Science of the Total Environment 792 (2021) 148406

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Dengue disease dynamics are modulated by the combined influences of precipitation and landscape: A machine learning approach

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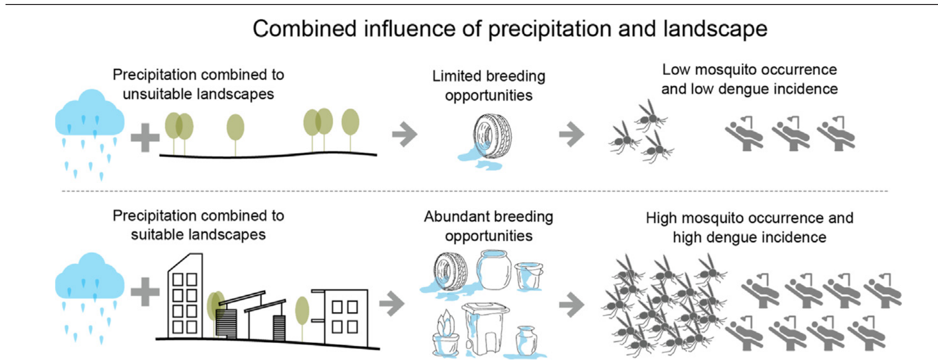
HIGHLIGHTS

- Dengue dynamics are influenced by the combined effects of precipitation and landscape.
- Landscape factors are strongly influential in increasing the sensitivity of mosquito occurrence.
- Climate factors strongly increase the sensitivity of dengue incidence.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 21 January 2021
Received in revised form 25 May 2021
Accepted 8 June 2021
Available online 10 June 2021

Editor: Scott Sheridan

Keywords:
Recursive partitioning
Random forest
Dengue
Combined influences
Environmental factors

ABSTRACT

Background: Dengue is an endemic vector-borne disease influenced by environmental factors such as landscape and climate. Previous studies separately assessed the effects of landscape and climate factors on mosquito occurrence and dengue incidence. However, both factors concurrently coexist in time and space and can interact, affecting mosquito development and dengue disease transmission. For example, eggs laid in a suitable environment can hatch after being submerged in rain water. It has been difficult for conventional statistical modeling approaches to demonstrate these combined influences due to mathematical constraints.
Objectives: To investigate the combined influences of landscape and climate factors on mosquito occurrence and dengue incidence.
Methods: Entomological, epidemiological, and landscape data from the rainy season (July–December) were obtained from respective government agencies in Metropolitan Manila, Philippines, from 2012 to 2014. Temperature, precipitation and vegetation data were obtained through remote sensing. A random forest algorithm was used to select the landscape and climate variables. Afterward, using the identified key variables, a model-based (MOB) recursive partitioning was implemented to test the combined influences of landscape and climate factors on ovitrap index (vector mosquito occurrence) and dengue incidence.
Results: The MOB recursive partitioning for ovitrap index indicated a high sensitivity of vector mosquito occurrence on environmental conditions generated by a combination of high residential density areas with low precipitation. Moreover, the MOB recursive partitioning indicated high sensitivity of dengue incidence to the effects of

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https://doi.org/10.1016/j.scitotenv.2021.148406

precipitation in areas with high proportions of residential density and commercial areas.
Conclusions: Dengue dynamics are not solely influenced by individual effects of either climate or landscape, but rather by their synergistic or combined effects. The presented findings have the potential to target vector surveillance in areas identified as suitable for mosquito occurrence under specific climatic conditions and may be relevant as part of urban planning strategies to control dengue.

1. Introduction

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

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

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

Most previous studies investigated the effects of either dynamic climate factors (Carvajal et al., 2018; Zheng et al., 2019; Arcari et al., 2007; Tovar-Zamora et al., 2019; Bavia et al., 2020) or static spatial distributions of landscape attributes (Seidahmed et al., 2018; Vanwambeke et al., 2007; Vanwambeke et al., 2011; Sarfraz et al., 2012) on the temporal variations or spatial distributions of mosquito occurrence and dengue incidence. However, landscape and climate conditions concurrently coexist in time and space, and their spatiotemporal interrelation and influence on dengue dynamics may not be occurring separately. In small areas where rainfall is equally distributed, surface runoff flows from highlands to lowlands due to gravity, increasing water concentration in lowlands compared with that in highlands. Comparative studies reported high mosquito densities in flooded lowlands compared with nonflooded highlands (Nasir et al., 2017; Rydzanicz et al., 2011). One study reported that the high mosquito abundance in lowlands was influenced by floods that reach mosquito eggs that were previously laid in the environment (Hashizume et al., 2012). Another study demonstrated that during the dry season, mosquito abundance was high in residential areas given the availability of permanent water-holding containers that served as breeding sites (Little et al., 2017); in the wet season, mosquito reproduction expanded to other nonresidential areas. These studies found an uneven effect of precipitation on mosquito abundance potentially due to different preexisting LU types (Nasir et al., 2017; Rydzanicz et al., 2011; Little et al., 2017). The characteristics of a local area's landscape can also influence its microclimate (Chang et al., 2007; Lin et al., 2018; Thani et al., 2017; Shashua-Bar et al., 2011), potentially affecting the ecology of the mosquito (Murdock et al., 2017) and dengue transmission. For example, areas with a high percentage of impervious surfaces (e.g., paved roads, built-up areas) with less vegetation coverage can absorb high amounts of solar radiation and produce more heat compared to areas with less impervious surfaces and extensive vegetation coverage (Koch-Nielsen, 1999). Therefore, the combined influence of landscape and climate factors on mosquito and dengue incidence must be quantitatively assessed (Sallam et al., 2017). No studies have yet attempted to assess the combined influence of climate and landscape features on dengue disease dynamics.

Previous studies that utilized environmental factors to develop dengue epidemiology models faced challenges when jointly considering climate and landscape attributes, preventing us from better understanding dengue disease distribution. One such challenge is the availability of secondary datasets (Sarfraz et al., 2012; Vanwambeke et al., 2007). Climate data such as temperature and precipitation are typically obtained from ground weather stations (WS). However, using such data is limited by the limited number of ground WS. Therefore, remotely sensed climatic variable data have been utilized in epidemiological studies to address the lack of routinely collected data from ground meteorological stations (Kapwata and Gebreslasie, 2016; German et al., 2018). The recent introduction of platforms that integrate remote sensing and cloud computation such as Google Earth Engine (GEE) (Gorelick et al., 2017) enhances free access and processing of a wide variety of satellite-derived products for precipitation, temperature, vegetation, and LU with notable flexibility, even in large areas (DeVries et al., 2020). However, many studies that utilize LU based on satellite image classification contain certain limitations. In this type of map, built-up areas are often merged into a single category (Vanwambeke et al., 2006; Ibarra, et al., 2014; German et al., 2018), preventing the ability to further distinguish the subcategories of land utilization such as residential, commercial, industrial, etc. These different categories of LU may have different ecological responses to mosquito and dengue dynamics that need to be accurately captured (Thammapalo et al., 2007); hence, detailed maps might amplify the chances to capture fine scale variations of mosquito habitats and dengue incidence. Although labor intensive, detailed LU maps produced by local governmental agencies based on field surveys can help uncover patterns of dengue disease at a fine scale in urban areas (Nazri et al., 2011).

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

This study aimed to examine the combined influences of landscape and climate features on mosquito vector occurrence and dengue incidence across Metropolitan Manila, the Philippines. We focused on identifying which specific combinations of climatic conditions and landscape attributes could potentially lead to an increased sensitivity of mosquito occurrence and dengue incidence. We employed some advanced machine learning algorithms due to its growing utilization to explore the influence of landscape features or climate on dengue disease (Carvajal et al., 2018; Guo et al., 2017; Ong et al., 2017; Chen et al., 2018; Baquero et al., 2018) and mosquito occurrence (Mwanga et al., 2019; Jiménez et al., 2019; Früh et al., 2018; Zheng et al., 2019). By selecting important environmental features for RFs, we further examined and described the optimal combination of landscape and climate variables that influence dengue incidence and mosquito occurrence using model-based (MOB) recursive partitioning.

2. Material and methods

2.1. Study area

Metropolitan Manila is the National Capital Region (NCR) of the Philippines, located at Southwestern Luzon (14°50′N Latitude, 121°E Longitude). With 100% urbanization (Asian Development Bank, 2014), the NCR is the most densely populated area in the country (18,165.1 persons/km^2 spread over an administrative land area of 636 km^2) (Asian Green City Index, 2011). It comprises 16 cities and one municipality with a total population of 12,877,253 (Philippines Statistics Authority, 2019). Each city or municipality is further subdivided into the smallest administrative division, a "Barangay," commonly known as a village, with 1706 total villages. A collection of villages can be merged into a "zone" depending on the city's administrative boundaries.

The majority of the target area is covered by residential (54.07%), industrial (9.41%), and commercial (7.45%) areas. The urban development of Metropolitan Manila occurred through a gradual replacement of agricultural LU with industrial and commercial LU, and a massive increase in residential areas. The constant spatial and population growth has led to LU pressure and instigated substandard housing in areas with a high risk of flooding (Zoleta-Nantes, 2000).

The climate of Metropolitan Manila during the rainy season (from July to December) is characterized by strong monsoon rain and tropical storms (World Bank, 2014; BBC News, 2012). Heavy rain associated with a lack of drainage infrastructure contributes to flooding (Zoleta-Nantes, 2000).

2.2. Data sources and processing

2.2.1. Administrative boundaries

The map of the administrative boundaries of Metropolitan Manila (Fig. 1a) was obtained from the Philippine GIS Data clearinghouse (www.philgis.org). Metropolitan Manila includes 1706 villages (barangays) with most within the City of Manila ($n = 897$; 53%). In this study, the villages of Manila, Caloocan, and Pasay were merged together into "zones" to facilitate consistency in village size because most villages are very small with an average area of 0.06 km^2. Additionally, 86% ($n = 771$) of the villages have an area of <0.06 km^2. The average area of each village in Metropolitan Manila (excluding the City of Manila) is 0.41 km^2. This study used the City of Manila, Caloocan, and Pasay's designated zone names to merge villages. Overall, 464 villages or zones were subsequently analyzed in this study. The population statistics were obtained from the Philippine Statistics Authority agency (www.psa.gov.ph). Since the Philippine population census is conducted every five years, we obtained the 2010 (Philippines Statistics Authority, 2012) and 2015 (Philippines Statistics Authority, 2019) census data and used the compounded population growth rate to calculate the population for the years 2012 and 2013. The sum of the projected population of the merged villages (Manila, Caloocan, and Pasay) was also calculated.

2.2.2. Entomological surveillance

In 2012, governmental institutions (Department of Science and Technology (DOST), Department of Education, Department of Health, Department of Interior, and local governments) implemented a nationwide surveillance program that installed DOST Orvicidal/Larvicidal traps (OL-traps) to monitor *Aedes* mosquitoes to help control dengue transmission and reduce dengue cases (DOST, n.d., DOST Mosquito Ovicidal/Larvicidal (OL) Trap for Dengue Prevention, 2013). Surveillance programs in many countries have utilized ovitraps as a routine surveillance tool because they are relatively low-cost and reliable in attracting gravid *Aedes* females for oviposition (Silver, 2007; Ritchie et al., 2003). In Metropolitan Manila, ovitraps were installed in public places such as schools, institutes, and other education facilities. A total of 719 georeferenced surveillance locations providing weekly reported Ovitrap indices (OIs) were extracted from the reporting website (http://oltrap.pchrd.dost.gov.ph/) (DOST, n.d.) from July 2012 to December 2014. Afterward, each georeferenced surveillance location was matched with its corresponding village, with only 268 of the 464 villages containing mosquito surveillance location(s). We aggregated the OIs into a monthly index by dividing the cumulative OI by the total number of sampling locations. Given the low numbers and inconsistent reporting during the months of January to June, the study only included the aggregated monthly OI from July to December of 2012, 2013, and 2014.

2.2.3. Epidemiological data

The total number of weekly reported dengue cases from January 2012 to December 2014 for all 464 villages was obtained from the National Epidemiology Center, Department of Health, Philippines. Most of the reported dengue cases during this period were suspected or probable cases according to standard definitions and were not confirmed in a laboratory. We calculated the monthly dengue incidence by dividing the total number of dengue cases each month by the total population of the village multiplied by a population factor of 10,000. The dengue incidence was transformed by adding 1 to all values and obtaining its natural logarithm [$\log_e (n + 1)$].

2.2.4. Climatic factors

Remote sensing (RS) is a promising tool in epidemiological studies (German et al., 2018; Misslin and Daudé, 2017; Buczak et al., 2014; Araujo et al., 2015). This study used the Tropical Rainfall Measurement Mission (TRMM) product 3B43 to obtain the monthly average rainfall. This gridded quasi-global product consists of monthly average precipitation measured in hourly bases with 0.25° of spatial resolution (Huffman and Bolvin, 2018). The Terra Moderate Resolution Image Spectroradiometer (MODIS) collected the average land surface temperature. The products MOD11A2 and MYD11A2 from MODIS Terra and Aqua satellites consists of the average temperature collected within an eight-day period for both daytime and nighttime temperatures with 1 km spatial resolution (USGS, n.d.-a). GEE (Gorelick et al., 2017) was used to download the RS raster images, apply scaling factor (0.02), and convert temperature values from the default Kelvin (K) to degrees Celsius (°C). This product suffers from missing data, particularly during the rainy season, given the high cloud cover and other atmospheric disturbances. To overcome this limitation, a Kriging interpolation method was applied to estimate the missing temperature values for each village using ArcGIS software version 10.2 (ESRI, Redlands, CA). This method weights the surrounding measured values to derive a surface of predicted values for an unmeasured location for each month (ESRI, 2016). Since each village can be covered by multiple pixels of the raster images

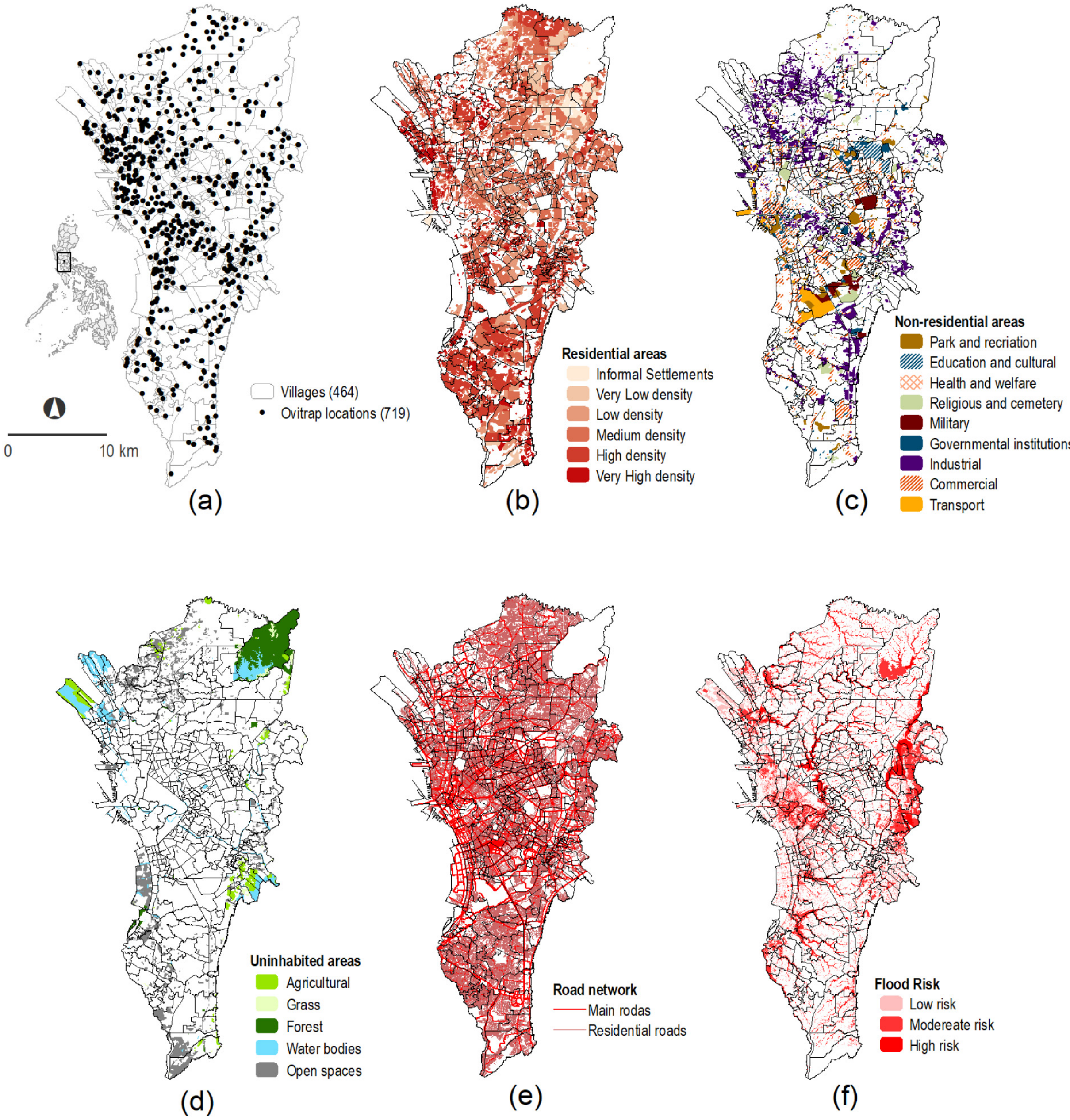

Fig. 1. Administrative boundaries of Metropolitan Manila showing: (a) Ovitrap locations; Landscape features: (b) Residential areas classified according to densities, (c) Nonresidential areas, (d) Uninhabited areas, (e) Road networks, and (f) Flood risk.

of precipitation and temperature, the spatially weighted average value of all pixels within each village was calculated per month. The validation of RS data for further use in the study was done by performing Pearson correlation analysis using the complete time series precipitation or interpolated temperature against precipitation or temperature observed from the three available ground WS across the study area from January 2012 to December 2014. The RS data utilized for validation corresponded to the monthly spatially weighted average value of the pixels around 1 km radius of each WS correlated to the value of precipitation or temperature observed from a particular ground WS, respectively. Essentially, these analyses showed a very high positive correlation ($r > 0.9$, $p < 0.01$), suggesting that RS data can precisely render the spatiotemporal trend of climatic data observed from ground WS; making it appropriate for further analysis. Detailed results from these analyses are presented in Supplementary file 1.

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

2.2.5. Landscape data

The local LU map of Metropolitan Manila (2004) was obtained from the Philippine Geoportal website (www.geoportal.gov.ph) managed by the Bureau of National Mapping and Resource Authority and the

Metropolitan Manila Development Authority (NAMRIA, n.d.). This map contains 30 LU types (agricultural, grass, forest, water bodies, open spaces, parks and recreation, education and cultural, health and welfare, religious and cemetery, military, governmental institutions, industrial, commercial, transport, residential areas of very low, low, medium, high, and very high density, and informal settlements). The largest portion (54.07%) was covered by residential areas (very low, low, medium, high, and very high house densities) with multi-story dwelling places (1–2, 3–4, 5, or more stories). This study only considered the house density categories (very low, low, medium, high, and very high) given the very small proportion of multi-story categories of more than three stories (0.01%–0.07%). Nonresidential areas such as industrial, commercial, and public facilities comprised 37% of Metropolitan Manila. A small portion was covered by natural landscape aspects such as water bodies and forests (10%). The 2004 LU map had a time gap with our dengue incidence data (2012–2014); thus, we updated the map to the period covered by our study so that all input parameters in the model had the same time range. This map was subjected to updates based on open street maps (OSM), processed and distributed by Geofabrik GmbH (www.geofabrik.de). The OSM data contained modifications that occurred before December 2016 (Geofabrik GmbH, 2019). Prior knowledge of the study area was used to manually inspect and validate the map modifications. We noted some LU changes that occurred between 2004 and 2014 in specific areas with the expansion of residential and commercial areas into open spaces (Supplementary file 2). Although LU is expected to change over time, LU in the 10-year period was not significantly different, which may reflect the well-established and consolidated urban land utilization distribution in Metropolitan Manila. Therefore, in this study, we considered the LU map of 2014 as a static variable that accurately rendered the land utilization distribution for 3 years (2012–2014). LU variables included the percentage of land covered by each LU class (i.e., agriculture, water bodies, commercial, residential) per village (Fig. 1b–d). The percentage of each LU class was calculated as follows. Firstly, we calculated the area of each LU class per village. Then, the percentage of each class was determined over the total area of the villages. All edits and calculations of LU areas per village was performed in ArcGIS software, version 10.2.

Road network density (RND) assesses the urbanization gradient (Suarez-Rubio and Krenn, 2018), which influences mosquito abundance and dengue transmission (Bostan et al., 2017). The road network map was obtained from the Philippine GIS Data Clearinghouse website (http://philgis.org/) and classifies roads as primary, secondary, tertiary, residential, and others (PhilGIS, 2012). The RND for each category was calculated by dividing the total length of roads by the total village area. Since the RND of each category of primary, secondary, and tertiary roads was less than 0.001 m/m^2, we merged them into a single category, “main roads” (Fig. 1e). Terra MODIS Normalized Difference of Vegetation Index (NDVI) was derived from the product MOD13Q1 version 6. The NDVI consists of measures of the reflected photosynthetic activity on vegetation and is generated every 16 days at 250-m spatial resolution (USGS, n.d.-b). All images were downloaded through GEE and processed using ArcGIS to obtain their monthly averages per village.

2.2.6. Data matching

To conform with the limited availability of OI data, DI and all explanatory variables were also restricted to those from July–December (rainy season) 2012–2014 in the analysis. Furthermore, all variables were spatially weighted by the area of the village for each month. The final dataset was obtained from village-month mean values (Table 1).

2.3. Cross-correlation analysis

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

2.4. Model development with variable selection

The model development was made in two steps. First, RF algorithm was used for variable selection. Second, the selected variables were utilized to investigate the potential combined influences between climatic and landscape factors toward OI and Dengue incidence with MOB recursive partitioning. Our combined approach of RF followed by MOB recursive partitioning enable us to see the nonlinear variable interactions.

2.4.1. Random forest for variable selection

RF is a bootstrap aggregation (bagging) ensemble method that generates a large number of independent bootstrapped trees from random small subsets of the dataset (Breiman, 2001). RF is used to solve a variety of classification and regression problems due its ability to handle large numbers of predictor variables even in the presence of complex interactions (Garge et al., 2013). Two regression models were implemented in this study. Dengue incidence was regressed with lagged climate factors, LU types, and OI, with 27 explanatory variables. Additionally, the OI was regressed with lagged climate factors and LU types, with 26 explanatory variables. Since RF variable importance can be sensitive to tuning parameters, we performed a grid search by looping a model implementation over several parameters combination for OI and Dengue incidence. The loop trains several RF models by gradually supplying and increasing the values of four parameters namely: number of variables (*mtry*), number of trees (*ntree*), percentage of bootstrap sample and node size. Afterwards, the best parameters combination is selected from the model with the lowest Out-of-Bag error. Both OI and Dengue incidence models were implemented with parameters set at $ntree = 500$, bootstrap sample = 80% and node size = 8. The *mtry* was set at 5 and 9 for OI and Dengue incidence respectively. RF models were estimated using the “*ranger*” package (Wright et al., 2020) implemented in the R software version 3.6.2 (R Core Team, 2017).The other parameters were set as default in the package.

Table 1
Spatiotemporal data characteristics.

Data	Source	Raw Temporal resolution	Raw spatial resolution	Adopted temporal resolution	Adopted spatial resolution
Dengue cases	DOH	Weekly	Tabular: Village	Monthly	Village
Ovitrap Index (%)	DOST	Monthly	Vector: point	Monthly	Village
Precipitation (mm/h)	TRMM	Monthly	Raster: 0.25°	Monthly	Village
Land Surface Temperature (°C)	MODIS	8-day	Raster: 1 km	Monthly	Village
Normalized Difference of Vegetation Index	MODIS	16-day	Raster: 250 m	Monthly	Village
Land use (Ha)	NAMRIA, Geofabrik	Static 2004, 2014	Vector: Village	Static	Village
Road Network (m)	PhilGIS	Static	Vector: Village	Static	Village
Flood risk	LiPAD	Static	Raster: 5 m	Static	Village

To identify the most important predictors of dengue incidence and mosquito occurrence, we assessed variable importance (VI), which was measured as the mean decrease in MSE in the RF models. VI is calculated based on the number of times the explanatory variable is used for splitting, weighted by the improvement to the model as a result of each split, averaged over all trees (Elith et al., 2008). For the VI and respective *p*-values, we applied the permutation importance method, which computes an unbiased VI measure (Altmann et al., 2010). Positive importance values with p-values less than 0.05 were selected for the subsequent MOB recursive partitioning analysis.

2.4.2. Model-based recursive partitioning

To investigate the combined influences of the selected explanatory variables to OI and Dengue incidence, we used a Model-Based (MOB) recursive partitioning (Zeileis et al., 2008; Pirkle et al., 2018). MOB is reminiscent of the classification and regression tree (CART) algorithms, which recursively split the datasets into subsets at each step based on independent variables (Pirkle et al., 2018). MOB algorithm performs iteratively through the following steps: (1) fit a user-defined linear regression equation to the data; (2) investigate if the model parameters depends on other covariates; (3) if yes, split the model and data into two groups with respect to the covariate with a threshold that brings the largest changes in the linear model parameters based on M-fluctuation test; and (4) repeat the procedure (1–3) in each of the resulting subsamples. The process is repeated until a particular stopping criterion is reached. Our stopping criteria were at the following parameters: 5% level of significance ($alpha = 0.05$) and maximum depth of the tree equal to 4 ($maxdepth = 4$). These constraints contribute to avoid model overfitting (Zeileis et al., 2008, Pirkle et al., 2018), and simplification of the tree structure for better interpretability since only the most significant predictors are considered (Kopf et al., 2010). The *P*-values were Bonferroni corrected to control a false positive rate. We used the Linear Model Tree (*lmtree*) interface implemented in "*partykit*" package (Hothorn and Zeileis, 2015) in R Software (R Core Team, 2017).

The models were implemented via two steps. First, we utilized all selected explanatory variables to build a decision tree to see the overall distributions of the OI and dengue incidence. From this step, we identify the predictors most strongly associated with the distribution of the OI and Dengue incidence. We used these associations as a linear model that MOB explores. Then, using a MOB, we explored covariates that modulate the associations. We regressed OI with High residential density areas as a linear model, of which parameter dependency was explored with precipitation, residential RND, temperature, medium residential density areas, vegetation, health institution areas, very high residential density areas, flood risk, commercial areas, and industrial areas. For Dengue incidence, we used precipitation as the linear model predictor, using the following variables as potential modulators: temperature, commercial areas, high residential density areas, vegetation, OI, flood risk, and residential RND.

3. Results

3.1. Cross-correlation analysis

Precipitation yield had the highest positive and significant correlation with dengue incidence ($r = 0.69$, $p = 0.00$) at a one-month lag, followed by OI ($r = 0.52$, $p = 0.05$) and temperature ($r = 0.52$, $p = 0.05$), both at a three-month lag. Vegetation displayed a negative and significant correlation ($r = -0.71$, $p = 0.00$) at a one-month lag (Table 2). Vegetation showed the highest positive correlation with the OI ($r = 0.77$, $p = 0.00$) at a three-month lag, followed by temperature ($r = 0.73$, $p = 0.00$) and precipitation ($r = 0.48$, $p = 0.04$), both at a zero-month lag. A dataset that contained lagged climate factors at the most significant lag for each variable (highest correlation coefficient and $p < 0.05$) was used as input dataset.

Table 2
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	0.05	–	–	–
Precipitation	1	0.69	0.00	0	0.48	0.04
Temperature	3	0.52	0.05	0	0.73	0.00
Vegetation	1	−0.71	0.00	3	0.77	0.00

3.2. Variable selection

Fig. 2 shows the varied importance of the selected variables in the two RF models. The OI was significantly associated with 11 variables (three climatic factors and eight landscape factors). High residential density areas were ranked first, followed by precipitation, residential RND, temperature, medium residential density areas, vegetation, health institution areas, very high residential density areas, flood risk, commercial areas, and industrial areas (Fig. 2a). Dengue incidence was significantly associated with eight variables (three climatic factors, four landscape factors, and OI). Precipitation was ranked first, followed by temperature, commercial areas, high residential density areas, OI, vegetation, flood risk, and residential RND (Fig. 2b). These variables were used in the subsequent modeling.

3.3. Model-based recursive partitioning

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

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

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

We employed further analyses to infer the interactive effect of the most important predictor (precipitation) with other environmental

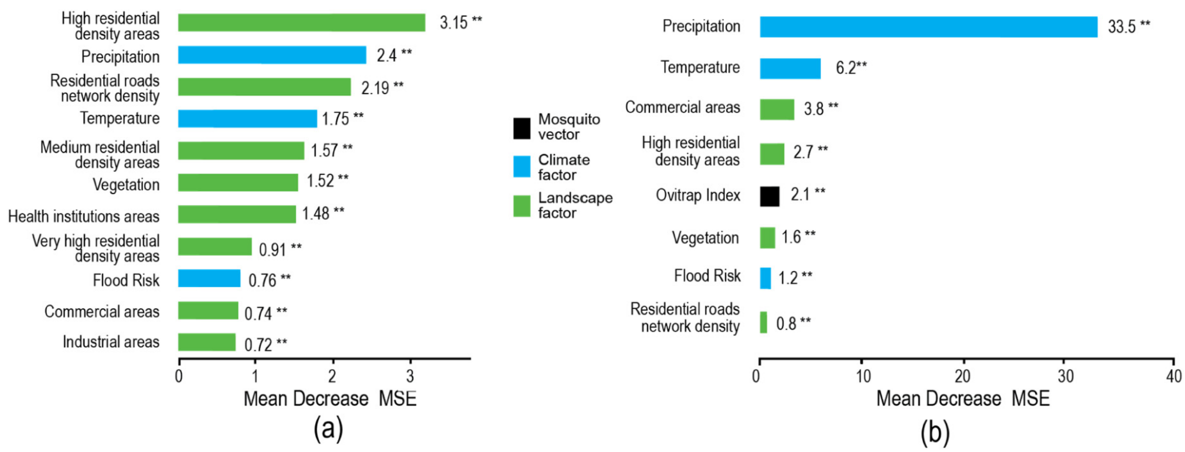

Fig. 2. Varied importance measures of the variables with the most significant associations with (a) ovitrap index and (b) dengue incidence; (**) statistically significant at $p < 0.05$.

factors on dengue incidence (Fig. 4b). We specified precipitation as the main predictor and the remaining variables as interacting factors. Higher slopes and R-squared values were found in relation to two different interaction patterns and were considered influential toward dengue incidence. The first pattern involved interactions between precipitation, commercial areas, and high residential density areas (nodes

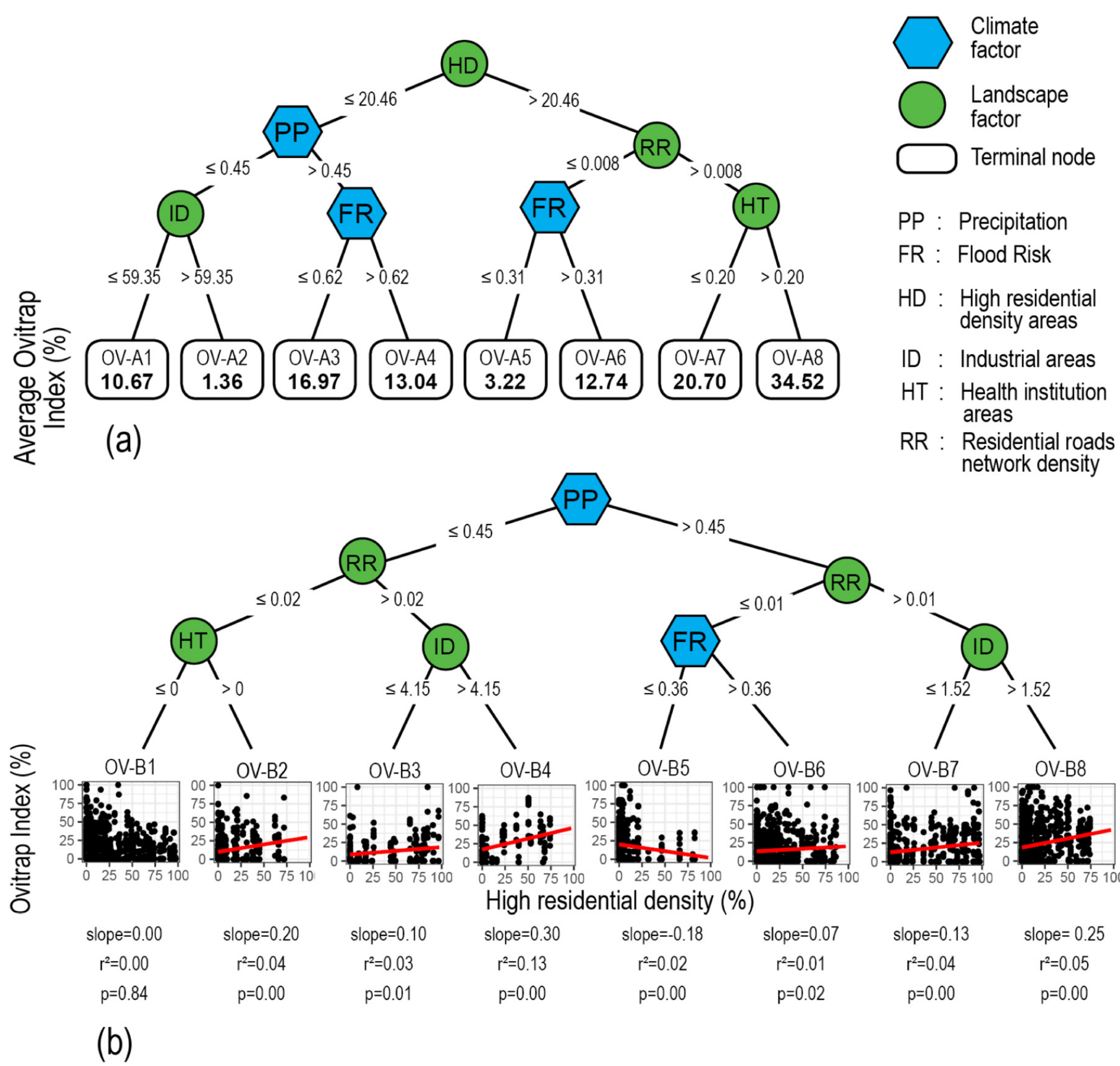

Fig. 3. Recursive partitioning trees for identifying the (a) most influential variables on the ovitrap index and (b) interactive effects between environmental factors and the ovitrap index.

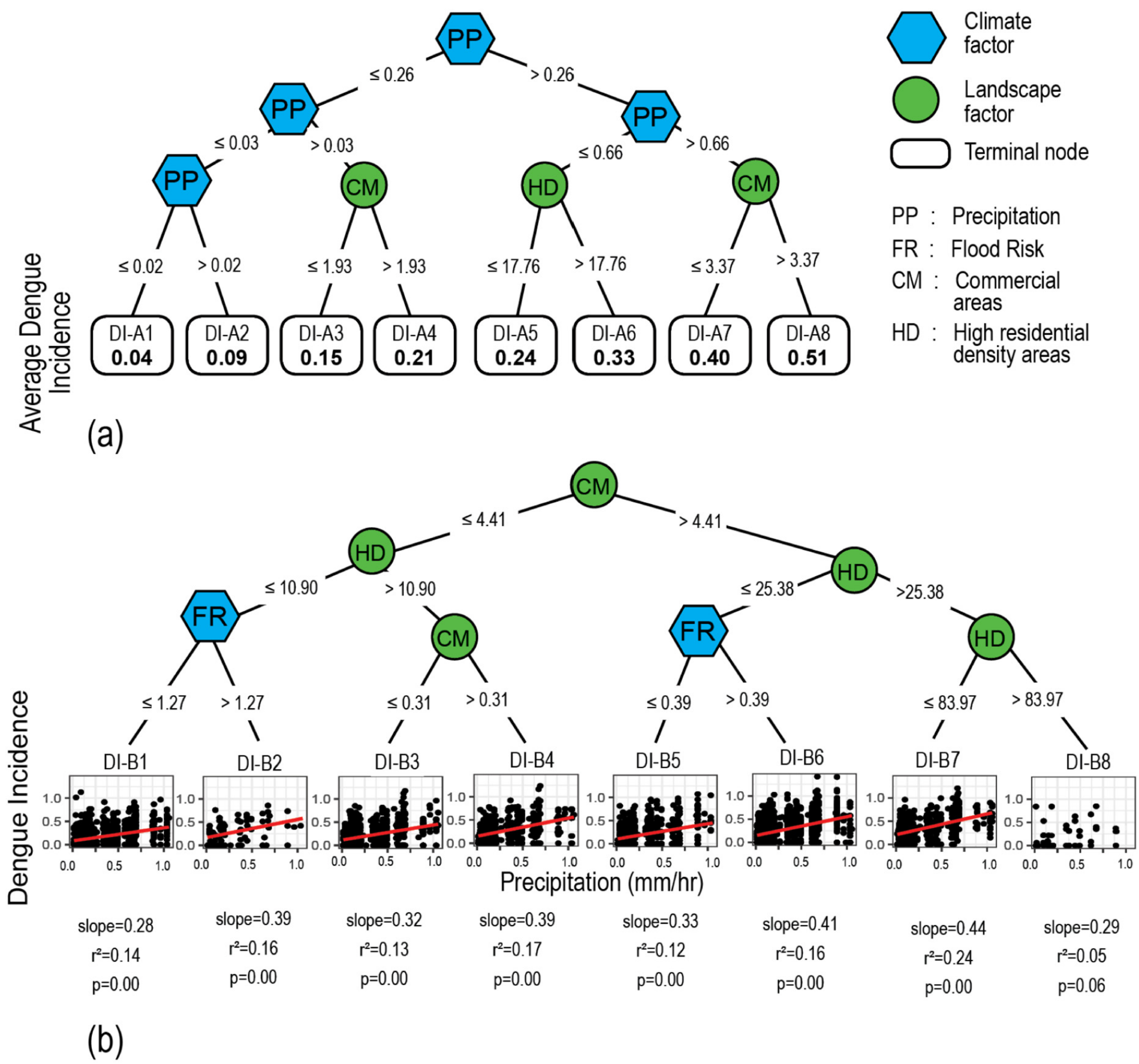

Fig. 4. Recursive partitioning trees for identifying the (a) most influential variables on dengue incidence and (b) the interactive effects between environmental factors and dengue incidence.

DI-B7 and DI-B4, with slopes of 0.44 ($R^2 = 0.24$, $p = 0.00$) and 0.39 ($R^2 = 0.17$, p = 0.00), respectively). The second pattern involved interactions between precipitation, commercial areas, high residential density areas, and flood risk (nodes DI-B6 and 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).

4. Discussion

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

In general, ovitraps can detect the presence of both *Ae. aegypti* and *Ae. albopictus*. However, the OI data utilized in this study does not contain any information on the proportion of these two species. Therefore, our discussion in this section focuses solely on *Ae. aegypti*, because previous studies that surveyed selected areas of Metropolitan Manila indicated a high infestation rate of *Ae. aegypti* (>80%) (Mistica et al., 2019; Carvajal et al., 2019), thereby making it the primary vector for dengue transmission.

Both the RF and MOB tree (Figs. 2a and 3a) analyses clearly indicate the importance of high residential density areas on the overall distribution of the OI. We employed further analyses by specifying high residential density areas as the main predictor and the remaining variables as interacting factors (Fig. 3b). The influence of high residential density areas on mosquito occurrence became clearer under certain environmental conditions specifically with lower precipitation (≤0.45 mm/h). The two nodes OV-B4 and OV-B8 with the highest slopes (0.30 and 0.25, respectively) were both formed in high industrial areas (>4.15 and > 1.52%, respectively) and high residential road areas (>0.02 and > 0.01 m/m^2, respectively), and node OV-B4 was formed in a low precipitation condition (≤0.45 mm/h). Since *Ae. aegypti* preferentially breeds in small water containers exposed to the outdoors (Carvajal et al., 2019; Ngugi et al., 2017), little rainfall might be sufficient to maintain optimal levels of water suitable for mosquito emergence. Although the aforementioned previous studies have reported a positive association of precipitation and mosquito occurrence, our results reveal that the effect of precipitation in increasing the sensitivity of mosquito occurrence may prevail at a certain threshold. Conversely, enhanced rainfall might flush out mosquito eggs and larvae from breeding containers: thus, reducing the chances for mosquito survival and population in high residential density areas (Dickin et al., 2013).

Residential RND was the partitioning variable on the second level of the MOB tree. Furthermore, nodes OV-B4 and OV-B8, which had the highest slopes, were partitioned with higher residential road densities (>0.02 and > 0.01 m/m^2, respectively). These results suggest a high sensitivity of mosquito occurrence to high residential density areas with a higher density of residential roads. Roads not only serve as transportation networks for people and goods but are also simultaneously accompanied by drainage components (e.g., roadside drains or canals, drain sumps), which collect surface water runoff for discharge in appropriate locations to avoid inland water flooding. However, in many cases, efficient drainage in residential areas can be compromised by the encroachment of concrete structures or garbage clogging the canals (Lagmay et al., 2015). These interferences can inhibit complete water flow, resulting in spots of accumulated water, which can create favorable habitats for *Ae. aegypti* (Paploski et al., 2016). Growing evidence has suggested a positive association between drainage and the occurrence of *Ae. aegypti* in Singapore (Seidahmed et al., 2018), Brazil (Souza et al., 2017), and Australia (Montgomery et al., 2004). Our results, specifically in the nodes OV-B4 and OV-B8, suggest that the high density of roads may contribute to an increased mosquito occurrence. However, these results should be carefully interpreted as they may reflect the actual poor conditions of the road network drainage in the study area.

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

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

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

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

4.2. Interactive effects between precipitation and landscapes in modulating dengue incidence

Both RF (Fig. 2b) and MOB tree (Fig. 4a) analyses showed the significant influence of precipitation in regulating the sensitivity to dengue incidence with high proportions of high residential density and commercial areas. On the MOB tree (Fig. 4a), precipitation was the partitioning variable on the first and second levels, whereas high residential and commercial areas were selected as partitioning variables on level 3. Overall, dengue incidence MOB trees supported the significant influence of precipitation on dengue incidence. The significant influence of precipitation agrees with previous studies in the Philippines (Carvajal et al., 2018; Su, 2008) and Malaysia (Dickin et al., 2013), which reported precipitation as a main driver of the temporal variation of dengue incidence. These studies assumed that the high correlation between precipitation and dengue incidence is due to the increasing mosquito density during the rainy season.

In the variable selection step, precipitation showed a very strong influence on dengue incidence compared with other environmental factors. We conducted further analyses to evaluate the combined influence of precipitation with other environmental factors in modulating dengue incidence (Fig. 4b). The association between precipitation and dengue incidence was notable particularly in areas covered by high residential and commercial areas, suggesting a high influence of these LU types in modulating dengue incidence. The highest slope (0.44, $R^2 = 0.24$, $p = 0.00$) was reported for node DI-B7 (Fig. 4b), which incorporates interactions between precipitation, commercial areas (>4.41%), and high residential density areas (between 25.38 and 83.97%). Herewith, this nodal pathway was considered the most influential environmental condition for increasing dengue incidence with high precipitation. The second highest slope (0.39, $R^2 = 0.17$, $p = 0.00$) was reported for node DI-B4 and formed with environmental conditions of commercial areas (0.31 < commercial areas ≤4.41%) and high residential density areas (>10.90%). With these influential patterns observed in terminal nodes DI-B7 and DI-B4, we suggest that certain ecological factors in commercial and high residential areas can enhance dengue transmission with precipitation. Previous studies have shown that residential and commercial areas experience the most damaged houses during extreme rainfall and flood events in Metropolitan Manila (Porio, 2014, a, Porio, 2011, b). Damage to families' shelters, followed by massive displacements, might subject many people to deteriorated conditions with limited capacity to observe disease prevention and vector control measures. The high human exposure to vectors in these areas might create an avenue for high dengue transmission. A highly sensitive influence of precipitation on increasing dengue incidence was observed under high flood risk conditions (DI-B6 and DI-B2). These terminal nodes 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, 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 0.33 ($R^2 = 0.12$, $p = 0.00$), respectively) displayed less sensitivity in increasing dengue incidence. These examples illustrate that the increased sensitivity of dengue transmission in residential and commercial areas with high precipitation can also be caused by floods. Floods can contribute to increased mosquito density and force people to live confined in deteriorated conditions of habitability with high exposure to vectors. The combination of human presence and exposure to vectors has been linked to high dengue transmission in residential (Scott and Morrison, 2010, de Moura Rodrigues et al., 2015) and commercial areas (Honório et al., 2009; Thammapalo et al., 2007). Due to the anthropophilic nature of *Ae. Aegypti*, high human presence and exposure in these areas may increase feeding opportunities for mosquitoes and increase the chances of dengue fever infections (Koyadun et al., 2012). Because many people are exposed in areas with high precipitation levels, it becomes easier for mosquitoes to bite and infect many people in a short time, thus increasing the incidence of dengue (Akter et al., 2017).

We expected that the resulting dengue incidence and ovitrap MOB trees (Figs. 4a and 3a) would yield similar tree topology patterns. This expectation assumed that the high dengue incidence during the rainy season is a result of high mosquito abundance influenced by precipitation. However, our result was contrary to our assumption and could be explained by methodological limitations. The OI is based on the percentage of positive ovitraps with the presence or absence of vectors; however, it has a limited capacity in precisely displaying the range of mosquito density in the environment transmitting dengue. Although ovitraps are fast and cost-effective tools for monitoring the presence of mosquitoes, the OI has a low association with dengue incidence compared with adult mosquito abundance data (de Melo et al., 2012). Additional correlation analyses (data no shown) of the OI and dengue incidence from the terminal nodes of Fig. 3a and b were not significantly correlated. Therefore, the mosquito occurrence data (OI) utilized in this study might be responsible for the dissimilarities in the ovitrap and dengue incidence MOB tree topology patterns.

4.3. Accessibility of data, modeling approach, and limitations

Most previous epidemiological studies faced limitations when integrating climatic and landscape data given the scarcity of data and modeling techniques. Although we consider landscape to be static in this study, the model development did not distinguish dynamic or static terms. Since the physical characteristics of each village did not change significantly over the three years, we assumed that these characteristics remained the same for each month of the study period. Based on this assumption, we utilized a data structure from previous studies that repeated the values of the static variables for the monthly values of the climate variables in each village (Kaul et al., 2018). This design allowed us to analyze dengue dynamics as a function of the combined influences of climate dynamics over the static landscape.

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

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

The utilization of RS in our study constituted a great asset for accessing spatiotemporal temperature, precipitation, and vegetation data for each village. These types of data overcome the limited accessibility of such information at fine scales in areas where the spatial coverage of weather stations is coarse (German et al., 2018). By using Google Earth Pro, we were able to use cloud computation to conduct all preliminary processing of the data, which significantly shortened the working time. Moreover, detailed LU maps can distinguish the risk of dengue and mosquito occurrence at a fine scale. Many studies that used coarse LU classification, for example, reported that *Ae. aegypti* and dengue incidence are positively correlated with residential areas (Vanwambeke et al., 2007; Vanwambeke et al., 2011; Sarfraz et al., 2012). In this study, we demonstrated that the distributions of mosquito and dengue can also vary depending on the type of density in these residential areas.

Our study, however, has certain limitations. As mentioned in the methods, the entomological data used in this study are incomplete and only correspond to the months of July–December of 2012–2014. This period covers the rainy season in Metropolitan Manila. Therefore, the lack of data for the dry season (January–June) may cause potential bias in our study. Furthermore, ovitraps were installed in only 298 of 464 villages across Metropolitan Manila. Complete data from all villages may increase the robustness of our analysis and better describe the mechanistic understanding of associations between the dengue metrics and environment factors. On the other hand, longer time series of Dengue epidemiological data along with the respective serotypes circulating would provide important insights on the dengue dynamics by accounting for possible herd immunity within the target population. Other socio-economic factors can also be included as they are being reported as important factors governing the abundance of mosquito and transmission of dengue (Santos et al., 2020). Nevertheless, our findings may still reflect the actual circumstances of LU and climatological characteristics of the study area. The results of the combinatory influences of landscape and climate may differ in other urban cities, particularly in rural areas in the Philippines and other dengue-endemic countries. Nonetheless, the methodology presented in this study can infer interplays between climate and landscape on mosquito occurrence and dengue incidence. To improve Dengue dynamics modeling, other approaches such as empirical dynamic modeling can be considered when complete and longer time series data is available.

5. Conclusions

Our study design was capable of integrating and assessing the combined influences of both climate and landscape factors toward dengue disease dynamics. It suggests discordant patterns wherein the OI is primarily influenced by landscapes and modulated by the effects of low levels of precipitation. Dengue incidence is primarily influenced by precipitation and modulated by landscape types. These results show that the dynamics of dengue disease are not solely influenced by individual effects of either climate or landscape, but rather by their synergistic and combined effects. The presented findings have the potential to target vector surveillance in areas identified as suitable for mosquito occurrence under specific climatic conditions. Furthermore, the study findings may be relevant as part of urban planning strategies to control dengue in areas of increased sensitivity to dengue transmission.

In recent years, vector control efforts in eliminating mosquito breeding sites have intensified in residential areas by identifying and destroying breeding sites. However, we demonstrated that the existence of potential breeding sites in the landscape is not the only reason for dengue transmission. These efforts should be accompanied by effective improvements in urban planning toward a more resilient landscape against mosquito-vectored diseases.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.148406.

CRediT authorship contribution statement

Micanaldo Ernesto Francisco: Software, Formal analysis, Data curation, Visualization, Writing – original draft. **Thaddeus M. Carvajal:** Conceptualization, Data curation, Writing – original draft. **Masahiro Ryo:** Methodology, Validation, Writing – review & editing. **Kei Nukazawa:** Data curation, Writing – review & editing. **Divina M. Amalin:** Writing – review & editing. **Kozo Watanabe:** Conceptualization, Validation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank Katherine M. Viacrusis, Lara Fides T. Hernandez, and Howell T. Ho from Trinity University of Asia for collecting and providing the data on notified dengue fever cases. This study was supported in part by the Japan Society for the Promotion of Science (JSPS) Grant-in-Aid Fund for the Promotion of Joint International Research (Fostering Joint International Research (B)) under grant number 19KK0107, JSPS Grant-in-Aid for Scientific Research (A) under grant number 19H01144, the JSPS Core-to-Core Program B. Asia-Africa Science Platforms under grant number JPJSCCB20190008, and the Endowed Chair Program of the Sumitomo Electric Industries Group Corporate Social Responsibility Foundation.

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