

Table 1. Transmission and Disease Severity Characteristics Between Two Successive Waves of Chikungunya, Reunion Island, 2005–2006

Indicator/Reunion Island Population	Total	Wave 1	Wave 2	P Value
Duration of the outbreak event (months)	17	6	11	...
Reunion Island children subset, ^a n	200 321	51 462	148 859	...
Infected children (attack rate), %	30.5	11.9	37.0	<.0001
Girls, %	50.2	50.4	50.1	.3940
Boys, %	49.8	49.6	49.9	...
0–5 years, %	34.4	34.2	34.4	.7280
6–8 years, %	23.4	25.8	23.1	...
9–14 years, %	42.2	40.0	42.5	...
Person-years	160 185	25 731	134 454	...
Incidence, per 1000 person-years	377.2	239.0	403.2	<.0001
Symptomatic infections, %	70.2	51.9	72.3	.1829
Inapparent infections, %	29.8	48.1	27.7	...
Symptomatic-to-inapparent ratio	1:0.424	1:0.927	1:0.383	...
95% confidence interval	(0.423–0.426)	(0.919–0.935)	(0.381–0.384)	...
Score of symptoms, $\mu \pm \sigma$	2.18 \pm 0.18	1.16 \pm 0.47	2.30 \pm 0.19	.0219
Painful joints, $\mu \pm \sigma$	3.67 \pm 0.42	1.66 \pm 1.01	3.90 \pm 0.45	.0413
Persistent arthralgia, %	27.8	50.0	25.0	.4900
Minimum temperature (°C), $\mu \pm \sigma$	20.49 \pm 0.25	19.87 \pm 0.78	20.56 \pm 0.26	.4625
Maximum temperature (°C), $\mu \pm \sigma$	28.63 \pm 0.23	27.11 \pm 0.68	28.80 \pm 0.24	.0807
Average temperature (°C), $\mu \pm \sigma$	24.05 \pm 0.24	23.52 \pm 0.90	24.11 \pm 0.24	.5495
Reproductive numbers	3.7 (2.1 to 11.0)	8.4 (6.0 to 11.0)	3.4 (2.1 to 4.5)	...
Post convalescent enzyme-linked immunosorbent assay immunoglobulin G titers, $\mu \pm \sigma$	1.80 \pm 0.10	1.30 \pm 0.22	1.83 \pm 0.11	.1376

^a In this population-based study, a random sample was stratified on the community characteristics to ensure the representativeness of the participants. The study was completed with meteorological data to investigate contextual risk factors [3], along with a follow-up survey, the TELECHIK cohort study, to estimate the long-term consequences [4].

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Reply to Gérardin et al

TO THE EDITOR—We thank Gérardin and colleagues [1] for their comments on our article and for reexamining pediatric

data [2] from the 2005–2006 chikungunya epidemic on La Réunion Island. Upon splitting the original dataset to reflect the 2 epidemic waves of chikungunya virus (CHIKV) transmission on La Réunion, the authors found, among other results, an inverse relationship between the probability of CHIKV infection in an initially naive population (ie, seroprevalence, what they call the attack rate) and the probability of an inapparent outcome given infection, the latter a probabilistic expression of the symptomatic-to-inapparent (S:I) ratio. Our studies of the chikungunya epidemics experienced by a pediatric cohort [3] in Managua, Nicaragua, showed this association with both epidemiological risks and rates [4, 5]. Research from a community-based cohort study in the Philippines also documented this relationship with risks and rates [6, 7]. More broadly, this inverse association was first put forward in the chikungunya field by Manimunda et al [8], and it has since been remarked upon by others [9].

Here, we present evidence in favor of Manimunda et al's hypothesis that we collected from the literature. Following PRISMA guidelines [10], we conducted a systematic review of the chikungunya literature in the PubMed database, without any restrictions. Our only search term was "chikungunya," and we screened 3480 articles. We extracted data for studies reporting the ratio of symptomatic and inapparent infections among serologically confirmed CHIKV infections in initially naive populations who experienced a chikungunya epidemic. We corresponded with study authors when questions arose regarding their data or study design to ensure consistency and accuracy. The results are presented in Figure 1 and Supplementary Table 1.

Assuming a Gaussian model, the overall correlation between the probability of CHIKV infection and asymptomatic infection, after weighting by the sample size and the size of the CHIKV-infected population, is -0.67 (95% confidence interval, $-0.98, -0.36$; $P < .001$; Figure 1A). This weighted Pearson correlation

is robust to exclusion of any one study population. A sensitivity analysis based on iterative jackknife [11] estimates of the weighted Pearson correlation estimator shows that the correlation estimates range from a maximum value of -0.55 ($P < .01$) with the removal of our 2014 Nicaraguan pediatric data [5] to a minimum value of -0.76 ($P < .0001$) with the removal of Nakkhara et al's data [12]. Figure 1B summarizes the same data with a flexible LOESS model [13], which more accurately reflects the variability of the association of interest in the published literature. The inverse association holds reliably for studies that report at most a 40% CHIKV seroprevalence in initially naive populations that have experienced a recent CHIKV epidemic. At higher seroprevalence levels, the variance of the association is large, owing to small sample sizes and variable percentages of asymptomatic infection at high seroprevalence levels.

As indicated in our original article, such a relationship between force of infection and the S:I ratio has been observed with other infectious diseases,

including dengue and malaria [14, 15]. Thus, this inverse association may represent a broader phenomenon observed across multiple infectious diseases, which has yet to be fully explained.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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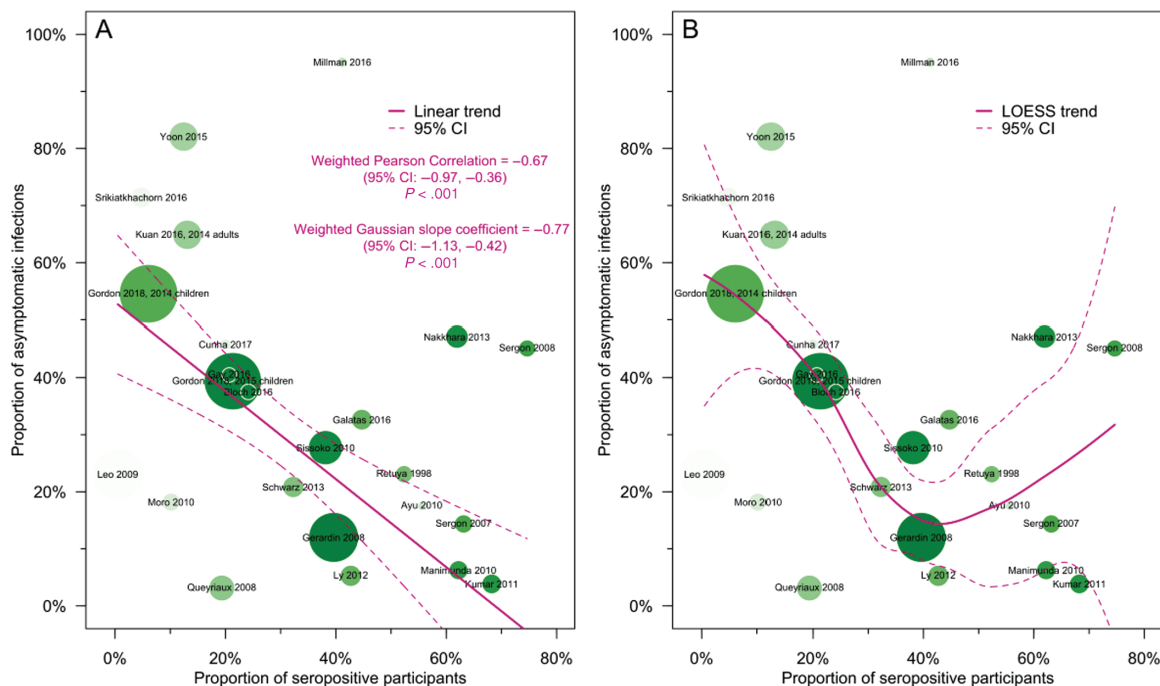


Figure 1. Risk of chikungunya virus (CHIKV) infection and asymptomatic presentation in the published literature. Scatterplot elements correspond to data in Supplementary Table 1 and references in Supplementary Materials. The radius of each study's data point is scaled to the sample size and shaded to the size of the CHIKV-infected population. A, Data summarized with a Gaussian model. B, Data summarized with a LOESS model. Abbreviation: CI, confidence interval.

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