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The Mosquito, the Virus, the Climate: An Unforeseen Réunion in 2018

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Key Points:
- Unseasonably warm temperatures and increased tropical-cyclone-related rainfall led to the large 2018 dengue outbreak in Réunion
- Subseasonal forecasts successfully predicted temperature and rainfall events in Réunion, up to 4 weeks in advance
- Forecasts would have provided enough lead time to activate early-warning systems, vector-control strategies, and medical readiness

Supporting Information:
- Supporting Information S1

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Abstract The 2018 outbreak of dengue in the French overseas department of Réunion was unprecedented in size and spread across the island. This research focuses on the cause of the outbreak, asserting that climate played a large role in the proliferation of the *Aedes albopictus* mosquitoes, which transmitted the disease, and led to the dengue outbreak in early 2018. A stage-structured model was run using observed temperature and rainfall data to simulate the life cycle and abundance of the *Ae. albopictus* mosquito. Further, the model was forced with bias-corrected subseasonal forecasts to determine if the event could have been forecast up to 4 weeks in advance. With unseasonably warm temperatures remaining above 25°C, along with large tropical-cyclone-related rainfall events accumulating 10–15 mm per event, the modeled *Ae. albopictus* mosquito abundance did not decrease during the second half of 2017, contrary to the normal behavior, likely contributing to the large dengue outbreak in early 2018. Although subseasonal forecasts of rainfall for the December–January period in Réunion are skillful up to 4 weeks in advance, the outbreak could only have been forecast 2 weeks in advance, which along with seasonal forecast information could have provided enough time to enhance preparedness measures. Our research demonstrates the potential of using state-of-the-art subseasonal climate forecasts to produce actionable subseasonal dengue predictions. To the best of the authors' knowledge, this is the first time subseasonal forecasts have been used this way.

Plain Language Summary Between December 2017 and February 2018, there was a large outbreak of dengue in the French overseas department of Réunion. Tropical-cyclone-related rainfall events and higher-than-average temperatures played a role in the dengue outbreak, which could have been forecast 4 weeks in advance. The size of the *Aedes albopictus* mosquito population in Réunion was modeled with temperature and rainfall data to replicate the population size that would have been present during the time of the outbreak. Rainfall and temperature forecasts were input into the mosquito model, for 1 to 4 weeks prior to the target date of 8 January, to better understand if the increased mosquito population could have been calculated in advance. Due to abnormally warm temperatures hovering around 25°C for most of the year, along with large rainfall events during the 2017–2018 transition, the mosquito population did not diminish toward the end of 2017, contrary to normal behavior, likely contributing to the large dengue outbreak in early 2018. Additionally, model results suggest accurate prediction of the onset and size of the outbreak 2 weeks in advance, which could have provided enough time to enhance preparedness measures.

1. Introduction

Despite heightened levels of attention and the mobilization of intensive vector-control efforts over the last several decades, Réunion, an island in the Indian Ocean, experienced an unprecedented epidemic of dengue during the early months of 2018. A total of 1,388 cases were reported between 1 January and 15 April 2018, and 6,942 cases by the end of the year, a 6,000% increase from 2017 (Kles et al., 1994; World Health Organization [WHO], 2019; Kreisel, 2018). The first dengue epidemic occurred in Réunion between 1977 and 1978 (Kreisel, 2018). Between 2004 and 2016, small dengue outbreaks have been observed on the island, with an average number of cases ranging from 1 to 281. In 2017, a larger outbreak was observed, with 1,086 cases reported; however, even compared to this outbreak, the magnitude of the 2018 event was unusual in size (Kreisel, 2018; Larrieu et al., 2012).

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Globally, dengue is a significant public health concern, estimated to cause nearly 100 million symptomatic cases per year, but tends to be confined to urban areas in tropical and subtropical regions, where the principal mosquito vector, *Aedes aegypti*, is endemic (Bhatt et al., 2013). Dengue can also be transmitted by the secondary mosquito vector *Aedes albopictus*. Unlike *Ae. aegypti,* the range distribution of *Ae. albopictus* also includes temperate regions of the globe, such as North America, Europe, and China (Kraemer et al., 2015). On Réunion, *Ae. albopictus* may be the more important vector as it has been found in higher relative abundances than has been *Ae. aegypti*, and *Ae. aegypti* larvae have been found only at the west coast of the island (WHO, 2019). The vector *Ae. albopictus* has rarely been associated with large dengue outbreaks, such as the one observed in 2018 (Lambrechts et al., 2010). Surveillance on *Aedes* vector density is important and operationalized for prioritizing areas and timing of vector control. One of the most widespread indices is the Breteau index (BI), which measures the number of *Aedes* larvae or pupae positive containers per 100 houses inspected (WHO, 2020).

The underlying causes for the sudden and unusual upsurge in cases of the 2018 outbreak have not been investigated in detail thus far. High susceptibility to dengue virus among the population, or genetic adaptation of the dengue virus to *Ae. albopictus* are plausible hypotheses (Kles et al., 1994). Additional suppositions include local water use, specifically water insecurity, water hoarding, and unidentified standing water, along with other socioeconomic conditions that may have stimulated the growth of local vector populations and hampered the preventative efforts taken by the local government (Akanda et al., 2020; Caprara et al., 2009; Delatte et al., 2013; Fred et al., 2018; Setbon & Raude, 2008).

We hypothesize that optimal temperatures for the vector and the virus during most of 2017, along with tropical-cyclone-related rainfall occurring between the end of 2017 and the beginning of 2018, created suitable environmental conditions and hampered vector-control activities, contributing to unusual vector abundance on the island. Previous research suggests that the combination of above-normal rainfall and temperatures is a prerequisite for the reproduction of ectotherm vectors such as *Ae. albopictus*, leading to high vector abundance (Dieng et al., 2012; Hawley, 1988; Jia et al., 2016; Liyanage et al., 2016; Lowe et al., 2018; Reinhold et al., 2018; Waldock et al., 2013). Favorable ambient climatic conditions enhance viral replication within vectors and lead to increased transmission in a vulnerable population (Liu-Helmersson et al., 2016). Additionally, we hypothesize that these rainfall events could have been forecast up to 4 weeks in advance, which, along with information about the high vector population and the dengue circulation at the moment, could have provided decision makers with the information needed to prevent or minimize the outbreak. Such tools could be regularly used by decision makers as a form of early-warning systems to protect against future outbreaks.

2. Data and Methods

2.1. Climate Attribution

In order to examine the contribution of climatic conditions to the 2018 dengue outbreak in Réunion, we analyzed the preceding climatic conditions and contextualized them using an 18-year baseline: 2000–2017. Our climate analysis used observed station-based gridded rainfall data (CPC-Unified; see Chen et al., 2008), and temperature and atmospheric circulation variables from the European Re-Analysis Interim project (Dee et al., 2011). We developed a process-based stage-structured model of the mosquito vector *Ae. albopictus* by drawing on previously calibrated models of *Ae. albopictus* (Jia et al., 2016; Metelmann et al., 2019), and of *Ae. aegypti* (Liu-Helmersson et al., 2019). Additionally, we used the BI for validating the predicted larvae and pupae from our model. This is not a straightforward comparison, but in the absence of the actual larvae and pupae frequencies, which have not been surveyed, we believe the temporal association between BI and the predicted larvae and pupae will give, for the circumstances, an indication of the model validity. The model was validated to local BI observations from Réunion (Boyer et al., 2014), exhibiting skillful results (Figure 1). See the supporting information for further details.

The model was then run for the baseline period on a "perfect prognosis" mode (Wilks, 1995), i.e., using climate observations of daily temperature and rainfall to generate past adult vector population from four compartments (i.e., emerging, blood feeding, gestating, and ovipositing); the approach is designed to help diagnose the role of climate in the present epidemic event and also as a measure of the maximum predictive skill provided by such a model. The adult *Ae. albopictus* abundance was standardized over time in order to

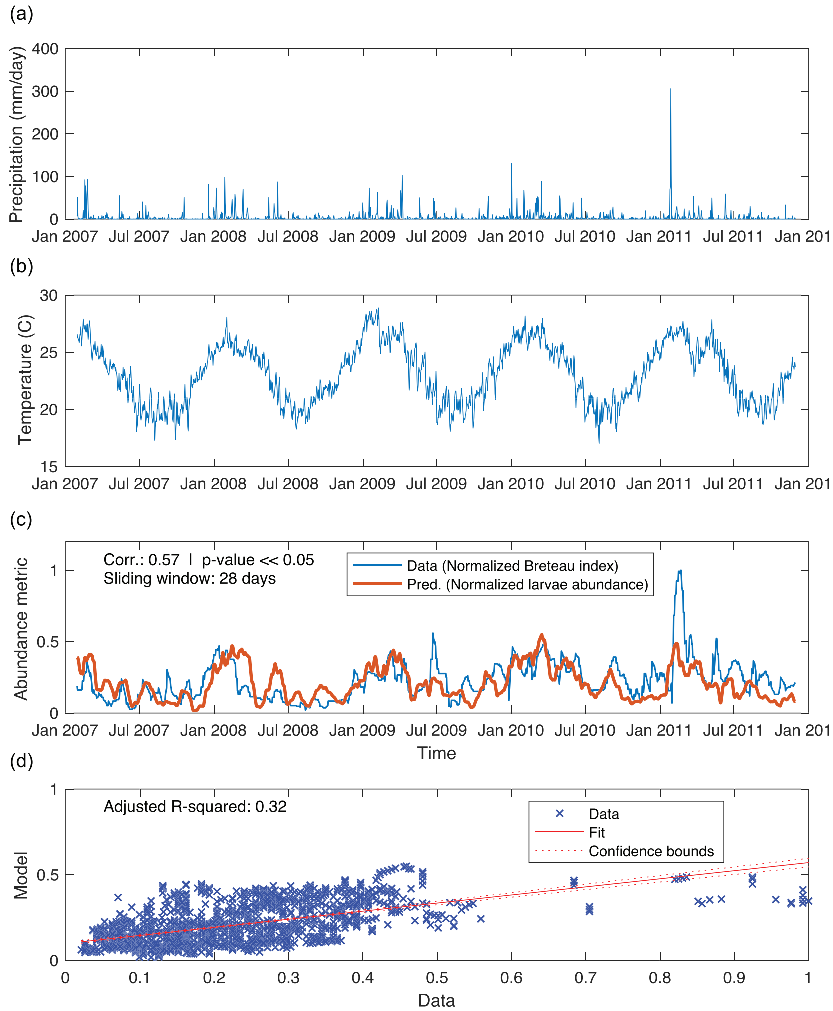

Figure 1. The stage-structured vector model performs well in comparison to Réunion Breteau index between 2007 and 2012 (Boyer et al., 2014). (a) Time series of precipitation data. (b) Time series of temperature data. (c) Time series of normalized Breteau index and normalized modeled larva abundance, where annotations indicate correlation between the two and that a sliding mean of 4 weeks was applied to the larvae abundance. (d) A linear regression model of the modeled larvae abundance against the Breteau index shows an adjusted *R*-squared of 0.32.

visualize statistical anomalies in vector population driven by climate factors. We obtained epidemiological data of dengue from Réunion from 2010 up to April 2018, provided by the European Centre for Disease Control (ECDC; Muñoz, 2020).

2.2. Subseasonal Skill Assessment

Additionally, we wanted to understand if the events leading to the outbreak could have been forecast in advance. Seasonal forecasts provide a first layer of information to assess if suitable conditions for an outbreak will happen in a coming season but cannot be specific enough as to indicate when within that season the epidemic could occur. Nonetheless, the relatively new subseasonal forecasts have the potential to provide that kind of information (Vitart et al., 2017). Using subseasonal climate forecasts produced by the European Centre for Medium-Range Weather Forecasts (ECMWF) model, available through the Seasonal to Subseasonal Prediction Project Database (Vitart et al., 2017; World Meteorological Organization, 2020), we analyzed if and how many weeks in advance the increase in mosquito population could have been forecast.

We conducted a subseasonal forecast skill assessment analysis for both temperature and rainfall, as described below, paying special attention to subseasonal rainfall forecast skill to see if the heavy rainfall episodes that occurred at the end of December 2017 and beginning of 2018 (yellow sections in Figures 2a

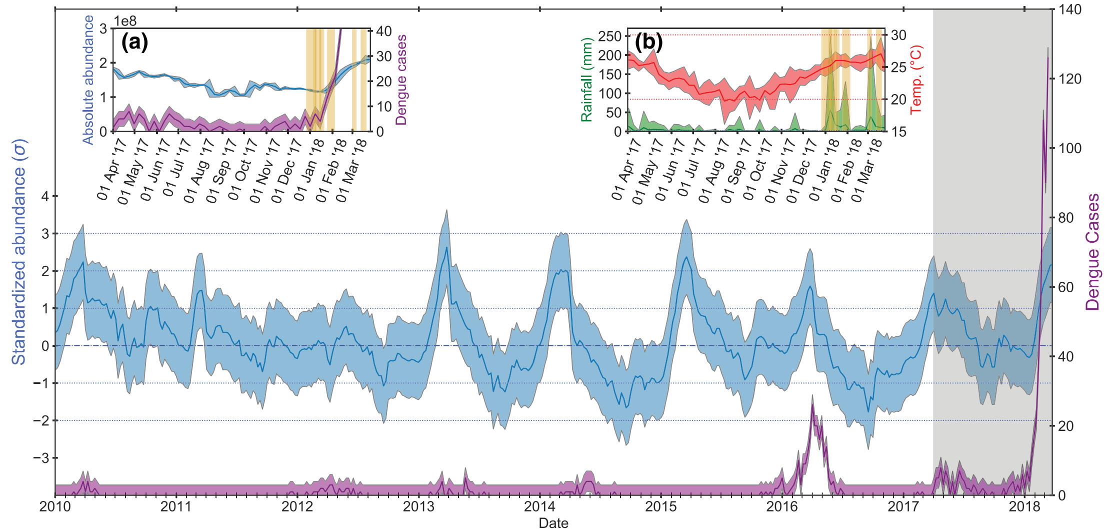

Figure 2. (main) Simulated weekly standardized abundance of *Aedes albopictus* adult population in Réunion (blue curve, units in standard deviations, σ), overlaid with weekly number of reported dengue cases by ECDC (purple curve). (a) As in the main panel, but for the period highlighted in gray: 1 April 2017 to 26 March 2018. Vertical scale for dengue cases ranges from 0 to 40 to better visualize variations before December 2017. (b) Weekly rainfall amounts (green curve) and temperature values (red curve) for the period highlighted in gray; horizontal red lines indicate suitable temperatures for the vector: 20–30°C. Periods highlighted in yellow in panels (a) and (b) indicate the timing and duration of each one of the seven tropical storms/cyclones referred to in the main text. The base period for standardization is 2010–2016. Shading represents the uncertainty envelope of each curve: For standardized vector abundance, it corresponds to $\pm 1\sigma$, while for dengue cases, rainfall, and temperature, it is defined by the observed difference in weekly maxima and minima.

and 2b) could have been forecast. Predictive skill, by definition (e.g., Murphey, 1988), involves the comparison of "how accurate" a forecast system is with respect to observations. To assess "how accurate" a forecast is, one needs to consider the best set of scores that measure the particular forecast attribute that wants to be analyzed (e.g., see Table 1 in Mason, 2018). The metrics chosen for this study are described below.

Four different lead time forecasts were used, each 45 days in length, for 1 to 4 weeks before the target week starting on 8 January 2018. For simplicity, we refer to each subseasonal forecast as Week 1, Week 2, Week 3, and Week 4 prior to the target week, corresponding to the initializations of 1 January 2018, 25 December 2017, 18 December 2017, and 11 December 2017, respectively. The week of 8 January was selected due to its proximity within the various tropical-cyclone-related rainfall events hypothesized to be partially responsible for the observed steep increase in dengue cases during and after that week.

For each of the four sets of 45-day-long forecasts, a large set of 160 ECMWF hindcasts was downloaded from the Subseasonal-to-Seasonal Database at the International Research Institute for Climate and Society's Data Library (IRIDL). Hindcasts are forecasts made with exactly the same model configuration for the same 45 forecast days in the past 20 years. For example, for the 1 January 2018 initialization, the forecasts consist of daily predictions from 1January to 14 February 2018, and the hindcasts (or "reforecasts") consist of the same days for the years 1998–2017. A 20-year record does not provide a statistically robust sample for skill analysis; hence, we used all initializations available in the 4 weeks prior to the initialization of the forecast. Since the ECMWF model provides two initializations per week (every Monday and Thursday), we used a total of 160 hindcasts (20 hindcasts $\times$ 2 initializations/week $\times$ 4 weeks), as indicated above.

The skill assessment process involved a cross-validation procedure for two key forecast attributes: association, measured by the Spearman rank correlation, and discrimination, measured by the two-alternative forced choice metric, or 2AFC (supporting information; Mason & Weigel, 2009). The cross-validation analysis used a leave-5-out moving window and was conducted using PyCPTv1.5 (Muñoz et al., 2019), a set of Python libraries designed to interface and enhance International Research Institute for Climate and Society's Climate Predictability Tool (CPTv16; Mason et al., 2020). PyCPT automatically downloads from the IRIDL the necessary hindcasts and observations to perform the skill assessment analysis.

For each set of subseasonal hindcasts, we corrected for mean and amplitude biases present in the temperature and rainfall time series. To do this, we shifted the mean and rescaled the standard deviation for each

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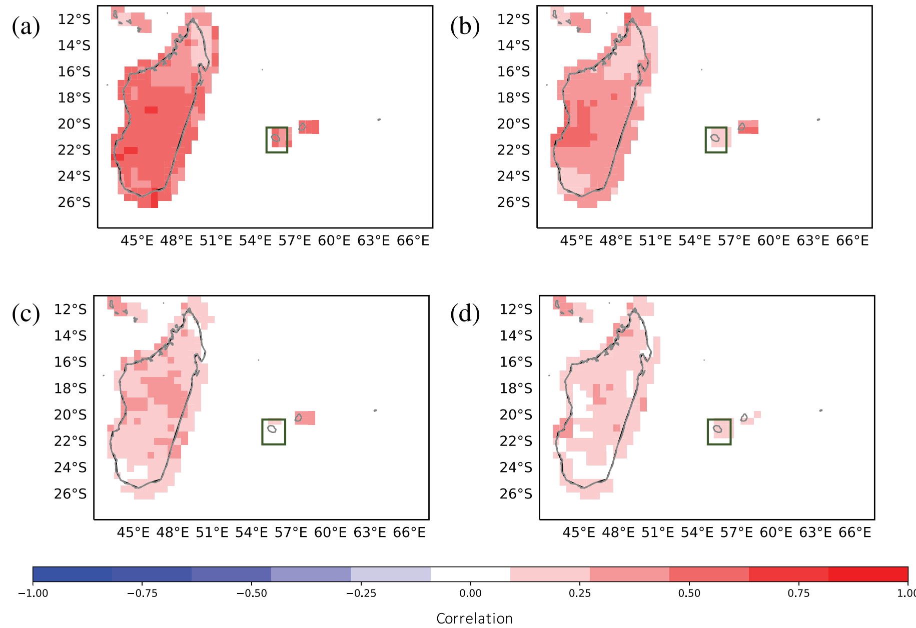

Figure 3. Forecast skill, measured by the Spearman rank correlation, for lead times (a) 1, (b) 2, (c) 3, and d) 4 weeks preceding the target week starting on 8 January 2018. A green square shows the location of Réunion.

variable and forecast initialization and then used this corrected daily temperature and rainfall time series to run the vector model in forecast mode. No climate forecast calibration was conducted beyond the mean and variability bias corrections.

3. Results

3.1. Climate Attribution

During 2017, then the warmest year on record without an El Niño event (NOAA, 2018), daily average surface temperature in Réunion provided suitable conditions for vector proliferation, even during most of the austral winter (in red in Figure 2). The average daily rainfall between May and the end of November on the island was around 2–3 mm/day, providing suitable conditions for mosquito reproduction. Starting on 27 December, a total of seven (European Commission, 2018) large-scale atmospheric systems in the South-West Indian Ocean (one tropical depression, one tropical storm, and five tropical cyclones, denoted by yellow sections in Figure 2) produced important rainfall events over Réunion (in green in Figure 2). Rainfall associated with these tropical systems is likely responsible for the increase in vector population during the end of 2017 and beginning of 2018, due to a compounding effect involving an increased number of larvae habitats and mosquitos and also the hampering of vector-control activities.

This effect is reflected in the reported number of dengue cases in Réunion in 2017, as they did not drop off to typical levels observed in previous years (see Figure 2, purple line); after a bimodal peak of dengue reports with maxima between April and June, the cases decreased but did not subside. The modeled vector population, in turn, grew from a relative minimum in June to near-normal values toward the end of 2017 and proceeded to grow more than 2 standard deviations, σ, during the beginning of 2018 (see blue curve in Figure 2), the sharp increase being concurrent with the initiation of the outbreak.

Therefore, we posit that sustained high levels of mosquito population co-occurring with an actively circulating DEN2 serotype virus set up the scenario for the 2018 epidemic, which was triggered by a combination of suitable environmental temperatures and impacts of tropical-cyclone-related rainfall. The compounding impact of these events for both the mosquitoes and the virus during most of 2017 and the beginning of 2018 created additional larvae habitats and a more difficult landscape for conducting vector-control activities.

3.2. Subseasonal Skill Assessment

Skill assessment for the beginning of the outbreak shows (Figures 3 and S1) the uncalibrated rainfall predictions to be skillful even 4 weeks ahead of time. Forecast skill for surface temperature (not shown) was also

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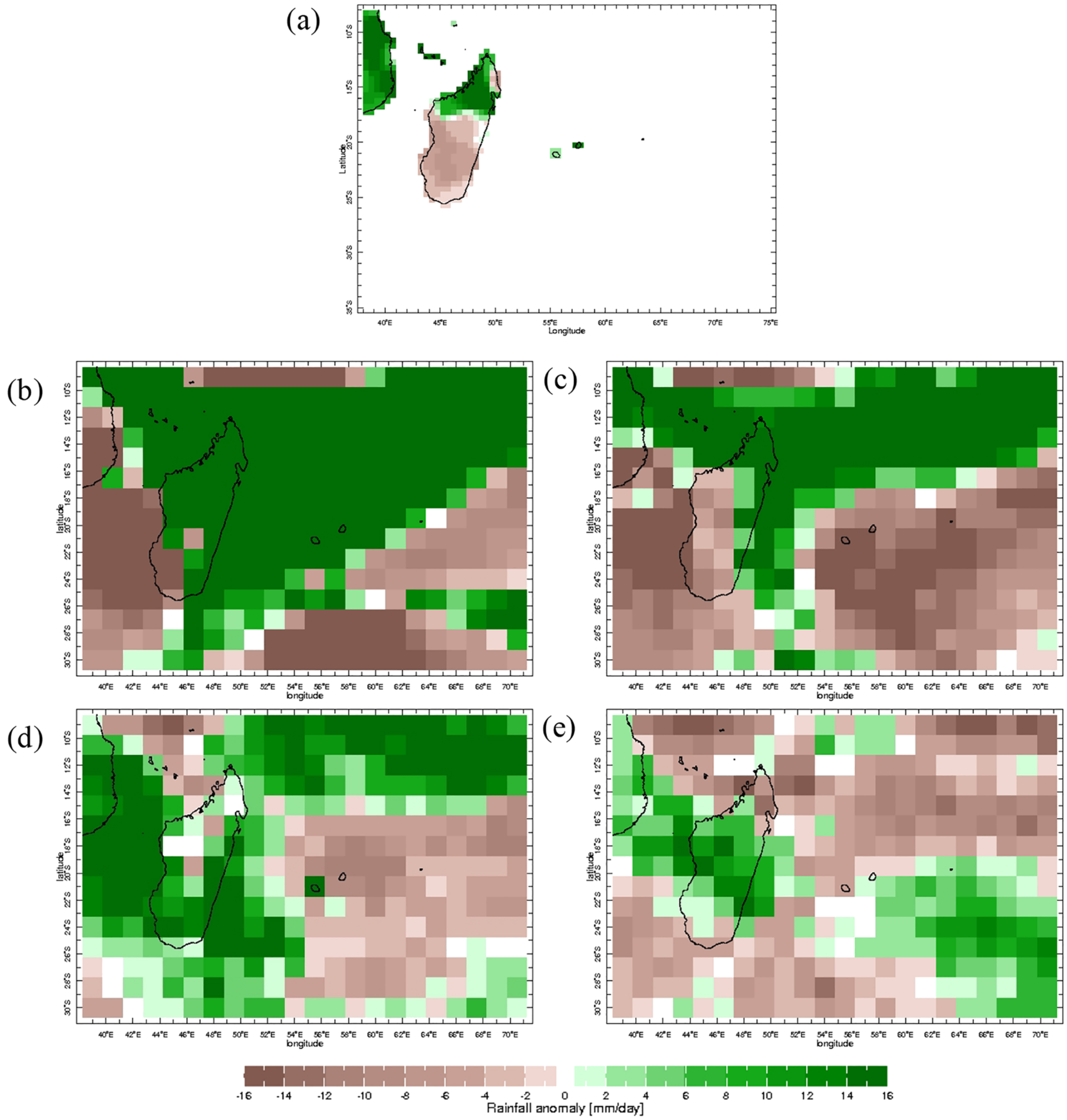

Figure 4. (a) Observed and forecast rainfall anomaly (mm/day) produced (b) 1, (c) 2, (d) 3, and (e) 4 weeks preceding the target week of 8 January 2018.

high up to 6 weeks ahead of time; temperature tends to vary little during the analyzed season (Figure 2b), which makes it considerably easier to predict than rainfall. Specifically, by using forecasts for 1 to 4 weeks (Figure 4) preceding 8 January 2018, the targeted week of one of the larger rainfall events, we found that models were able to forecast above-normal rainfall over Réunion 3 weeks in advance, corresponding to the initialization of 18 December 2018. The forecasts predicted an anomalous amount of 10–15 mm of above-average rainfall for Réunion and the surrounding region, consistent with the pass of tropical cyclones Ava and Berguitta (Bouhet, 2018; European Commission, 2018). We found that the forecast model has improved skill over the baseline (based on the long-term rainfall average for the period under consideration, commonly known as "climatology") for all weeks analyzed. Further research should consider if and how spatially calibrated model output (e.g., Muñoz et al., 2017), addressing mean, variability, and spatial biases, may be able to further improve the forecast skill with additional lead times at the subseasonal time scale.

Upon integrating this forecast information into the mosquito model (Figure 5), there is potential for the use of subseasonal forecasts in predicting mosquito vector abundance, especially for adult mosquitos, up to

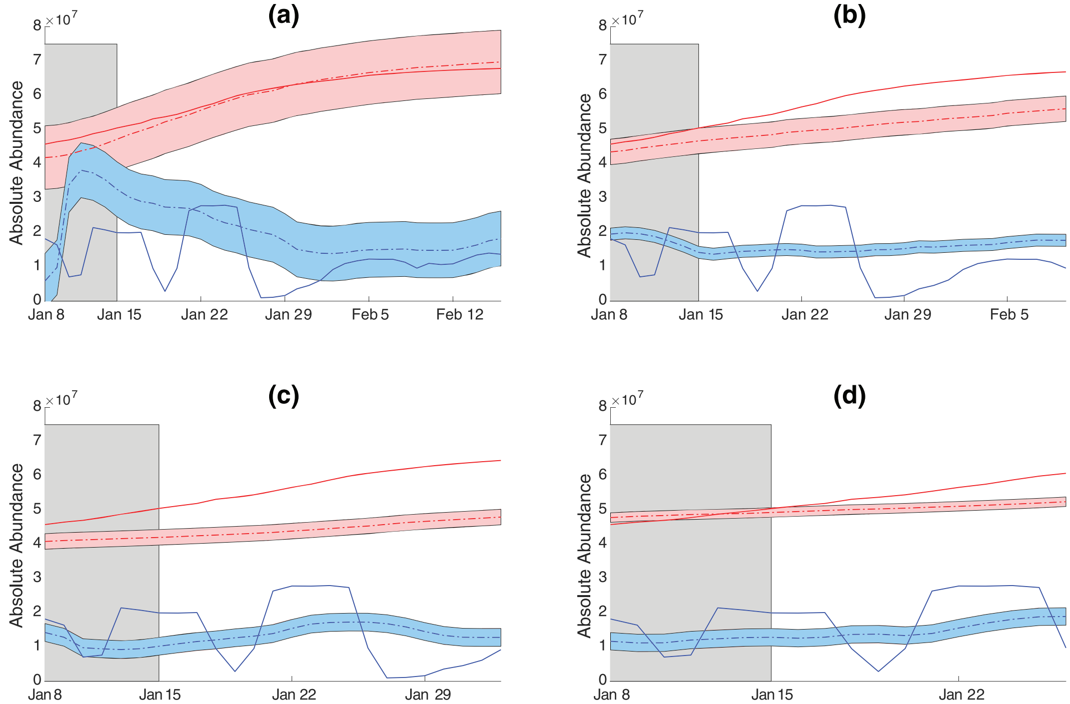

Figure 5. Forecast (dashed, with standard deviation shading) and reference (simulation used observed climate data; solid) adult (red) and larvae (blue) mosquito abundance, produced (a) 1, (b) 2, (c) 3, and (d) 4 weeks preceding the target week of 8 January 2018. Each forecast was produced forcing the vector model with output from the ECMWF model (51-member ensemble mean) and has a horizon of 45 days. The analysis focuses on the week starting on 8 January 2018 (gray shading).

4 weeks in advance, and perhaps also for larvae in the case of the Week 1 forecast (Figure 5). Indeed, always focusing on the week starting on 8 January 2018, the Week 1 forecast shows (Figure 5a) that as larvae reach a peak, adult abundances grow a few days after that, as expected, and although the timing is not perfect in the larvae forecast, the adult abundance matches almost perfectly the simulated one. The match between the simulated and forecast adult population abundance is weaker for the Week 2 and Week 4 forecasts (Figures 5b and 5d), although still of potential use for decision makers. Nonetheless, there is room for improvement in the Week 3 forecast (Figure 5c).

Though the subseasonal rainfall forecasts indicate that up to 3 weeks out, there is a positive rainfall amount tendency, there is not a clear translation of this behavior into an increase in adult mosquito abundance. However, the subseasonal forecasts in this study are spatially uncalibrated. Spatially calibrated climate forecasts have the potential for increased skill in mosquito abundance at a lead time of 3 to 4 weeks in future analysis. This suggests that it is and was possible—at least for this particular case—to create and utilize an early-warning system in an effort to protect the citizens of Réunion.

4. Discussion and Concluding Remarks

Based on this analysis, we posit that climate factors substantially contributed to the onset and magnitude of the 2018 outbreak of dengue in Réunion. Together, climate factors created a compounding effect related to (1) suitable temperatures during most of 2017 that increased vector activity and viral replication rates above usual levels and (2) tropical cyclone rainfall at the end of 2017 and beginning of 2018 that supported the formation of additional larvae habitats and mosquito proliferation, which hampered vector-control efforts on the island due to the tropical cyclone emergencies.

Compared to previous years in the analysis, 2017 is the only year that concurrently exhibits (a) the largest number of weeks per year with mosquito abundance around or above 1 before winter, (b) close to the long-term-normal mosquito population values during and after winter, and (c) the largest number of weeks per year with nonzero dengue cases reported (Figure 2). These conditions imply that a balance between a high vector survival rate (even through the relatively warm winter) and the number of infected humans with dengue might have been a key ingredient setting the stage of the 2018 epidemic. Health-related authorities in Réunion should pay attention to these combinations of conditions, along with increasing surveillance of *Aedes* vectors for management, in order to be better prepared for potential outbreaks, which are expected to become more common due to global warming.

Most importantly, we contend that this particular epidemic event could have been successfully predicted by utilizing models such as the one used in this study, forced by seasonal and subseasonal climate forecasts (Kirtman et al., 2014; L'Heureux et al., 2015; Vitart et al., 2017). In this particular example, the International Institute for Climate and Society's (2019) seasonal forecast system predicted above-normal rainfall conditions over Réunion for the November 2017 to January 2018 season since at least October 2017. Given this forecast, and the warmer-than-normal temperatures observed during the year, it would have been possible to establish an early-warning status of a potential dengue outbreak, targeting the end of 2017. Skillful predictions in this context could have provided public health authorities with sufficient time to initiate an early-response strategy to try to minimize the impact of this epidemic event. However, to produce a fully functioning early-warning system, skillful forecasts for all seasons of the year would need to be produced.

Utilizing subseasonal dengue outbreak predictions allows for the assessment of expected costs and benefits of implementing early-warning systems and other response activities. One of the largest challenges for using these predictions derives from uncertainty in the forecasts. Due to the inherent uncertainties in prediction and local circumstances that shape high-transmission dengue events, false alarms may occur. Benefits from this analysis include the potential to allow decision makers to avoid otherwise unexpected health system costs or experience other burdens due to the disease in the event of an outbreak. Identifying the net benefit, by taking the difference of the benefits and costs, allows for the comparison of response strategies and makes explicit the trade-offs between forecast skill, response effectiveness, and monetary costs. The information generated by such assessments can be used to inform preparedness and response planning under uncertainty.

Limitations of this research include the need to use additional dengue and climate models to better assess uncertainties in the study and to conduct a formal model evaluation for a long period of time, which also involves access to quality-controlled local climate, entomological, and epidemiological data. We recognize that several other factors may have impacted the spread of dengue during this outbreak that have not been included in this study, including human mobility, spatial dependence of the vector, and the circulation of new serotypes. In particular, due to increased tropical storms on the island, human mobility likely decreased during this time, leading to residents sheltering in their homes and being potentially more exposed to transmission in more rural regions.

Additionally, while the effects of environmental factors, such as rainfall and temperature, on dengue have been well established, the relationship between vector proliferation and dengue incidence is not well understood (Bowman et al., 2014) and the limited number of studies to date have produced somewhat contradictory results (de Albuquerque et al., 2018; de Melo et al., 2012; Degener et al., 2014; Liyanage et al., 2019; Pessanha et al., 2014). One potential reason suggested is that most dengue risk factors are likely to exhibit spatial dependence, and this spatial dependence should be considered in further research (Scott & Morisson, 2003; Vargas et al., 2015). Given that the main premise of an early-warning system is to initiate timely and appropriate response and inform vector-control interventions, it is important to identify the temporal and spatial relationship between vector proliferation and dengue risk.

Finally, dengue has been circulating on Réunion for some time; nevertheless, the introduction of a new serotype, and also a new lineage, can spur epidemics. In the case of the 2018 outbreak, DENV-2 appeared to be the dominant serotype, but DENV-1 and DENV-4 have also been detected (European Commission, 2018). Given the past circulation and cocirculation of serotypes, we pose climate may have played an important role in the 2018 anomaly, as indicated in this analysis. That does not exclude the other factors involved, of course.

For future modeling research, we recommend that subseasonal hindcasts be spatially calibrated using pattern-based calibration to minimize biases in the mean, variability, and spatial patterns; similar efforts have been recently conducted regarding environmental suitability for *Aedes*-borne disease transmission at seasonal time scales (Muñoz et al., 2017; Muñoz et al., sub-judice). Additionally, we suggest that future studies investigate whether this particular dengue outbreak co-occurred with the adaptation of the virus to the vector, a possibility that cannot be ruled out by this analysis. Adaptability, along with human mobility, can pose a great threat to other countries that are otherwise unexposed to specific *Aedes*-borne diseases, such as dengue. As a consequence, from this and future outbreaks, areas across the world with high connectivity to Réunion, or other high-risk areas, are likely to receive viremic travelers. If the timing is right to the local receptivity of the vector, this transmission could initiate epidemics outside the island and pose a great threat to other vulnerable populations.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

Data for dengue cases can be found below (Muñoz, 2020), and any forecast or historical data can be found at the IRI Data Library (Vitart et al., 2017).

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