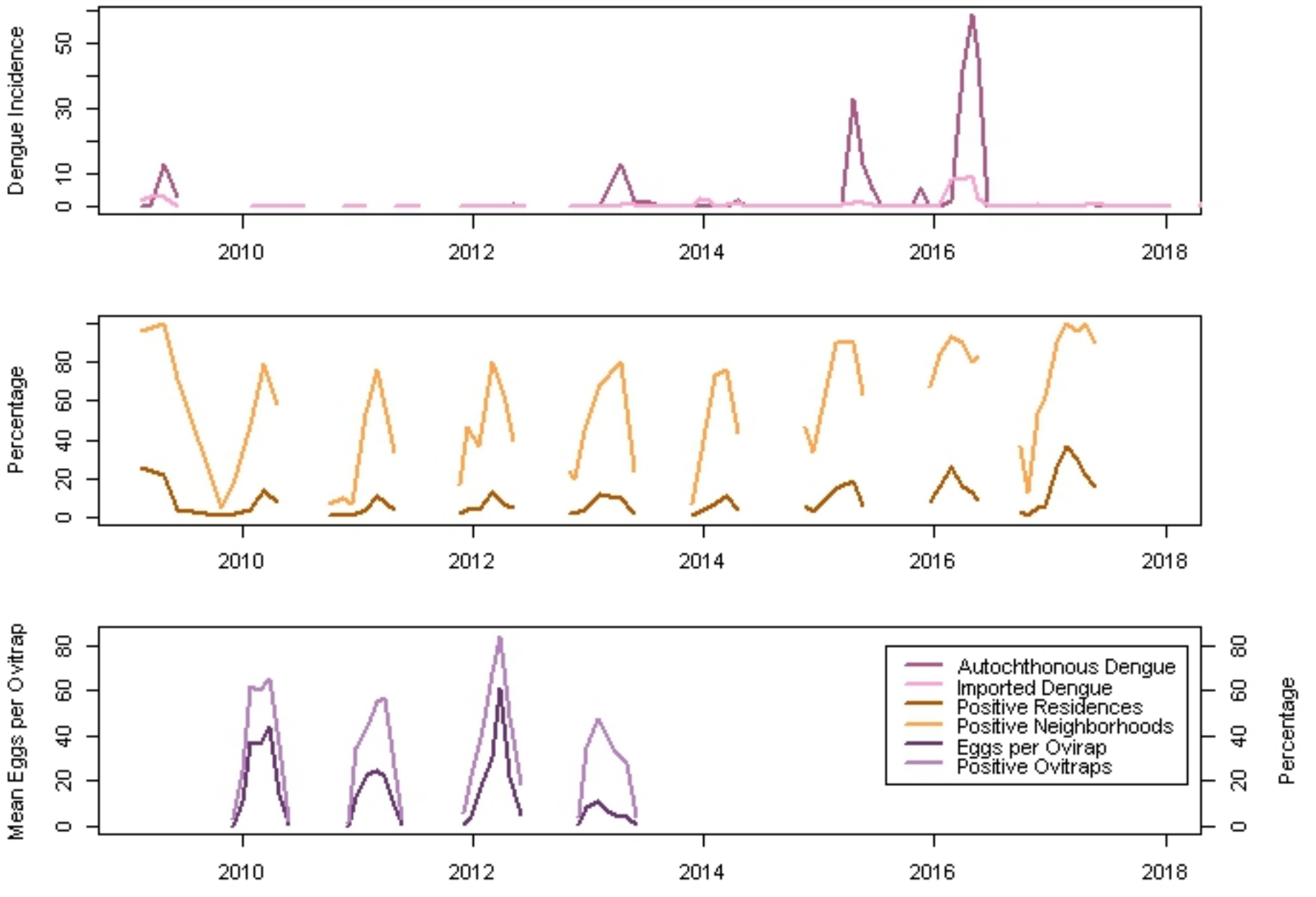
793 **Supplemental Figure 1**. Location of 177 sites where ovitraps were placed to collect

794 *Aedes aegypti* eggs in the city of Córdoba, from November 2009 to October 2013.

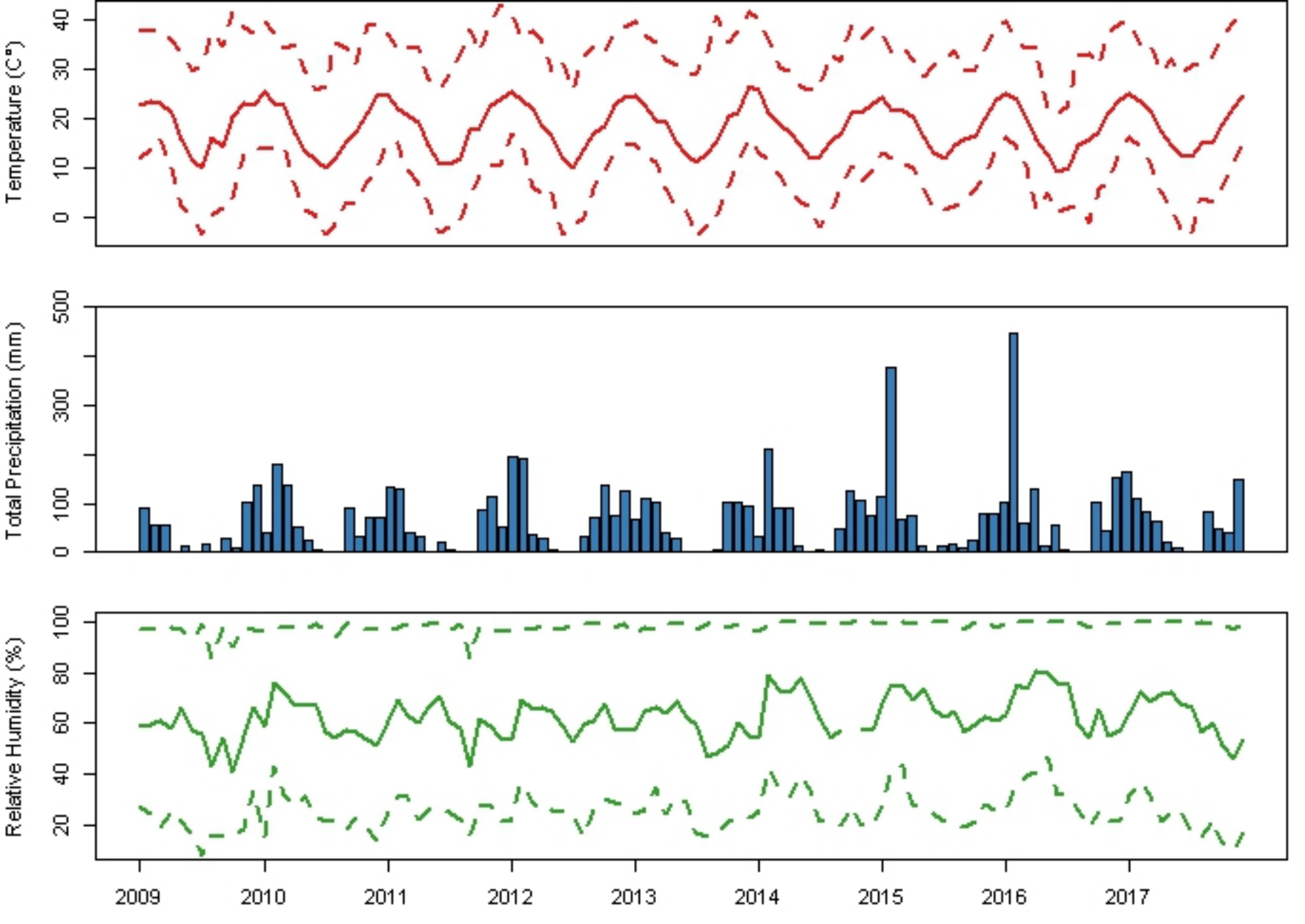
795


Equator
Tropic of
Capricorn
N
W
E
S
1000 0 1000 2000 3000 Kilometers
A
2.5 0 2.5 5 7.5 Kilometers
B

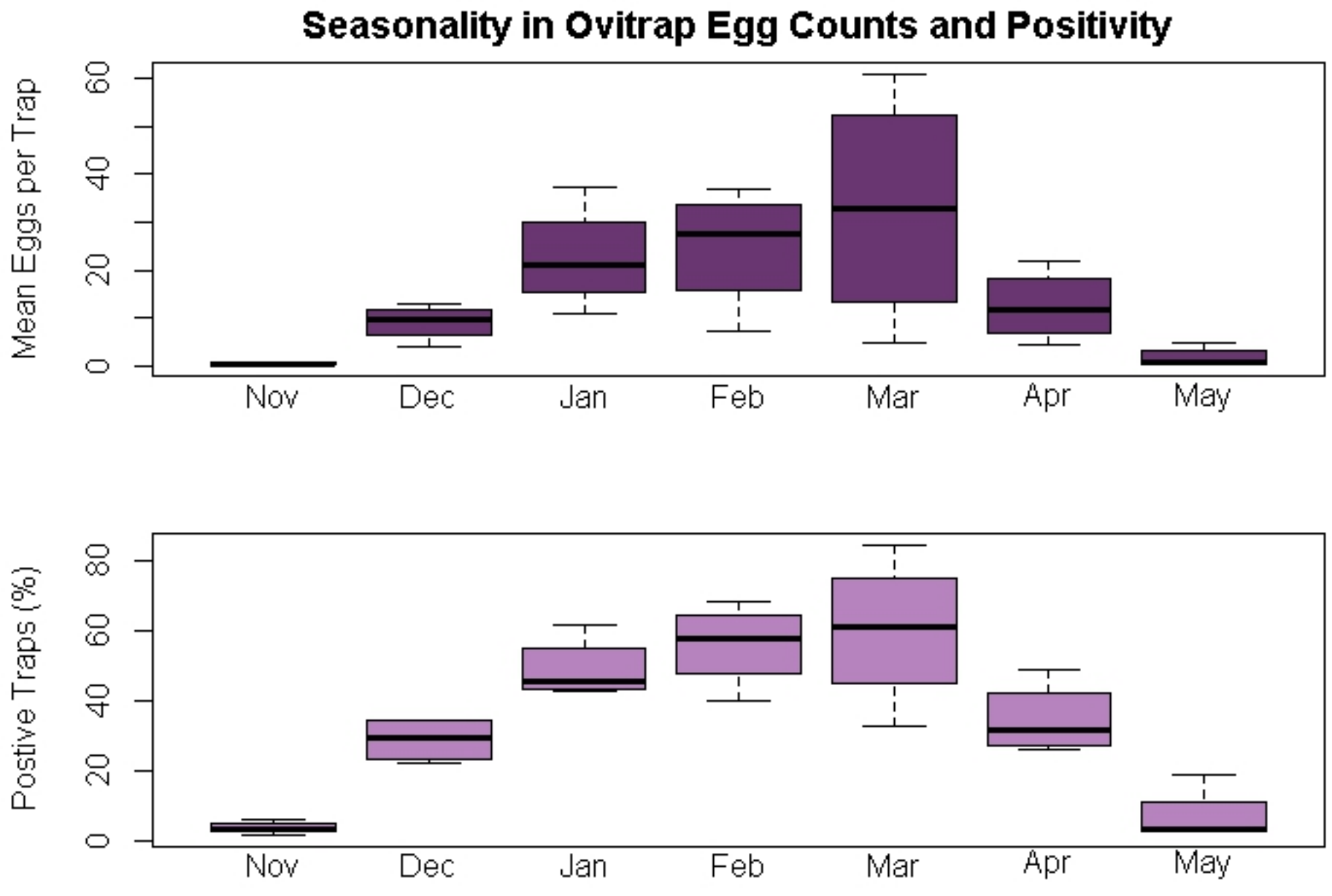
Figure


Dengue Incidence
0
10
30
50
2010
2012
2014
2016
2018
Percentage
0
20
40
60
80
2010
2012
2014
2016
2018
Mean Eggs per Ovitrap
0
20
40
60
80
Percentage
0
20
40
60
80
2010
2012
2014
2016
2018
Autochthonous Dengue
Imported Dengue
Positive Residences
Positive Neighborhoods
Eggs per Ovirap
Positive Ovitraps

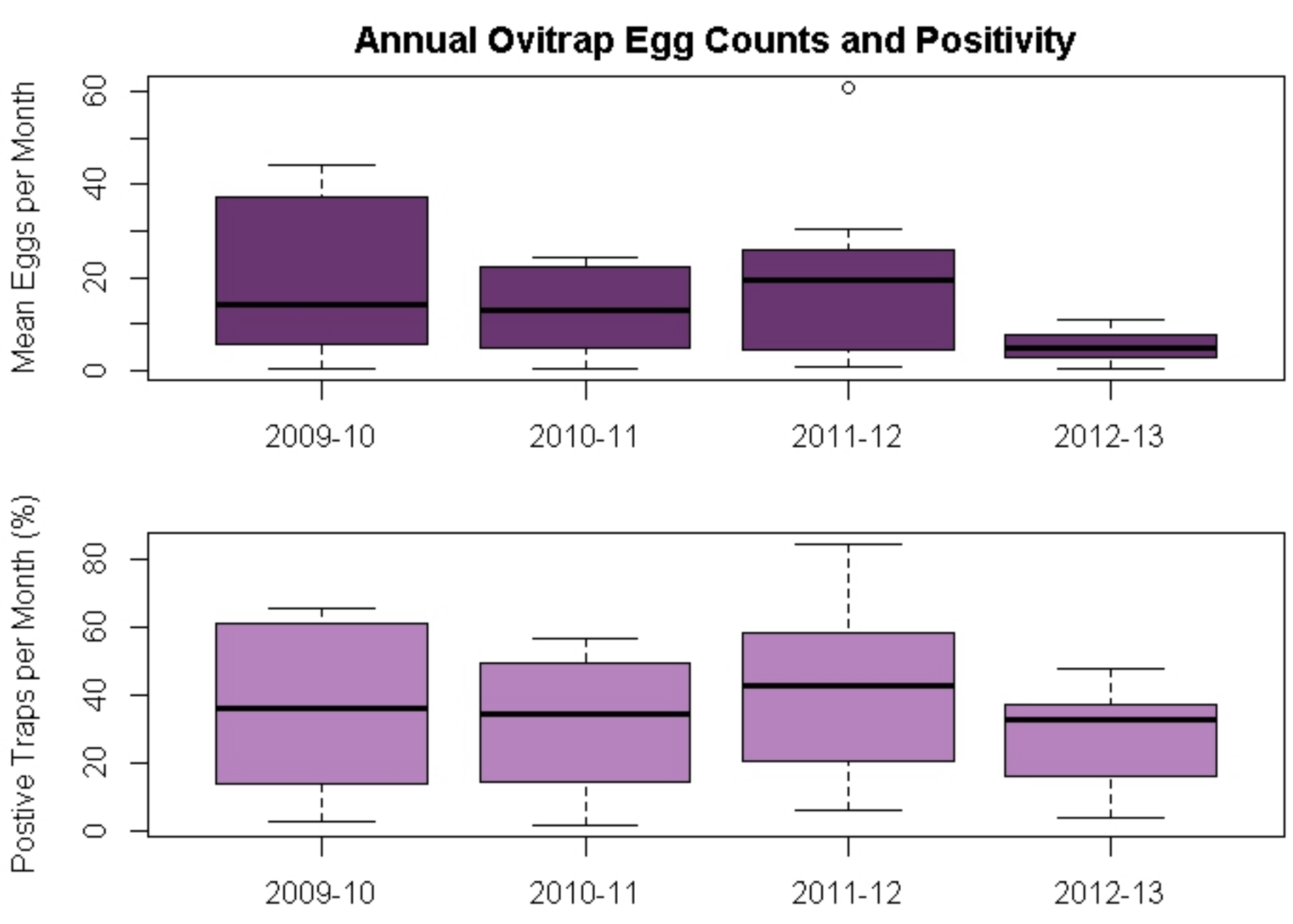
Figure


Temperature (C°)
0
10
20
30
40
Total Precipitation (mm)
0
100
300
500
Relative Humidity (%)
20
40
60
80
100
2009
2010
2011
2012
2013
2014
2015
2016
2017

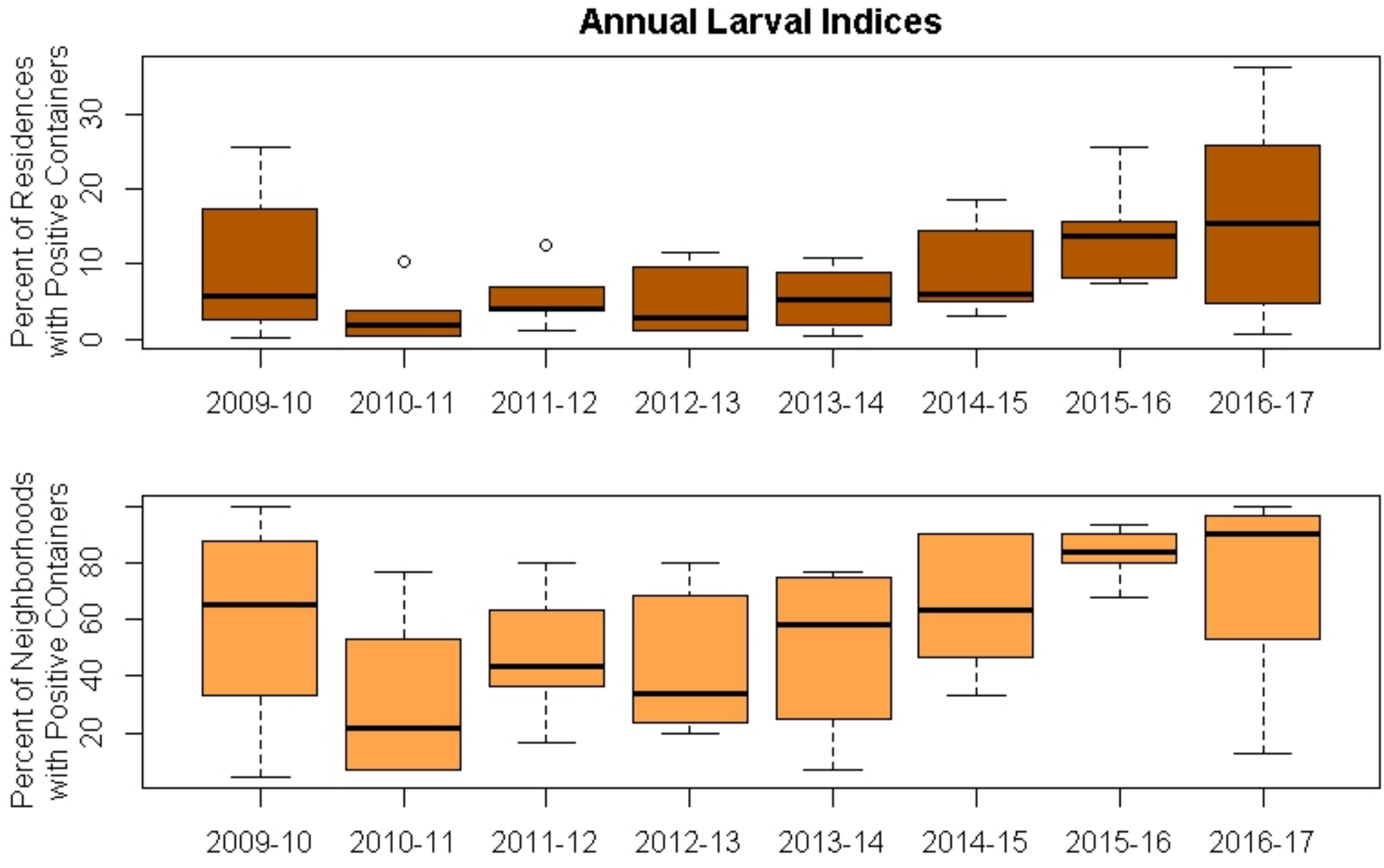
Figure


Seasonality in Ovitrap Egg Counts and Positivity
Mean Eggs per Trap
0
20
40
60
Nov
Dec
Jan
Feb
Mar
Apr
May
Postive Traps (%)
0
20
40
60
80
Nov
Dec
Jan
Feb
Mar
Apr
May

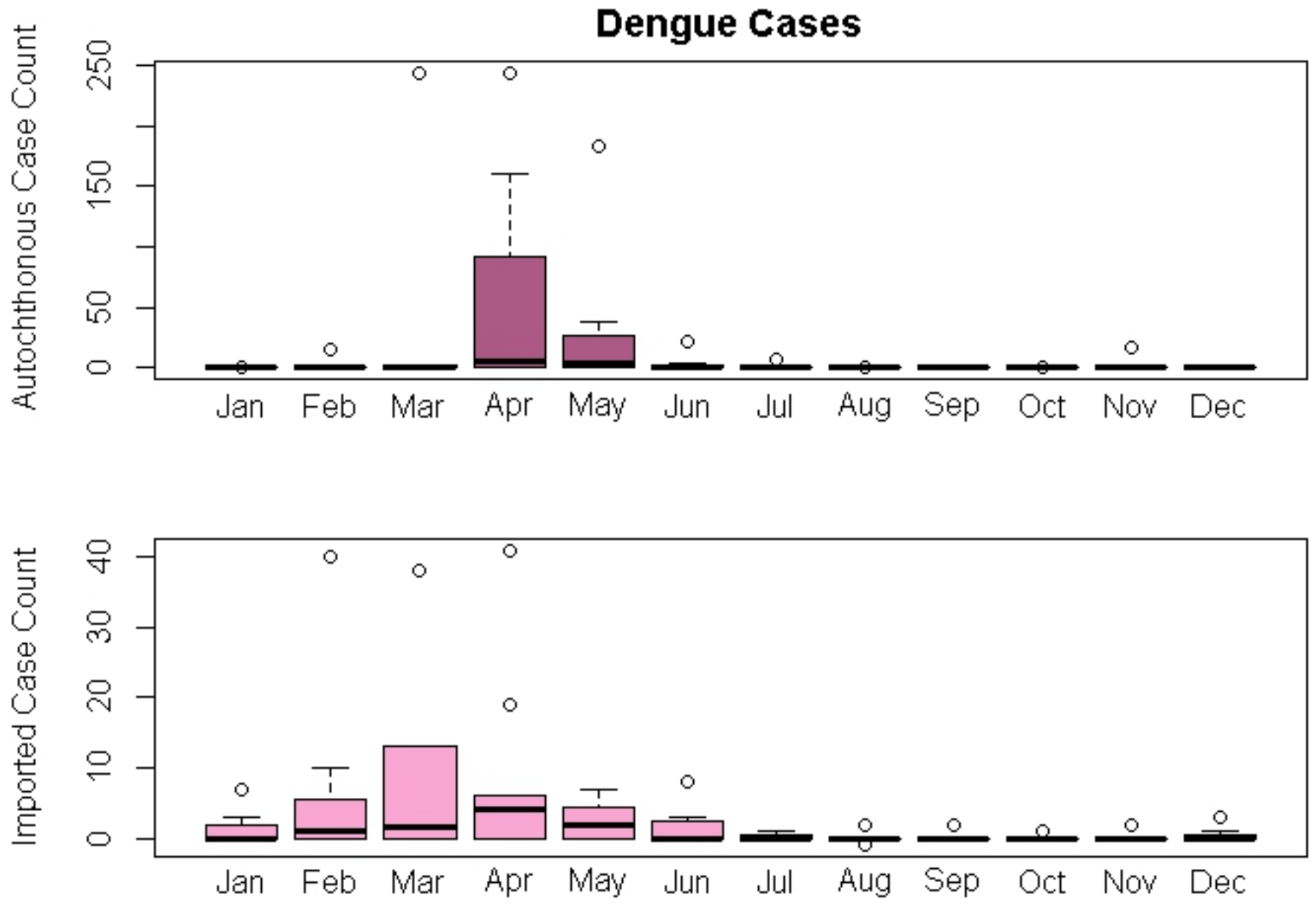
Figure


Annual Ovitrap Egg Counts and Positivity
Mean Eggs per Month
0
20
40
60
2009-10
2010-11
2011-12
2012-13
Postive Traps per Month (%)
0
20
40
60
80
2009-10
2010-11
2011-12
2012-13

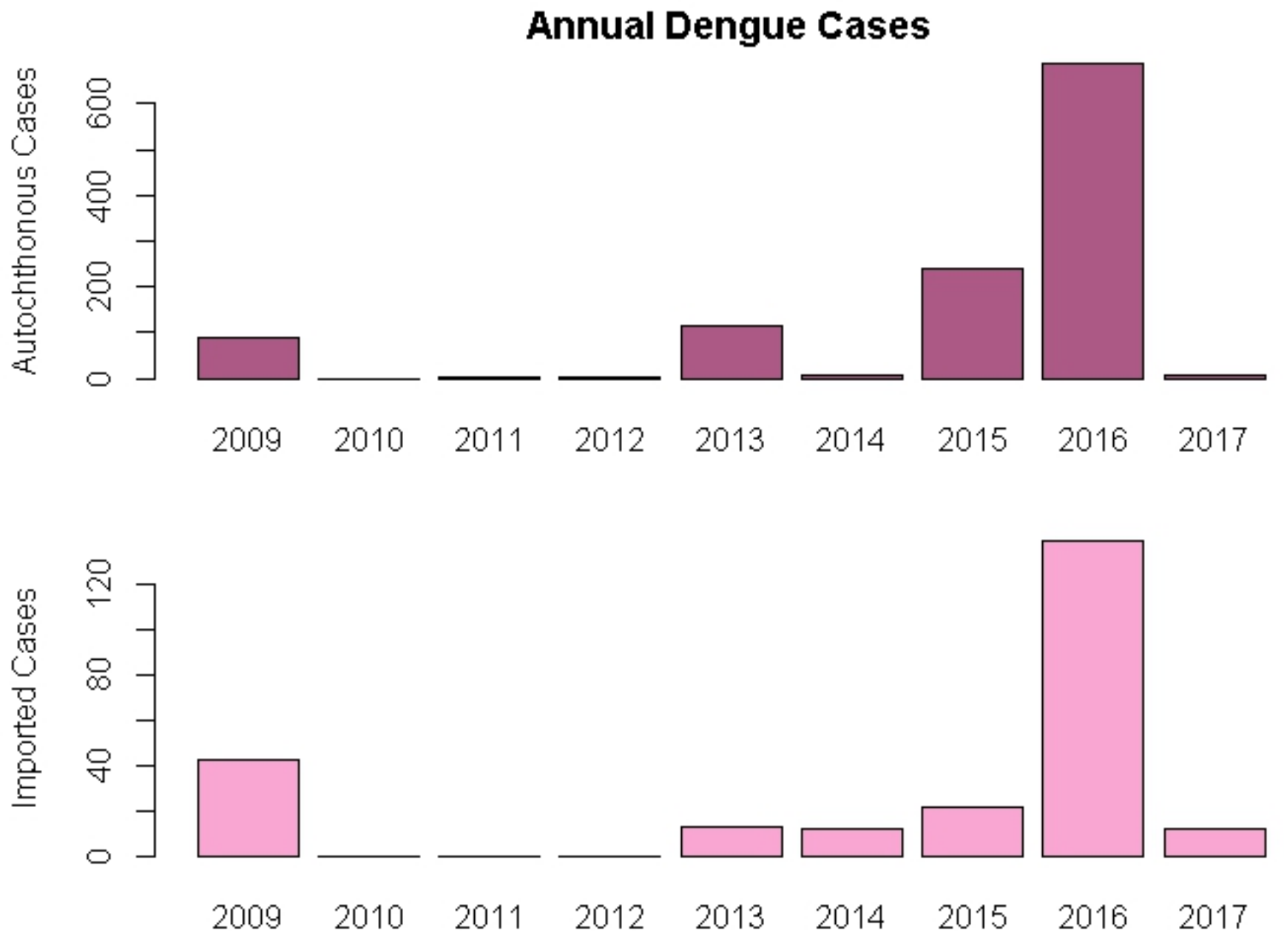
Figure


Annual Larval Indices
Percent of Residences with Positive Containers
0
10
20
30
2009-10
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
Percent of Neighborhoods with Positive COntainers
20
40
60
80
2009-10
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17

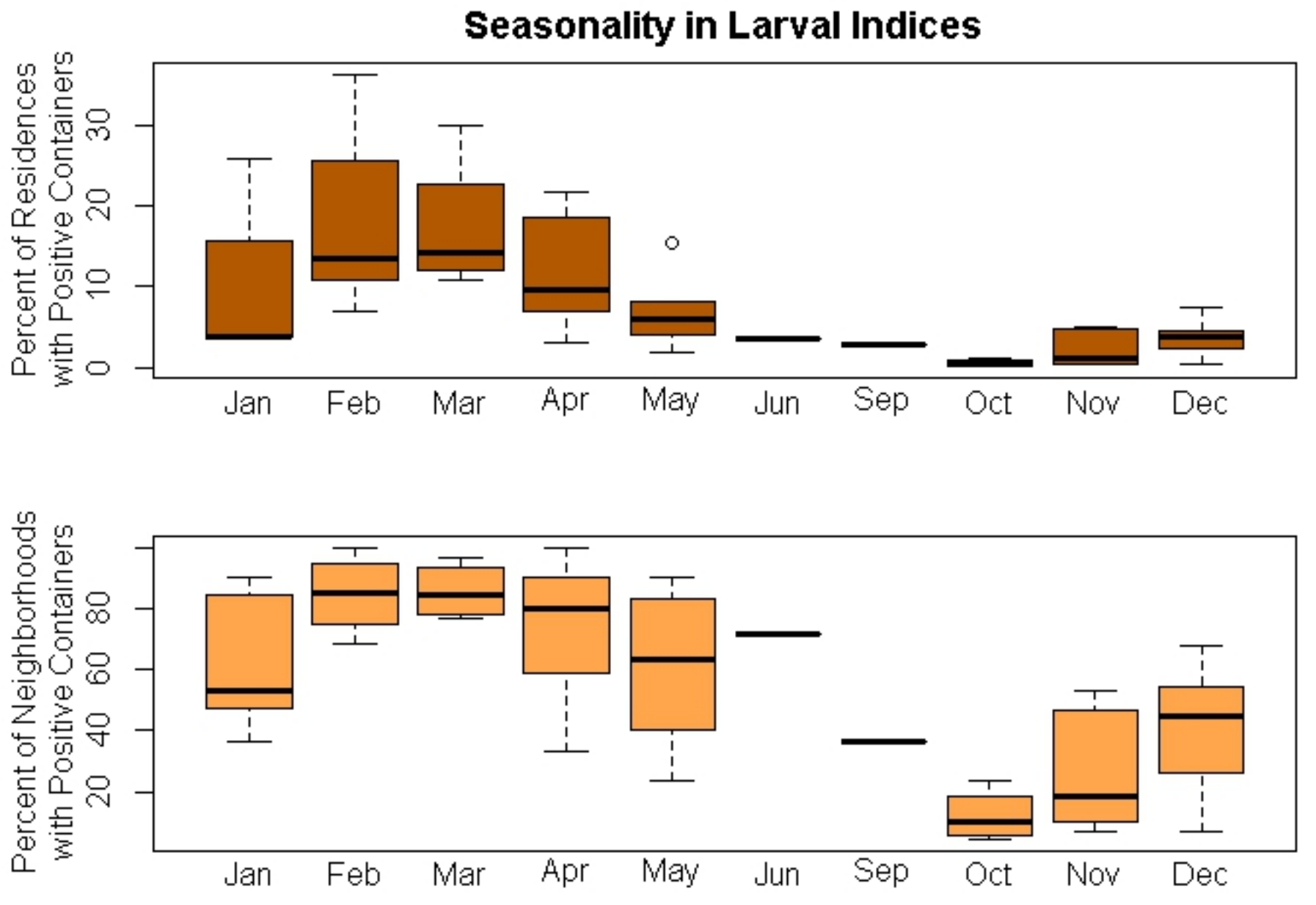
Figure


Dengue Cases
Autochthonous Case Count
0
50
150
250
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Imported Case Count
0
10
20
30
40
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

Figure


Annual Dengue Cases
Autochthonous Cases
0
200
400
600
2009
2010
2011
2012
2013
2014
2015
2016
2017
Imported Cases
0
40
80
120
2009
2010
2011
2012
2013
2014
2015
2016
2017

Figure


Seasonality in Larval Indices
Percent of Residences with Positive Containers
0
10
20
30
Jan
Feb
Mar
Apr
May
Jun
Sep
Oct
Nov
Dec
Percent of Neighborhoods with Positive Containers
20
40
60
80
Jan
Feb
Mar
Apr
May
Jun
Sep
Oct
Nov
Dec

Figure