

1 **Dengue Disease Dynamics are Modulated by the Combined Influence of Precipitation and Landscapes: A**
2 **Machine Learning-based Approach**

3

4 **AUTHORS**

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18

19 ABSTRACT

20 Background: Dengue is an endemic vector-borne disease influenced by environmental factors such as
21 landscape and climate. Previous studies separately assessed the effects of landscape and climate factors
22 on mosquito occurrence and dengue incidence. However, both factors interact in time and space to
23 affect mosquito development and dengue disease transmission. For example, eggs laid in a suitable
24 environment can hatch after being submerged in rain or flood water.

25 Objectives: This study aimed to investigate the combined influences of landscape and climate factors on
26 mosquito occurrence and dengue incidence.

27 Methods: Entomological, epidemiological, and landscape data from the rainy season (July-December)
28 were obtained from respective government agencies in Metro Manila, Philippines, from 2012 to 2014.
29 Temperature, precipitation, and vegetation data were obtained through remote sensing. A random forest
30 algorithm was used to select the landscape and climate variables. Afterwards, using the identified key
31 variables, a model-based (MOB) recursive partitioning was implemented to test the combinatory
32 influences of landscape and climate factors on the ovitrap index and dengue incidence.

33 Results: The MOB recursive partitioning for the ovitrap index indicated that mosquito occurrence was
34 higher in high residential density areas, where industrial areas also exist and are well connected with
35 roads. Precipitation was another key covariate modulating the effects of landscape factors, possibly by
36 expanding breeding sites and activating mosquito reproduction. Moreover, the MOB recursive
37 partitioning indicated that precipitation was the main predictor of dengue incidence, with a stronger
38 effect in high residential density and commercial areas.

39 Discussion: Precipitation with floods has epidemiologically important implications by damaging shelters
40 and causing population displacement, thus increasing exposure to dengue vectors. Our findings suggest

41 that the intensification of vector control during the rainy season can be prioritized in residential and
42 commercial areas to better control dengue disease dynamics.

43

44 INTRODUCTION

45 Dengue is an endemic vector-borne disease influenced by environmental factors such as climate
46 and landscape. Dengue-endemic countries such as the Philippines consider this arboviral disease an
47 economic and health burden (Buczak, et al. 2014). Environmental factors, particularly climate and
48 landscape, play a significant role in regulating the temporal variation and spatial distribution of dengue
49 and the vectors *Aedes aegypti* and *Ae. albopictus* (Hayden, et al. 2010). These factors can mediate
50 human-mosquito interactions by expanding the vector's habitat and increasing its abundance, thus
51 advancing dengue disease transmission (Thongsripong, et al. 2013).

52 Previous studies demonstrated that climate factors such as precipitation and temperature
53 significantly affect both mosquito abundance (Barrera, Amador and MacKay 2011, Naish, et al. 2014) and
54 dengue incidence (Phanitchat, et al. 2019, Carvajal, Viacrusis, et al. 2018). For example, the high
55 availability of breeding sites for mosquitoes during the rainy season in Southeast Asian countries (e.g.,
56 Philippines, Singapore, Thailand, and Indonesia) contributes to the increased number of annual dengue
57 cases (Su 2008, Hashizume, et al. 2012). Many studies have reported that the increasing number of cases
58 is associated with the high number of available mosquito breeding sites that can hold or contain
59 rainwater, thereby facilitating high mosquito abundance (Seidahmed, et al. 2018, Arcari, Tapper and
60 Pfueller 2007). Additionally, high temperatures are responsible for extending adult mosquito longevity,
61 accelerating virus replication, and enhancing the mosquito biting rate (Kilpatrick, et al. 2008, Chan and
62 Johansson 2012).

63 Recent studies have shown that different land use (LU) types (residential, industrial, and
64 agricultural areas) may have different impacts on dengue incidence (Kesetyaningsih, et al. 2018, Sheela,
65 et al. 2017, Sarfraz, et al. 2012, Vanwambeke, Lambin, et al. 2007, Cheong, Leitão and Lakes 2014) given
66 the uneven spatial distribution of vectors in these terrestrial habitats (Piovezan, et al. 2019). Areas with
67 human settlements contribute to a high incidence of dengue (Cheong, Leitão and Lakes 2014, Sarfraz, et
68 al. 2012) due to the high availability of man-made water-holding containers that serve as breeding sites
69 (Ngugi, et al. 2017) and humans as a host preference for blood meals (Higa 2011).

70 Most previous studies investigated the effects of either dynamic climate factors (Carvajal,
71 Viacrusis, et al. 2018, Zheng, et al. 2019, Arcari, Tapper and Pfueller 2007, Tovar-Zamora, et al. 2019,
72 Bavia, et al. 2020) or static spatial distributions of landscape attributes (Seidahmed, et al. 2018,
73 Vanwambeke, Lambin, et al. 2007, Vanwambeke, N.Bennett and Kapan 2011, Sarfraz, et al. 2012) on the
74 temporal variations or spatial distributions of mosquito occurrence and dengue incidence. However,
75 landscape and climate conditions can change concurrently in time and space, and their spatiotemporal
76 interrelation may play a decisive role in determining the positive or negative effects on mosquitoes and
77 dengue, such as interference during flood events. In small areas where rainfall is equally distributed,
78 rainwaters flow from highlands to lowlands due to gravity, and patterns of water flow and retention can
79 greatly differ in LU type due to surface roughness texture and permeability. Comparative studies reported
80 high mosquito densities in flooded lowlands compared with non-flooded highlands (Nasir, et al. 2017,
81 Rydzanicz, Kącki and Jawień 2011). One study reported that the high mosquito abundance in lowlands
82 was influenced by floods that reach mosquito eggs that were previously laid in the environment
83 (Hashizume, et al. 2012). Another study demonstrated that during the dry season, mosquito abundance
84 was high in residential areas given the availability of permanent water-holding containers that served as
85 breeding sites (Little, Bajwa and Shaman 2017); in the wet season, mosquito reproduction expanded to
86 other non-residential areas. These studies found an uneven effect of precipitation on mosquito

87 abundance due to different ecological responses in different local landscapes (Nasir, et al. 2017,
88 Rydzanicz, Kącki and Jawień 2011, Little, Bajwa and Shaman 2017). The characteristics of a local area's
89 landscape can also influence its microclimate (Chang, Li and Chang 2007, Lin, et al. 2018, Thani,
90 Mohamad and Abdullah 2017, Shashua-Bar, Pearlmutter and Erell 2011), potentially thus affecting the
91 ecology of the mosquito and dengue transmission. For example, areas with a high percentage of
92 impervious surfaces (e.g., paved roads, built-up areas) with less vegetation coverage can absorb high
93 amounts of solar radiation and produce more heat compared to areas with less impervious surfaces and
94 extensive vegetation coverage (Koch-Nielsen 1999). Therefore, the combinatory influence of landscape
95 and climate factors on mosquito and dengue incidence must be quantitatively assessed (Sallam, et al.
96 2017). No studies have yet attempted to assess the combined influence of climate and landscape features
97 on dengue disease dynamics.

98 Previous studies that utilized environmental factors to develop dengue epidemiology models
99 faced challenges when jointly considering climate and landscape attributes, preventing us from better
100 understanding dengue disease distribution. One such challenge is the availability of secondary datasets
101 (Sarfraz, et al. 2012, Vanwambeke, Lambin, et al. 2007). Climate data such as temperature and
102 precipitation are typically obtained from ground weather stations. However, using such data is limited by
103 the limited number of ground weather stations. Therefore, remotely sensed climatic variable data have
104 been utilized in epidemiological studies to address the lack of routinely collected data from ground
105 meteorological stations (Kapwata and Gebreslasie 2016, German, et al. 2018). With the introduction of
106 platforms that integrate remote sensing and cloud computation such as Google Earth Engine (GEE)
107 (Gorelick, et al. 2017), it is possible to freely access and process many types of satellite-derived products
108 with notable flexibility, even in large areas (DeVries, et al. 2020). However, many studies that utilize LU
109 based on satellite images contain certain limitations. In this type of map, built-up areas are often treated
110 as a single category (Vanwambeke, et al. 2006, Ibarra, et al. 2014, German, et al. 2018), preventing the

111 ability to further distinguish the subcategories of land utilization such as residential, commercial,
112 industrial, etc. These different categories of LU have different ecological responses to mosquito and
113 dengue dynamics (Thammapalo, et al. 2007); hence, detailed maps might amplify the chances to capture
114 fine scale variations of mosquito habitats and dengue incidence. Although labor intensive, detailed LU
115 maps produced by local governmental agencies based on field observations can help uncover patterns of
116 dengue disease at a fine scale by capturing the different categories of land utilization in urban areas
117 (Nazri, et al. 2011).

118 Another challenge is finding an appropriate method to model complex interactive mechanisms
119 between multiple environmental factors (Little, Bajwa and Shaman 2017, Sarfraz, et al. 2012). In the
120 recent decade, modeling techniques in machine learning methods such as random forests (RFs) (Breiman
121 2001) have been adopted to analyze complex databases and handle anomalies found in datasets such as
122 outliers and multi-collinearity among covariates. Data-intensive modeling has gained popularity in
123 spatiotemporal ecological modeling at the landscape or larger scales to better explain ecological or
124 epidemiological patterns by capturing nonlinear variable interactions (Ryo, Yoshimura and Iwasaki 2018,
125 Ryo, Harvey, et al. 2017b, Ryo and Rilling 2017a). The results of this approach improved RF model
126 accuracy (Leontjeva and Kuzovkin 2016) and better predictability of species' habitat distribution with the
127 inclusion of maximum entropy (Stanton, et al. 2012).

128 This study aimed to examine the combinatory influence of landscape and climate features on
129 mosquito occurrence and dengue incidence across Metropolitan Manila, the Philippines. We employed
130 some advanced machine learning algorithms due to its growing utilization to explore the influence of
131 landscape features or climate on dengue disease (Carvajal, Viacrusis, et al. 2018, Guo, et al. 2017, Ong, et
132 al. 2017, Chen, et al. 2018, Baquero, Santana and Chiaravalloti-Neto 2018) and mosquito occurrence
133 (Mwanga, et al. 2019, Jiménez, et al. 2019, Früh, et al. 2018, Zheng, et al. 2019). By selecting important
134 environmental features for RFs, we further examined and described the optimal combination of

135 landscape and climate conditions that influence dengue disease and mosquito occurrence using model-
136 based (MOB) recursive partitioning.

137

138 MATERIALS AND METHODS

139 Study area

140 Metropolitan Manila is the National Capital Region (NCR) of the Philippines, located at
141 Southwestern Luzon (14°50'N Latitude, 121°E Longitude). With 100% urbanization (Asian Development
142 Bank 2014), the NCR is the most densely populated area in the country (18,165.1 persons/km² spread
143 over an administrative land area of 636 km²) (Asian Green City Index 2011). It comprises 16 cities and one
144 municipality with a total population of 12,877,253 (Philippines Statistics Authority 2019). Each city or
145 municipality is further subdivided into the smallest administrative division, a “Barangay,” commonly
146 known as a village, with 1,706 total villages. A collection of villages can be merged into a “zone”
147 depending on the city’s administrative boundaries.

148 The majority of the target area is covered by residential (54.07%), industrial (9.41%), and
149 commercial (7.45%) areas. The territorial development of Metro Manila occurred through a gradual
150 replacement of agricultural LU by industrial, commercial, and a massive increase in residential areas. The
151 constant spatial and population growth has led to LU pressure and instigated substandard housing in
152 areas with a high risk of flooding (Zoleta-Nantes 200).

153 The climate in Metro Manila is divided into two major seasons: the dry season (November to
154 April) and the wet season (the rest of the year) (DOST 2014). The rainy season from June to September is
155 characterized by strong monsoon rain and tropical storms (World Bank 2014). Heavy rain associated with
156 a lack of drainage infrastructure leads to a high vulnerability for flooding (Zoleta-Nantes 200).

157 Data Sources and Processing

158 **Administrative boundaries**

159 The map of the administrative boundaries of Metropolitan Manila (Figure 1a) was obtained from
160 the Philippine GIS Data clearinghouse (www.philgis.org). Metropolitan Manila includes 1,706 villages
161 (barangays) with most within the City of Manila (n = 897; 53%). In this study, the villages of Manila,
162 Caloocan, and Pasay were merged together into “zones” to facilitate consistency in village size because
163 most villages are very small with an average area of 0.06 km. Additionally, 86% (n = 771) of the villages
164 have a total area of <0.06 km². The average total area of each village in Metropolitan Manila (excluding
165 the City of Manila) is 0.41 km². This study used the City of Manila, Caloocan, and Pasay’s designated zone
166 names to merge villages. Overall, 464 villages or zones were subsequently analyzed in this study. The
167 population statistics were obtained from the Philippine Statistics Authority agency (www.psa.gov.ph).
168 Since the Philippine population census is conducted every five years, we obtained the 2010 (Philippines
169 Statistics Authority 2012) and 2015 (Philippines Statistics Authority 2019) census data and used the
170 compounded population growth rate to calculate the population for the years 2012 and 2013. The sum of
171 the projected population of the merged villages (Manila, Caloocan, and Pasay) was also calculated.

172 **Entomological surveillance**

173 In 2012, governmental institutions (Department of Science and Technology (DOST), Department
174 of Education, Department of Health, Department of Interior, and local governments) implemented a
175 nationwide surveillance program that installed DOST Ovicidal/Larvicidal traps (OL-traps) to monitor
176 *Aedes* mosquitoes to help control dengue transmission and reduce dengue cases (DOST n.d., DOST
177 Mosquito Ovicidal/Larvicidal (OL) Trap for Dengue Prevention 2013). Surveillance programs in many
178 countries have utilized ovitraps as a routine surveillance tool because they are relatively low-cost and
179 reliable in attracting gravid *Aedes* females for oviposition (Silver 2007, Ritchie, et al. 2003). In Metro
180 Manila, ovitraps were installed in public places such as schools, institutes, and other education facilities. A
181 total of 719 georeferenced surveillance locations containing reported Ovitrap indices (OIs) were extracted

182 from the reporting website (<http://oltrap.pchrd.dost.gov.ph/>) (DOST n.d.) from July 2012 to December
183 2014. Afterwards, each georeferenced surveillance location was matched with its corresponding village,
184 with only 268 of the 464 villages containing mosquito surveillance location(s). We aggregated the OIs into
185 a monthly index by dividing the cumulative OI by the total number of sampling locations. Given the low
186 numbers and inconsistent reporting during the months of January to June, the study only included the
187 aggregated monthly OI from July to December of 2012, 2013, and 2014 (Additional file 3).

188 **Epidemiological data**

189 The total number of weekly reported dengue cases from January 2012 to December 2014 for all
190 464 villages was obtained from the National Epidemiology Center, Department of Health, Philippines. We
191 calculated the monthly dengue incidence by dividing the total number of dengue cases each month by
192 the total population of the village multiplied by a population factor of 10,000. The dengue incidence was
193 transformed by adding 1 to all values and obtaining its natural logarithm [$\log_e (n + 1)$].

194 **Climatic factors**

195 Remote sensing (RS) is a promising tool in epidemiological studies (German, et al. 2018, Misslin
196 and Daudé 2017, Buczak, et al. 2014, Araujo, et al. 2015). This study used the Tropical Rainfall
197 Measurement Mission (TRMM) product 3B43 to obtain the monthly average rainfall. This gridded quasi-
198 global product consists of monthly average precipitation measured in hourly bases with 0.25° of spatial
199 resolution (Huffman and Bolvin 2018). The Terra Moderate Resolution Image Spectroradiometer (MODIS)
200 collected the average land surface temperature. The product MOD11A2 consists on the average
201 temperature collected within an eight-day period for both daytime and nighttime temperatures with 1
202 km spatial resolution (USGS n.d.). GEE (Gorelick, et al. 2017) was used to download the RS raster images,
203 apply scaling factor (0.02), and convert temperature values from the default Kelvin (K) to degrees Celsius
204 (°C). This product suffers from missing data, particularly during the rainy season (August-October), given

205 the high cloud cover and other atmospheric disturbances. To overcome this limitation, a Kriging
206 interpolation method was applied to complete monthly temperature records for each village using ArcGIS
207 software version 10.2 (ESRI, Redlands, CA). This method weights the surrounding measured values to
208 derive a surface of predicted values for an unmeasured location (ESRI 2016). Since each village can be
209 covered by multiple pixels of the raster images of precipitation and temperature, the mean value of all
210 pixels within each village (spatial) was calculated per month (temporal) and used for further analyses.

211 A flood hazard map of Metro Manila was obtained from the LiDAR Portal for Archiving and
212 Distribution (LiPAD) website (<https://lipad.dream.upd.edu.ph>) (LiPAD 2018). This flood map indicates the
213 flood susceptibility level at a 10-m spatial resolution (NOAH 2015). There are three categories of flood
214 susceptibility: (a) low (flood water height ranging from 0.1–0.5 m), b) moderate (0.5–1.5 m), and (c) high
215 (above 1.5 m). Initially, the percentage of land covered by each flood risk category was calculated by
216 village and multiplied by a weighing value from 1 (low) to 3 (high) according to the risk category. The
217 average of these three values was calculated and utilized as the flood risk index per village. The degree of
218 flood susceptibility was estimated based on a five-year period of heavy rain scenarios and thus is limited
219 to spatial risk and does not consider the variation of risk throughout a year.

220

221 **Landscape factors**

222 The local LU map of Metropolitan Manila (2004) was obtained from the Philippine Geoportal
223 website (www.geoportal.gov.ph) managed by the Bureau of National Mapping and Resource Authority
224 and the Metropolitan Manila Development Authority (NAMRIA n.d.). This map contains 30 LU types
225 (agricultural, grass, forest, water bodies, open spaces, parks and recreation, education and cultural,
226 health and welfare, religious and cemetery, military, governmental institutions, industrial, commercial,
227 transport, residential areas of very low, low, medium, high, and very high density, and informal

228 settlements). The largest portion (54.07%) was covered by residential areas (very low, low, medium, high,
229 and very high densities) with multi-story dwelling places (1–2, 3–4, 5, or more stories). This study only
230 considered the house density categories (very low, low, medium, high, and very high) given the very small
231 proportion of multi-story categories of more than three stories (0.01%–0.07%). Non-residential areas
232 such as industrial, commercial, and public facilities comprised 37% of Metropolitan Manila. A small
233 portion was covered by natural landscape aspects such as water bodies and forests (10%). The 2004 LU
234 map had a dengue incidence time gap (2012–2014); thus, we updated the map to the period covered by
235 our study so that all input parameters in the model had the same time range. This map was subjected to
236 updates based on open street maps (OSM), processed and distributed by Geofabrik GmbH
237 (www.geofabrik.de). The OSM data contained modifications that occurred before December 2016
238 (Geofabrik GmbH 2019). Prior knowledge of the study area was used to manually inspect and validate the
239 map modifications. LU variables included the percentage of land covered by each LU class (i.e., agriculture,
240 water bodies, commercial, residential) per village (Figure 1b–d). The percentage of each LU class was
241 calculated as follows. Firstly, we calculated the area of each LU class per village. Then, the percentage of
242 each class was determine over the total area of the villages. All edits and calculations of LU areas per
243 village was performed in ArcGIS software, version 10.2.

244 Road network density (RND) assesses the urbanization gradient (Suarez-Rubio and Krenn 2018),
245 which influences mosquito abundance and dengue transmission (Bostan, et al. 2017). The road network
246 map was obtained from the Philippine GIS Data Clearinghouse website (<http://philgis.org/>) and classifies
247 roads as primary, secondary, tertiary, residential, and others (PhilGIS 2012). The RND for each category
248 was calculated by dividing the total length of roads by the total village area. Since the RND of each
249 category of primary, secondary, and tertiary roads was less than 0.001 m/m², we merged them into a
250 single category, “main roads” (Figure 1e). Terra MODIS Normalized Difference of Vegetation Index (NDVI)
251 was derived from the product MOD13Q1 version 6. The NDVI consists of measures of the reflected

252 photosynthetic activity on vegetation and is generated every 16 days at 250-m spatial resolution (USGS
253 n.d.). All images were downloaded through GEE and processed using ArcGIS to obtain their monthly
254 averages per village.

255 **Cross-correlation analysis**

256 A cross-correlation analysis was conducted on the temporal variations of environmental factors
257 (precipitation, temperature, and vegetation) on the OI and dengue incidence. The mean value of
258 Metropolitan Manila area per month for each variable was utilized. We identified the best-lag based on
259 the highest Pearson correlation coefficient that was generated and its statistical significance ($p < 0.05$).
260 These analyses were implemented in R software version 3.6.2 using “*ggpubr*” package version 0.2.4
261 (Kassambara 2019). The best-lag timing for each variable was used for the latter analyses.

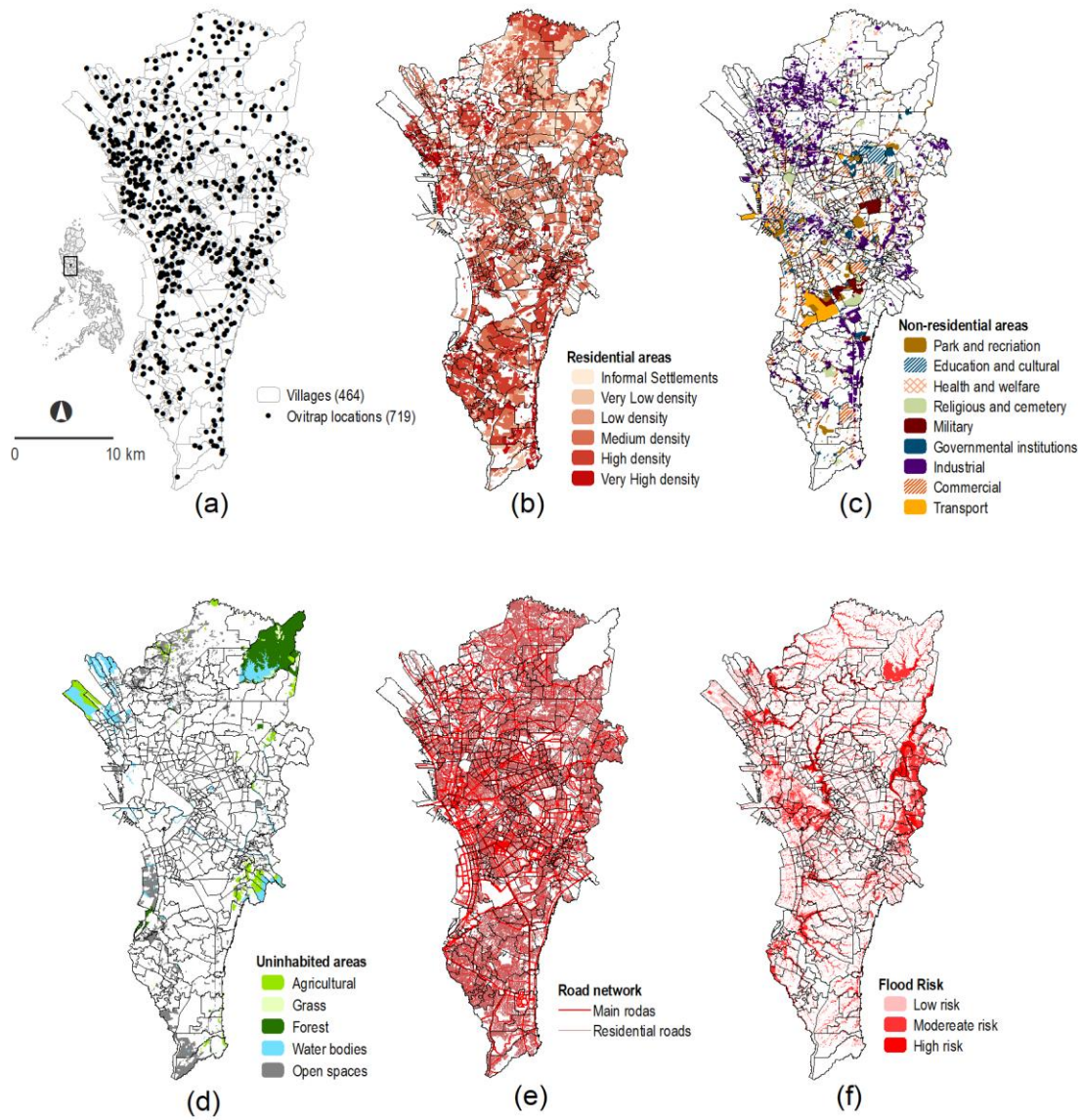
262 **Model development with variable selection**

263 RF is a bootstrap aggregation (bagging) ensemble method that generates a large number of
264 independent bootstrapped trees from random small subsets of the dataset (Breiman 2001). RF is used to
265 solve a variety of classification and regression problems due its ability to handle large numbers of
266 predictor variables even in the presence of complex interactions (Garge, Bobashev and Eggleston 2013).
267 Two regression models were implemented in this study. Dengue incidence was regressed with lagged
268 climate factors, LU types, and OI, with 27 explanatory variables. Additionally, the OI was regressed with
269 lagged climate factors and LU types, with 26 explanatory variables. RF models were estimated using the
270 “*ranger*” package (Wright, Wager and Probst 2020) implemented in the R software version 3.6.2 (R Core
271 Team 2017) with parameters set at $n_{tree} = 500$ and $m_{try} = 5$.

272 To identify the most important predictors of dengue incidence and mosquito occurrence, we
273 assessed variable importance (VI), which was measured as the mean decrease in MSE in the RF models. VI
274 is calculated based on the number of times the explanatory variable is used for splitting, weighted by the

275 improvement to the model as a result of each split, averaged over all trees (Elith, Leathwick and T.Hastie
276 2008). For the VI and respective p-values, we applied the permutation importance method, which
277 computes an unbiased VI measure (Zeileis, Hothorn and Hornik 2008). Positive importance values with p-
278 values less than 0.05 were selected for the subsequent MOB recursive partitioning analysis.

279 To investigate the interactions of the selected explanatory variables, we used MOB recursive
280 partitioning to build a decision tree hierarchy by recursively partitioning the data into several groups
281 using the variable that provides the best split per node (Zeileis, Hothorn and Hornik 2008). Recursive
282 partitioning was implemented via two steps. First, we utilized all selected explanatory variables to build a
283 decision tree to see the overall distributions of the OI and dengue incidence. From this step, we can also
284 identify the main predictors of the OI and dengue incidence. In the second step, we explicitly specified
285 the most important predictor found in the earlier step as the main explanatory variable in the model and
286 then explored covariates that modulate the associations between the main predictors and the response
287 variables. Herewith, we inferred how the OI and dengue incidence were modulated by the interaction
288 between the main predictor and other variables. We used the Linear Model Tree (*lmtree*) interface
289 implemented in “*partykit*” package (Hothorn and Zeileis 2015) in R Software (R Core Team 2017). For
290 each of the generated intermediate nodes, regression coefficients and *p-values* were computed to inform
291 the relevance of the splitting variable in a particular node. We set *p value* < 0.05 and maximum depth = 4
292 as the stopping criteria so that only the most important variables and intermediate nodes that were
293 statistically significant were used for modeling. These hyperparameters have been suggested to avoid
294 model overfitting (Zeileis, Hothorn and Hornik 2008, Pirkle, et al. 2018), and simplification of tree
295 structure was performing by only including the most relevant predictors (Kopf, Augustin and Strobl 2010).
296 The *p-values* were *Bonferroni* corrected to control a false positive rate. The slope coefficients, R-squared,
297 and p-values were obtained using the “*summary()*” function.



298

299 Figure 1: Administrative boundaries of Metropolitan Manila showing: (a) Ovitrap locations; Landscape
300 features: (b) Residential areas classified according to densities, (c) Non-residential areas, (d) Uninhabited
301 areas, (e) Road networks, and (f) Flood risk.

302

303 RESULTS

304 Cross-correlation analysis

305 Precipitation yield had the highest positive and significant correlation with dengue incidence (r
306 = 0.69, $p = 0.00$) at a one-month lag, followed by OI ($r = 0.52$, $p = 0.05$) and temperature ($r = 0.52$, $p =$
307 0.05), both at a three-month lag. Vegetation displayed a negative and significant correlation ($r = -0.71$, p
308 = 0.00) at a one-month lag (Table 1). Vegetation showed the highest positive correlation with the OI ($r =$
309 0.77, $p = 0.00$) at a three-month lag, followed by temperature ($r = 0.73$, $p = 0.00$) and precipitation ($r =$
310 0.48, $p = 0.04$), both at a zero-month lag.

311 Table 1: Cross-Correlation Analysis of Temporal Climate Factors in Dengue Incidence and Ovitrap Index

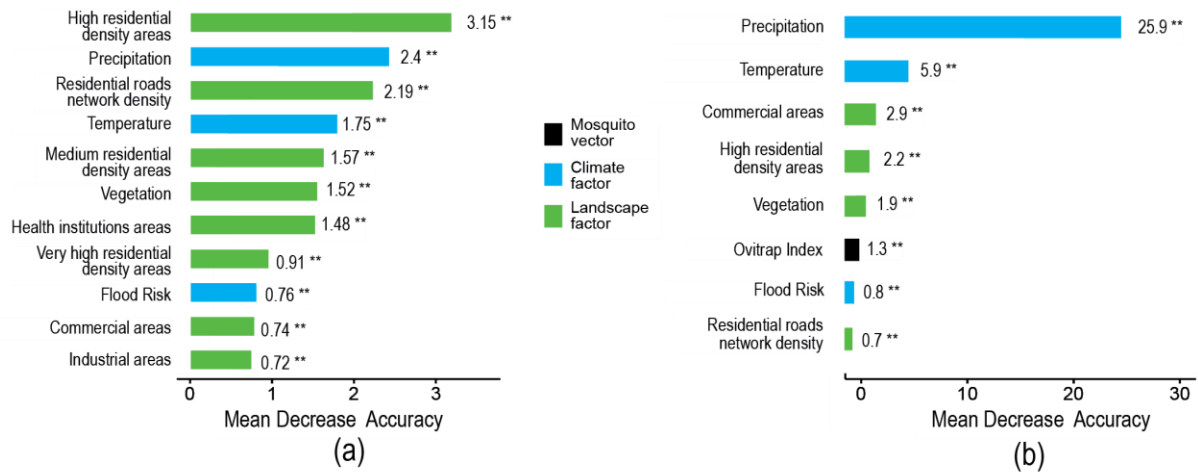
Variables	Dengue incidence			Ovitrap index		
	Lag month	r value	p value	Lag month	r value	p value
Ovitrap Index	3	0.52	$p = 0.05$	-	-	-
Precipitation	1	0.69	$p = 0.00$	0	0.48	$p = 0.04$
Temperature	3	0.52	$p = 0.05$	0	0.73	$p = 0.00$
Vegetation	1	-0.71	$p = 0.00$	3	0.77	$p = 0.00$

312

313 Variable selection

314 Figure 2 shows the variable importance of the selected variables in the two RF models. The OI
315 was significantly associated with 11 variables (three climatic factors and eight landscape factors). High
316 residential density areas were ranked first, followed by precipitation, residential RND, temperature,
317 medium residential density areas, vegetation, health institution areas, very high residential density areas,
318 flood risk, commercial areas, and industrial areas (Figure 2a). Dengue incidence was significantly
319 associated with eight variables (three climatic factors, four landscape factors, and OI). Precipitation was

320 ranked first, followed by temperature, commercial areas, high residential density areas, vegetation, OI,
 321 flood risk, and residential RND (Figure 2b). These variables were used in the subsequent modeling.

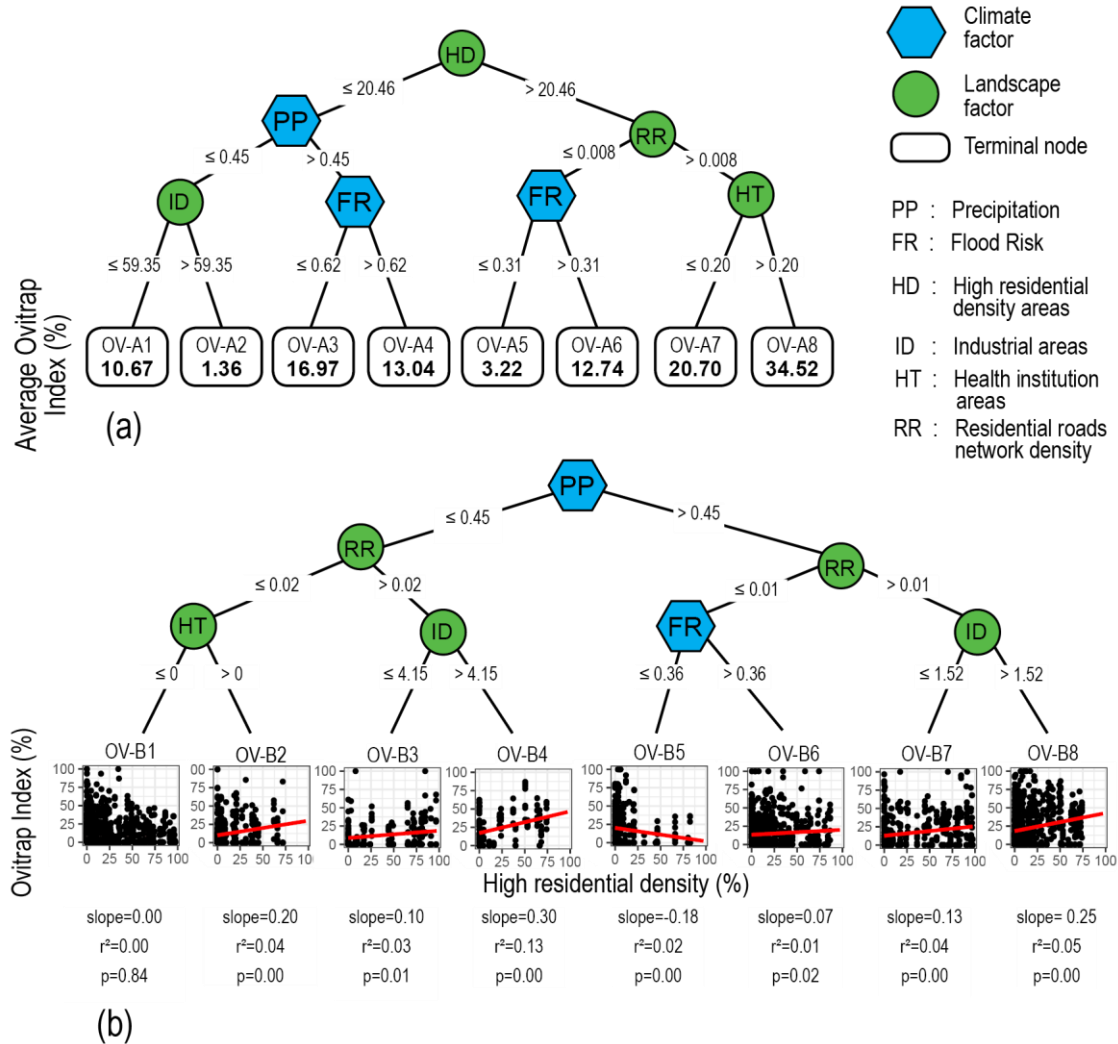


322
 323 Figure 2: Variable importance measures of the variables with the most significant associations with (a)
 324 ovitrap index and (b) dengue incidence; (**) statistically significant at p < 0.05.

325
 326 **Model-based recursive partitioning**

327 Figure 3a displays the MOB tree of the environmental conditions explaining the distribution of
 328 the OI. The tree is composed of three partitioning levels and eight terminal nodes. Each terminal node
 329 shows the average OI of a subset of the entire dataset based on selected landscape and climatic features
 330 and labeled accordingly as terminal nodes OV-A1 to OV-A8. In the MOB tree, high residential density was
 331 identified as the first-level partitioning variable and thus considered the most important environmental
 332 feature. The succeeding levels were comprised of residential RND, precipitation, industrial areas, health
 333 institutional areas, and flood prone areas. The order of the variables was agreed with the estimated
 334 variable importance (Figure 2a). The average OI from node OV-A1 to OV-A8 ranged from 1.36 to 34.52%.

335 We employed further analyses to identify the interactive effects of the most important
 336 predictor (i.e., high residential density) with other environmental factors on OI (Figure 3b). Higher slopes
 337 and R-squared values were found in nodes OV-B4 and OV-B8 (0.30 ($R^2 = 0.13$, $p = 0.00$) and 0.25 ($R^2 =$
 338 0.05 , $p = 0.00$), respectively), indicating that the effect of high residential density areas on OI is
 339 modulated by precipitation, residential roads, and industrial areas. Discordant associations of high
 340 residential density areas to OI were observed for flood risk. A negative slope of -0.18 ($R^2 = 0.02$, $p = 0.00$)
 341 was found when the flood risk was lower or equal to 0.36 (node OV-B5) whereas a positive slope of 0.07
 342 ($R^2 = 0.01$, $p = 0.02$) was found when the flood risk was greater than 0.36 (node OV-B6).

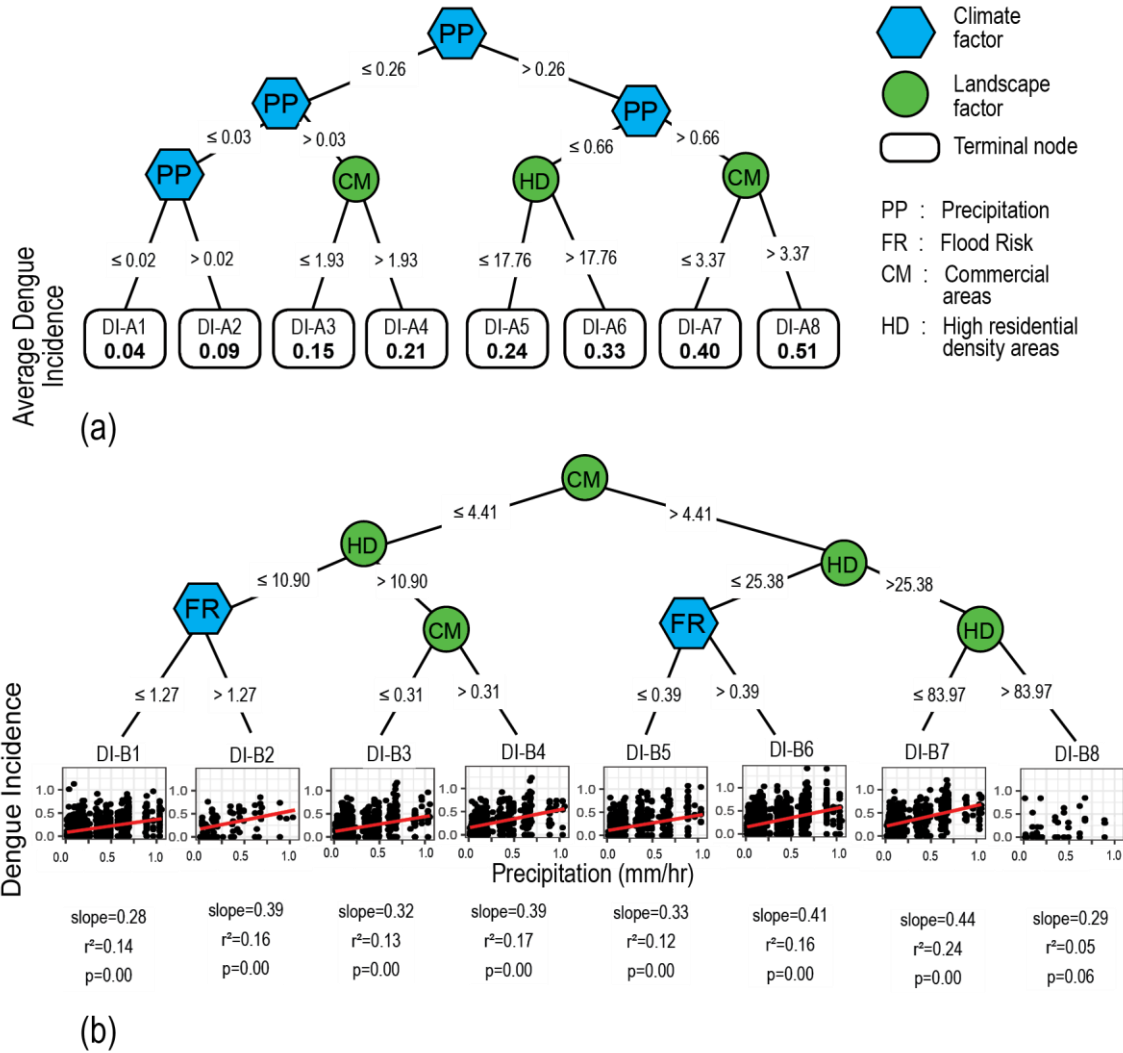


343

344 Figure 3: Recursive partitioning trees for identifying the (a) most influential variables on the ovitrap index
345 and (b) interactive effects between environmental factors and the ovitrap index.

346 Figure 4a shows the MOB tree of the influence of climatic and landscape factors on dengue
347 incidence. This tree is composed of eight terminal nodes generated from three partitioning levels. Each
348 terminal node shows the average dengue incidence of a subset of the entire dataset based on selected
349 climatic and landscape factors and is labeled accordingly as terminal nodes DI-A1 to DI-A8. Precipitation
350 was the partitioning variable in the first and second partitioning levels and thus considered the most
351 important environmental feature, similar to the RF analysis (Figure 2b). The succeeding partitioning levels
352 comprised commercial and high residential density areas. The average dengue incidence on the terminal
353 nodes DI-A1 to DI-A8 ranged from 0.04 to 0.51.

354 We employed further analyses to infer the interactive effect of the most important predictor
355 (precipitation) with other environmental factors on dengue incidence (Figure 4b). We specified
356 precipitation as the main predictor and the remaining variables as interacting factors. Higher slopes and
357 R-squared values were found in relation to two different interaction patterns and were considered
358 influential toward dengue incidence. The first pattern involved interactions between precipitation,
359 commercial areas, and high residential density areas (nodes DI-B7 and DI-B4, with slopes of 0.44 ($R^2 =$
360 0.24, $p = 0.00$) and 0.39 ($R^2 = 0.17$, $p = 0.00$), respectively). The second pattern involved interactions
361 between precipitation, commercial areas, high residential density areas, and flood risk (nodes DI-B6 and
362 DI-B2, with slopes of 0.41 ($R^2 = 0.16$, $p = 0.00$) and 0.39 ($R^2 = 0.16$, $p = 0.00$), respectively).



363

364 Figure 4: Recursive partitioning trees for identifying the (a) most influential variables on dengue incidence

365 and (b) the interactive effects between environmental factors and dengue incidence.

366 DISCUSSION

367 The interactive effects between high residential density, precipitation, and other landscapes in
368 modulating ovitrap index

369 Ovitrap, in general, can detect the presence of both *Ae. aegypti* and *Ae. albopictus*. However,
370 the OI data utilized in this study does not contain any information on the proportion of these two species.

371 Therefore, in this section, our discussion focuses solely on *Ae. aegypti*. This is because previous studies
372 that surveyed selected areas of Metropolitan Manila indicated a high infestation rate of *Ae. aegypti*
373 (>80%) (Mistica, et al. 2019, Carvajal, Ho, et al. 2019), thereby making it the primary vector for dengue
374 transmission.

375 Both the RF and MOB tree (Figures 2a and 3a) analyses clearly indicate the importance of high
376 residential density areas on the overall distribution of the OI. This finding is consistent with previous
377 studies reporting that high residential areas are potential sources of breeding sites and blood meals for
378 *Ae. aegypti* (Ngugi, et al. 2017). These areas are highlighted as the foremost breeding sites for *Ae. aegypti*
379 due to the permanent availability of breeding containers and humans, who serve as blood sources (Higa
380 2011, Ngugi, et al. 2017, Little, Bajwa and Shaman 2017). Herewith, residential areas exhibited ecological
381 requirements to serve as main mosquito habitats compared with other types of landscapes.

382 To determine how high residential density areas interact with other environmental factors in
383 modulating OI, we employed further analyses by specifying high residential density areas as the main
384 predictor and the remaining variables as interacting factors (Figure 3b). The influence of high residential
385 density areas on mosquito occurrence became clearer under certain environmental conditions. The two
386 nodes OV-B4 and OV-B8 with the highest slopes (0.30 and 0.25, respectively) were formed in high
387 industrial areas (>4.15 and >1.52%, respectively) and high residential road areas (>0.02 and >0.01 m/m²,
388 respectively), and node OV-B4 had a low precipitation condition (≤ 0.45 mm/hr). Since *Ae. aegypti*
389 preferentially breeds in small water containers exposed to the outdoors (Carvajal, Ho, et al. 2019, Ngugi,
390 et al. 2017), little rainfall might be sufficient to maintain optimal levels of water suitable for mosquito
391 emergence. Conversely, enhanced rainfall might flush out mosquito eggs and larvae from breeding
392 containers and reduce the sensitivity of the OI to changes in high residential density areas. The
393 destructive effect of significant precipitation on mosquito development has been suggested in another

394 work (Dickin, Schuster-Wallace and Elliott 2013); however, the possible precipitation thresholds remain
395 unclear.

396 Residential RND was the partitioning variable on the second level of the MOB tree.
397 Furthermore, nodes OV-B4 and OV-B8, which had the highest slopes, were partitioned with higher
398 residential road densities (>0.02 and >0.01 m/m², respectively). These results suggest an enhanced
399 vulnerability to mosquito occurrence in high residential density areas with a higher density of residential
400 roads. Roads not only serve as transportation networks for people and goods but are also simultaneously
401 accompanied by drainage components (e.g., roadside drains or canals, drain sumps), which collect surface
402 water runoff for discharge in appropriate locations to avoid flooding. However, in many cases, efficient
403 drainage in residential areas can be compromised by the encroachment of concrete structures or garbage
404 clogging canals (Lagmay, et al. 2015). These interferences can inhibit complete water flow, resulting in
405 spots of accumulated water, which can create favorable habitats for *Ae. aegypti* (Paploski, et al. 2016).
406 Growing evidence has suggested a positive association between drainage and the occurrence of *Ae.*
407 *aegypti* in Singapore (Seidahmed, et al. 2018), Brazil (Souza, et al. 2017) and Australia (Montgomery, et
408 al. 2004).

409 Notably, with increased precipitation (>0.45 mm/hr), high residential density areas showed an
410 opposite association to OI depending on the flood risk (Figure 3b). Increased flood risk led to a positive
411 association between high residential density areas and OI (node OV-B6) whereas reduced flood risk led to
412 a negative association (node OV-B5). Breeding containers located in high residential density areas with a
413 higher flood risk, despite being watered by rainwater or water for domestic usage, might have a higher
414 chance to be reached by flood waters. However, flood waters can also extend the range of potential
415 habitats for mosquitoes (Yee, et al. 2019). Even more unusual breeding sites such as underground septic
416 tanks were reported as favorable for *Ae. aegypti* reproduction in residential areas in Puerto Rico (R.
417 Barrera, et al. 2008). These conflicting potential effects of flood on mosquito habitats might explain the

418 higher vulnerability for mosquito occurrence in high residential density areas with higher flood risks (node
419 OV-B6) compared with high residential density areas with lower flood risks (node OV-B5).

420 Node OV-B1, which had less precipitation (≤ 0.45 mm/hr), residential roads (≤ 0.02 m/m²), and
421 no health institution areas ($\leq 0\%$), is an extreme situation of null sensitivity of the OI toward high
422 residential density areas. This node's slope (0.00, $R^2 = 0.00$, $p = 0.84$) might indicate that the mixture of
423 other types of landscapes with residential areas is essential to enhance the sensitivity of the OI in high
424 residential density areas. However, further work is necessary to test this hypothesis and explain potential
425 mechanistic effects.

426 The adaptation of *Ae. aegypti* closer to human settlements does not seem to be solely
427 influenced by environmental factors; certain human practices (e.g., housing in flood prone areas, weak
428 environmental sanitation, obstruction of drainage canals, water storage practices for domestic usage)
429 might contribute to the occurrence of mosquitoes. Therefore, environmental improvement and
430 integrated control measures at the community level to improve the environment surrounding households,
431 careful domestic water storage, and other sanitation practices are the most promising solutions for
432 reducing the occurrence of mosquitoes.

433 The environmental conditions associated with mosquito occurrence must be carefully
434 interpreted given the nature of the mosquito occurrence data (OI) utilized in this study. The OI is based
435 on the percentage of positive ovitraps and can detect the presence or absence of vectors. However, it has
436 limited capacity in displaying the precise range of mosquito density in the environment (Harburguer, et al.
437 2016). Therefore, the environmental conditions inferred from this ovitrap MOB tree might only display
438 the conditions for mosquito oviposition and not necessarily the conditions influencing mosquito
439 abundance.

440 **Interactive effects between precipitation and landscapes in modulating dengue incidence**

441 Both RF (Figure 2b) and MOB tree (Figure 4a) analyses showed a significant influence of
442 precipitation with a combinatory influence of high residential density and commercial areas in increasing
443 dengue incidence. The significant influence of precipitation agrees with previous studies in the Philippines
444 (Carvajal, Viacrusis, et al. 2018, Su 2008) and Malaysia (Dickin, Schuster-Wallace and Elliott 2013), which
445 reported precipitation as a main driver of the temporal variation of dengue incidence. These studies
446 assumed that the high correlation between precipitation and dengue incidence is due to the increasing
447 mosquito density during the rainy season. On the MOB tree (Figure 4a), precipitation was the partitioning
448 variable on the first and second levels whereas high residential and commercial areas were selected as
449 partitioning variables on level 3. Overall, dengue incidence MOB trees support the significant influence of
450 precipitation on dengue incidence.

451 Previous studies have discussed the impact of precipitation on the increased number of dengue
452 cases because of its role in increasing the number of available breeding sites for mosquitoes (Carvajal, Ho,
453 et al. 2019, Pasin, et al. 2018). However, the transference of viruses from mosquitoes to humans occurs
454 when the dynamics between the vector, the virus, and hosts are favorable (de Melo, Scherrer and Eiras
455 2012). These conditions include the ratio of infected mosquitoes, human behavior, human exposure, and
456 the ability of mosquitoes to transfer pathogens to humans (Thi, et al. 2017). Human behavior and
457 exposure can also be altered by meteorological conditions (Akter, et al. 2017). Precipitation combined
458 with floods, for example, can generate changes in the physical environment such as damaging shelters,
459 which can alter urban dynamics (e.g., population displacement, increase of human exposure to vectors),
460 thus favoring dengue transmission (Few, et al. 2004).

461 In the variable selection step, precipitation showed a very strong influence on dengue incidence
462 compared with other environmental factors. We conducted further analyses to evaluate the combinatory
463 influence of precipitation with other environmental factors in modulating dengue incidence (Figure 4b).
464 The association between precipitation and dengue incidence was further notable in these analyses,

465 particularly in areas covered by high residential and commercial areas, suggesting a vulnerability of these
466 landscapes in modulating dengue incidence. The highest slope (0.44, $R^2 = 0.24$, $p = 0.00$) was reported for
467 node DI-B7 (Figure 4b), which incorporates interactions between precipitation, commercial areas
468 (>4.41%), and high residential density areas (between 25.38 and 83.97%). Herewith, this nodal pathway
469 was considered the most influential environmental condition for increasing dengue incidence with high
470 precipitation. The second highest slope (0.39, $R^2 = 0.17$, $p = 0.00$) was reported for node DI-B4 and
471 formed with environmental conditions of commercial areas ($0.31 < \text{commercial areas} \leq 4.41\%$) and high
472 residential density areas (>10.90%). With these influential patterns observed in terminal nodes DI-B7 and
473 DI-B4, we suggest that certain ecological factors in commercial and high residential areas can enhance
474 dengue transmission with precipitation. Previous studies have shown that residential and commercial
475 areas experience the most damaged houses during extreme rainfall and flood events in Metropolitan
476 Manila (Porio 2014, a, Porio 2011, b). Damage to families' shelters, followed by massive displacements,
477 might subject many people to deteriorated conditions with limited capacity to observe disease
478 prevention and vector control measures. The high human exposure to vectors in these areas might create
479 an avenue for high dengue transmission. A highly sensitive influence of precipitation on increasing
480 dengue incidence was observed under high flood risk conditions (DI-B6 and DI-B2). These terminal nodes
481 showed higher slopes of 0.41 ($R^2 = 0.16$, $p = 0.00$) and 0.39 ($R^2 = 0.16$, $p = 0.00$), respectively. Conversely,
482 terminal nodes with lower flood risk (nodes DI-B1 and DI-B5, with slopes of 0.28 ($R^2 = 0.14$, $p = 0.00$) and
483 0.33 ($R^2 = 0.12$, $p = 0.00$), respectively) displayed less sensitivity in increasing dengue incidence. These
484 examples illustrate that the vulnerability for dengue transmission in residential and commercial areas
485 with high precipitation can be further enhanced by floods. Floods can contribute to increased mosquito
486 density and force people to live confined in deteriorated conditions of habitability with high exposure to
487 vectors. The combination of human presence and exposure to vectors has been linked to high dengue
488 transmission in residential (Scott and Morrison 2010, de Moura Rodrigues, et al. 2015) and commercial

489 areas (Honório, et al. 2009, Thammapalo, et al. 2007). Due to the anthropophilic nature of *Ae. Aegypti*,
490 high human presence and exposure in these areas may increase feeding opportunities for mosquitoes
491 and increase the chances of dengue fever infections (Koyadun, Butraporn and Kittayapong 2012).
492 Because many people are exposed in areas with high precipitation levels, it becomes easier for
493 mosquitoes to bite and infect many people in a short time, thus increasing the incidence of dengue (Akter,
494 et al. 2017).

495 We expected that the resulting dengue incidence and ovitrap MOB trees (Figure 3a and 3b)
496 would yield similar tree topology patterns. This expectation assumed that the high dengue incidence
497 during the rainy season is a result of high mosquito abundance influenced by precipitation. However, our
498 result was contrary to our assumption and could be explained by methodological limitations. The OI is
499 based on the percentage of positive ovitraps with the presence or absence of vectors; however, it has a
500 limited capacity in precisely displaying the range of mosquito density in the environment transmitting
501 dengue. Although ovitraps are fast and cost-effective tools for monitoring the presence of mosquitoes,
502 the OI has a low association with dengue incidence compared with adult mosquito abundance data (de
503 Melo, Scherrer and Eiras 2012). Additional correlation analyses (data not shown) of the OI and dengue
504 incidence from the terminal nodes of Figure 3a and 3b were not significantly correlated. Therefore, the
505 mosquito occurrence data (OI) utilized in this study might be responsible for the dissimilarities in the
506 ovitrap and dengue incidence MOB tree topology patterns.

507

508 **Accessibility of data, modeling approach, and limitations**

509 Most previous epidemiological studies faced limitations when integrating climatic and
510 landscape data given the scarcity of data and modeling techniques. Although we consider landscape to be
511 static in this study, the model development did not distinguish dynamic or static terms. Since the physical

512 characteristics of each village did not change significantly over the three years, we assumed that these
513 characteristics remained the same for each month of the study period. Based on this assumption, we
514 utilized a data structure from previous studies that repeated the values of the static variables for the
515 monthly values of the climate variables in each village (Kaul, et al. 2018). This design allowed us to analyze
516 dengue epidemiology as a function of the combinatory influences of climate dynamics over the static
517 landscape.

518 Many methods from conventional statistics and machine learning may, in principle, be used to
519 handle datasets with temporal and spatial dimensions. Usually a statistical model suggests empirical
520 relationships between variables to generate specific outcomes based on certain assumptions and a priori
521 knowledge of the modeled dynamics (Bzdok, Altman and Krzywinski 2018, Kapwata and Gebreslasie
522 2016). By contrast, machine learning does not require a specific model structure in advance. The
523 algorithm itself can automatically utilize the original input data to identify hidden patterns in complex
524 data structure (Richter and Khoshgoftaar 2018). Beforehand, statistics requires us to declare a formal
525 model that incorporates our knowledge of the system. Thus, before implementing a model, careful
526 inspection of the data is necessary (e.g., normal distribution) (Olden, Lawler and Poff 2008). Machine
527 learning makes minimal assumptions about the data structure and can be effective even when the data
528 are gathered without a carefully controlled experimental design (Bzdok, Altman and Krzywinski 2018).
529 Additionally, machine learning is less sensitive to outliers and can efficiently address higher
530 dimensionality variables even in the presence of complicated nonlinear interactions among covariates
531 (Olden, Lawler and Poff 2008). The increase in data complexity may inherit some disadvantages to
532 classical statistical methods. Instead, we utilized a machine learning approach such as RF for variable
533 selection and recursive partitioning for subset selection because of their ability to handle complex
534 datasets and evaluate nonlinear relationships in the data without having to satisfy the restrictive
535 assumptions required by conventional approaches.

536 Machine learning, specifically RF, is often the preferred modeling method in a wide variety of
537 epidemiological studies due to its capability to handle large datasets and accurately identify the best
538 predictors (Kapwata and Gebreslasie 2016). However, many studies only ranked the relative importance
539 of individual variables in influencing mosquitoes and dengue. Ranking the importance of variables alone is
540 not enough to infer the dynamics occurring in the environment and their influence on dengue
541 epidemiology (Sallam, et al. 2017). As discussed previously, there are multiple interacting factors in the
542 environment that could play important roles in influencing mosquito and dengue occurrence. RF was able
543 to handle the initial dataset and screen the most relevant variables associated with the OI and dengue
544 incidence. Although RF can identify the most important variables, it cannot explain the interactions
545 among covariates. Therefore, a recent study recommends also applying a machine learning method that
546 is relatively easy to interpret (Ryo, Angelov, et al. 2020). By utilizing the recursive partitioning method in
547 this study, we demonstrated important mechanistic interplays between environmental factors and
548 presented specific conditions influencing the OI and dengue incidence. Furthermore, the same variables
549 were identified as most influential on dengue and mosquitoes in RF and recursive partitioning. This
550 consistency of results indicates the appropriateness of the adopted study design in capturing
551 combinatory influences among environmental factors. However, since the data utilized are limited (July-
552 December), subsequent studies should be conducted to infer whether complete data (January-
553 December) with a similar modeling approach leads to different or similar results.

554 The utilization of RS in our study made it possible to access spatiotemporal temperature,
555 precipitation, and vegetation data for each village. These types of data overcome the limited accessibility
556 of such information at fine scales in areas where the spatial coverage of weather stations is coarse
557 (German, et al. 2018). By using Google Earth Pro, we were able to use cloud computation to conduct all
558 preliminary processing of the data, which significantly shortened the working time. Moreover, detailed LU
559 maps can distinguish the risk of dengue and mosquito occurrence at a fine scale. Many studies that used

560 coarse LU classification, for example, reported that *Ae. aegypti* and dengue incidence are positively
561 correlated with residential areas (Vanwambeke, Lambin, et al. 2007, Vanwambeke, N.Bennett and Kapan
562 2011, Sarfraz, et al. 2012). In this study, we demonstrated that the distributions of mosquito and dengue
563 can also vary depending on the type of density in these residential areas.

564 Our study, however, has certain limitations. As mentioned in the methods, the entomological
565 data used in this study are incomplete and only correspond to the months of July-December of 2012–
566 2014. This period covers the rainy season in Metro Manila. Therefore, the lack of dry season data
567 (January-June) causes potential bias in our study. Furthermore, ovitraps were installed in only 298 of 464
568 villages across Metro Manila. Complete data may better describe mechanistic understanding of
569 associations between the dengue metrics and ambient environment factors. Nevertheless, our findings
570 may still reflect the actual circumstances of LU and climatological characteristics of the study area. The
571 results of the combinatory influences of landscape and climate may differ in other urban cities,
572 particularly in rural areas in the Philippines and other dengue-endemic countries. Nonetheless, the
573 methodology presented in this study can infer interplays between climate and landscape on mosquito
574 occurrence and dengue incidence.

575 Our study demonstrated notable combinatory effects between climate and landscape in
576 relation to the occurrence of mosquitoes and dengue incidence. It suggests discordant patterns wherein
577 the OI is primarily influenced by landscapes and modulated by the effects of precipitation. Dengue
578 incidence is primarily influenced by precipitation and modulated by landscapes. Such understanding and
579 knowledge can further strengthen the design and implementation of prevention and control measures
580 against dengue vectors and disease.

581 In recent years, vector control efforts in eliminating mosquito breeding sites have intensified in
582 residential areas by identifying and destroying breeding sites. However, we demonstrated that the

583 existence of potential breeding sites in the landscape is not the only reason for dengue transmission.
584 These efforts should be accompanied by effective improvements in urban settings by making them more
585 resilient to mosquito-vectored diseases.

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594 The authors declare they have no actual or potential competing interests.

595

596 **Data sharing**

597 Entomological data are available from the Department of Science and Technology
598 (<http://oltrap.pchrd.dost.gov.ph/>); epidemiological data are available from the National Epidemiology
599 Center, Department of Health–Philippines, upon request; meteorological (Precipitation and Temperature)
600 and vegetation data from remote sensing are available through GEE
601 (<https://code.earthengine.google.com/>); land use data from the Geoportal Philippine website
602 (www.geoportal.gov.ph) are available upon request; population statistics of Metro Manila are available
603 from Philippine Statistics Authority (<http://www.psa.gov.ph>); and flood risk data are available from LiDAR
604 Portal for Archiving and Distribution website (<https://lipad.dream.upd.edu.ph>).

605

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