



Environmental variable importance for under-five mortality in Malaysia: A random forest approach

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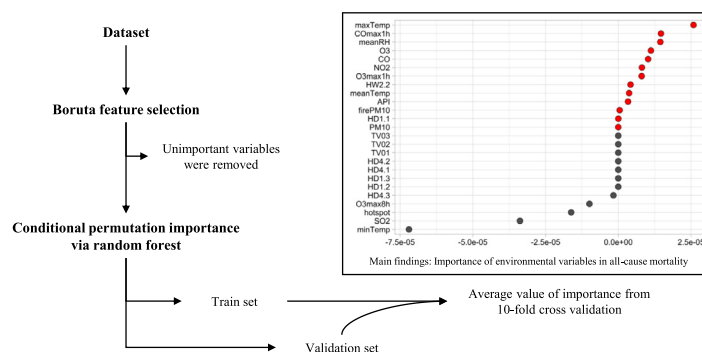
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HIGHLIGHTS

- Environmental variable importance for under-five mortality was evaluated.
- A conditional permutation importance via random forest approach was applied.
- Mortality causes and data structures were considered in the analyses.
- Heat-related, temperature variability, and haze-related variables were important.
- Important variables were consistent for all- and natural- but not external causes.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Environmental factors have been associated with adverse health effects in epidemiological studies. The main exposure variable is usually determined via prior knowledge or statistical methods. It may be challenging when evidence is scarce to support prior knowledge, or to address collinearity issues using statistical methods. This study aimed to investigate the importance level of environmental variables for the under-five mortality in Malaysia via random forest approach.

Method: We applied a conditional permutation importance via a random forest (CPI-RF) approach to evaluate the relative importance of the weather- and air pollution-related environmental factors on daily under-five mortality in Malaysia. This study spanned from January 1, 2014 to December 31, 2016. In data preparation, deviation mortality counts were derived through a generalized additive model, adjusting for long-term trend and seasonality. Analyses were conducted considering mortality causes (all-cause, natural-cause, or external-cause) and data structures (continuous, categorical, or all types [i.e., include all variables of continuous type and all variables of categorical type]). The main analysis comprised of two stages. In Stage 1, Boruta selection was applied for preliminary screening to remove highly unimportant variables. In Stage 2, the retained variables from Boruta were used in the CPI-RF analysis. The final importance value was obtained as an average value from a 10-fold cross-validation.

Abbreviations: ENSO, El Niño-Southern Oscillation; FIRMS, Fire Information for Resource Management System; GAM, Generalized additive model; MODIS, Moderate Resolution Imaging Spectroradiometer; NOAA, National Oceanic and Atmospheric Administration; PM, Particulate matter; WHO, World Health Organization.

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Result: Some heat-related variables (maximum temperature, heat wave), temperature variability, and haze-related variables (PM10, PM10-derived haze index, PM10- and fire-derived haze index, fire hotspot) were among the prominent variables associated with under-five mortality in Malaysia. The important variables were consistent for all- and natural-cause mortality and sensitivity analyses. However, different most important variables were observed between natural- and external-cause under-five mortality.

Conclusion: Heat-related variables, temperature variability, and haze-related variables were consistently prominent for all- and natural-cause under-five mortalities, but not for external-cause.

1. Introduction

The health effects of environmental variables (Murray et al., 2020), including ambient air pollutants (Atkinson et al., 2014; Cohen et al., 2017; Wong et al., 2008) and temperatures (Basu, 2009; Gasparrini et al., 2015; Guo et al., 2016), have been well-documented in previous studies. According to the Global Burden of Disease 2019 (GBD 2019), ambient particulate matter was among the top 10 leading risks for global mortality, whereas some studies also revealed the health risks from other gaseous pollutants (Chen et al., 2021; Newell et al., 2017; Phosri et al., 2019). A few studies from Southeast Asian countries have reported adverse health effects due to air pollution (Phosri et al., 2019; Phung et al., 2016; Wan Mahiyuddin et al., 2013) and temperature (Dang et al., 2019; Denpetkul and Phosri, 2021; Seposo et al., 2015; Yatim et al., 2021). The recurring vegetation fires in Southeast Asia (Jones, 2006; Reddington et al., 2014) further complicate quantification of air pollution attributable health effects in the region, as the fire smoke contains a variety of hazardous chemicals (Naehar et al., 2007), thus exposing individuals to fire-sourced pollutants (Cheong et al., 2019) in addition to anthropogenic pollutants (Sulong et al., 2017).

Malaysia is located in Southeast Asia and has a tropical climate. Besides urban air pollution, the country faces extreme air pollution issues due to vegetation fires (hereinafter referred to as “smoke haze”) in certain months of the year (Afroz et al., 2003), which may be exacerbated by climatic events, such as El Niño-Southern Oscillation (ENSO) (Wooster et al., 2012), although anthropogenic factors may also contribute (Field et al., 2016). El Niño, the warm phase of ENSO, occurred in 2015 and persisted until early 2016 (NOAA, 2021a). During this period, one of the most severe smoke haze episodes in Southeast Asia occurred (Koplitz et al., 2016), which has implications on health conditions. Nevertheless, the health effects in such a tropical climate country with a year-round hot and humid weather and recurring smoke haze are yet to be elucidated. Heat waves (Tong et al., 2014; Xu et al., 2018) and smoke haze (Ho et al., 2018; Liu et al., 2017; Morgan et al., 2010; Phung et al., 2022; Sahani et al., 2014; Sastry, 2002; Uttajug et al., 2021) indicators have been used in epidemiological studies to address extreme heat and pollution due to vegetation fires. These indicators, however, have been defined in several ways due to varying local characteristics or issues to be addressed. This increases the challenge in generalization and comparability across studies and regions.

Children are vulnerable to environmental factors due to their developing physiological and immunological systems. In 2018, 85 % of global child mortality (ages 0–14 years) consisted of those under-five years of age (UN IGME, 2019). However, the association between environmental variables and under-five mortality has not been well-examined (Karimi and Shokrinezhad, 2020; Xu et al., 2012). Some studies have reported the adverse health effects of ambient air pollution (Conceição et al., 2001) and household biomass burning (Naz et al., 2016), whereas one other study reported null association between fire smoke and under-five mortality (Phung et al., 2022). The effects of temperature and under-fives were also inconclusive (Xu et al., 2014). It is, therefore, difficult to derive the associations between each environmental variable and the health effects among under-fives. Thus, the selection of variables among the numerous environmental factors would be an essential step to allow prioritization of the important variables in a more time effective manner.

Various approaches have been applied in previous epidemiological studies, whereby prior knowledge and statistical selection have been the

main options in selecting the variables of interest (Talbot and Massamba, 2019; Walter and Tiemeier, 2009). However, these approaches have some limitations, as well as scarcity of related studies. Moreover, the selection of variables by statistical automation may be further complicated due to the high dimensionality of data or presence of confounding or correlated factors (Greenland, 1989; Keller, 2020). These shortcomings could be complemented by data-driven approaches (Keller, 2020). Variable importance via random forest is a machine learning technique, wherein the importance of variables is evaluated based on the error measures upon random permutation of the data (Strobl et al., 2008). Good screening and selection of appropriate variables could improve the performance and prediction in modeling (Chowdhury and Turin, 2020). Moreover, a conditional permutation importance via random forest should be used, as it would address the issue of bias when the data comprise highly correlated variables (Keller, 2020; Strobl et al., 2008). Although the conditional permutation for variable importance via random forest can be applied as a variable selection tool for epidemiological studies, to our knowledge, this was the first study to utilize this method considering epidemiological perspectives. While some studies have examined the weather variable importance level for daily mortality (Zhang et al., 2014), and the weather and social variables importance level for daily heatstroke morbidity (Wang et al., 2019), these studies did not adopt the permutation technique with conditioning, and did not account for potential collinearity. The feasibility of applications of conditional permutation for variable importance with random forest is worth exploring, by applying it to actual data to complement the suggestions based on simulations (Talbot and Massamba, 2019; Walter and Tiemeier, 2009).

This study aimed to investigate environmental variable importance in the association with under-five mortality using a random forest approach. Variable importance was explored in each sub-dataset of mortality cause: all-, natural-, and external-cause mortality. The nature of this study differed from a typical epidemiological approach, and was not designed to examine any effect estimate of the under-five mortality in relation to exposure to environmental variables, as demonstrated through epidemiological studies. Rather, this study contributes improved knowledge on whether this approach is feasible for future epidemiological studies.

2. Method

2.1. Data sources

This study utilized the nationwide data of daily under-five mortality counts in Malaysia spanning from January 1, 2014 to December 31, 2016. The data were obtained from the Family Health Development Division, Ministry of Health Malaysia. Causes of deaths were recorded based on the International Classification of Diseases Tenth Revision (ICD-10). We classified the under-five mortality into three groups: (i) all-cause (ICD-10: A00 – Y98); (ii) natural-cause (ICD-10: A00 – R99); and (iii) external injuries or accidental cause (hereinafter “external cause”) (ICD-10: S00 – T88, V00 – Y98). We applied a generalized additive model (GAM) adjusting for long-term trend and seasonality using a spline with seven degrees of freedom (7 df) on date. This derived the number of mortalities deviated from the spline in the GAM (Zhang et al., 2014). This deviation (hereinafter referred to as “number of mortality”) was used for the main analysis.

Environmental data were provided by the Department of Environment, Malaysia. Besides the main weather and air pollutant variables available in

Table 1
List and descriptions of all health and environmental variables.

Variable label	Variable	Unit	Descriptions or equations	Data source or reference
Health Variables				
nall	All-cause under-five mortality	Count	Difference (observed – expected) mortality counts. Splines adjusted for long-term and seasonality trend with 7 degrees of freedom per year (5 <i>df</i> and 10 <i>df</i> in sensitivity analysis)	Data provided by Family Health and Development Division, Ministry of Health, Malaysia
nat	Natural cause under-five mortality	Count	Difference (observed – expected) mortality counts. Splines adjusted for long-term and seasonality trend with 7 degrees of freedom per year (5 <i>df</i> and 10 <i>df</i> in sensitivity analysis)	Data provided by Family Health and Development Division, Ministry of Health, Malaysia
ext	External cause under-five mortality	Count	Difference (observed – expected) mortality counts. Splines adjusted for long-term and seasonality trend with 7 degrees of freedom (<i>df</i>) per year (5 <i>df</i> and 10 <i>df</i> in sensitivity analysis)	Data provided by Family Health and Development Division, Ministry of Health, Malaysia
Weather Variables				
meanTemp	Daily mean temperature	°C	24-h average	Data provided by Department of Environment, Malaysia
minTemp	Daily minimum temperature	°C	24-h minimum	Data provided by Department of Environment, Malaysia
maxTemp	Daily maximum temperature	°C	24-h maximum	Data provided by Department of Environment, Malaysia
meanRH	Daily mean relative humidity	%	24-h average	Data provided by Department of Environment, Malaysia
TV01	Temperature variability (1 day)	°C	sd(minTemp-lag-0, maxTemp-lag-0, minTemp-lag-1, maxTemp-lag-1)	Adapted from Guo et al., 2016
TV02	Temperature variability (2 days)	°C	sd(minTemp-lag-0, maxTemp-lag-0, minTemp-lag-1, maxTemp-lag-1, minTemp-lag-2, maxTemp-lag-2)	Adapted from Guo et al., 2016
TV03	Temperature variability (3 days)	°C	sd(minTemp-lag-0, maxTemp-lag-0, minTemp-lag-1, maxTemp-lag-1, minTemp-lag-2, maxTemp-lag-2, minTemp-lag-3, maxTemp-lag-3)	Adapted from Guo et al., 2016
HW1.1, HW1.2, HW1.3	HWx.y is heatwave by intensity-x and duration-y. x is meanTemp>90th percentile and y is 1, 2, and ≥ 3 consecutive days.	Binary	Heatwave: Indicated as “1” if meanTemp >90th percentile for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Tong et al., 2014
HW2.1, HW2.2, HW2.3	HWx.y is heatwave by intensity-x and duration-y. x is meanTemp>95th percentile and y is 1, 2, and ≥ 3 consecutive days.	Binary	Heatwave: Indicated as “1” if meanTemp >95th percentile for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Tong et al., 2014
HW3.1, HW3.2, HW3.3	HWx.y is heatwave by intensity-x and duration-y. x is meanTemp>99th percentile and y is 1, 2, and ≥ 3 consecutive days.	Binary	Heatwave: Indicated as “1” if meanTemp >99th percentile for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Tong et al., 2014
HW4	Heatwave alert level 1 (“Alert”) in Malaysia	Binary	Heatwave: Indicated as “1” if maxTemp remained 35–37 °C for ≥ 3 consecutive days	Adapted from Malaysian Meteorological Department (MetMalaysia, 2021)
HW5	Heatwave alert level 2 (“Heatwave”) in Malaysia	Binary	Heatwave: Indicated as “1” if maxTemp remained 37–40 °C for ≥ 3 consecutive days	Adapted from Malaysian Meteorological Department (MetMalaysia, 2021)
HW6	Heatwave alert level 3 (“Emergency”) in Malaysia	Binary	Heatwave: Indicated as “1” if maxTemp remained >40 °C for ≥ 3 consecutive days	Adapted from Malaysian Meteorological Department (MetMalaysia, 2021)
Air pollutants Variables				
PM10	Daily mean concentration of particulate matter with aerodynamic diameter below 10 µm (PM10)	µg/m ³	24-h average	Data provided by Department of Environment, Malaysia
O3	Daily mean concentration of ozone (O ₃)	ppb	24-h average	Data provided by Department of Environment, Malaysia
O3max1h	1-h maximum concentration of ozone (O ₃)	ppb	Maximum value of 1-h	Data provided by Department of Environment, Malaysia
O3max8h	8-h maximum concentration of O ₃	ppb	Maximum value of 8-h running average	Data provided by Department of Environment, Malaysia
NO2	Daily mean concentration of nitrogen dioxide (NO ₂)	ppb	24-h average	Data provided by Department of Environment, Malaysia
SO2	Daily mean concentration of sulfur dioxide (SO ₂)	ppb	24-h average	Data provided by Department of Environment, Malaysia
CO	Daily mean concentration of carbon monoxide (CO)	ppm	24-h average	Data provided by Department of Environment, Malaysia
COmax1h	1-h maximum concentration of CO	ppm	Maximum value of 1-h	Data provided by Department of Environment, Malaysia
API	Daily mean air pollutant index (API)	API value	24-h average	Data provided by Department of Environment, Malaysia
firePM10	Daily mean fire-PM10	µg/m ³	Difference between daily mean PM10 (region) and baseline average PM10 of the country throughout study period	Adapted from Morgan et al., 2010
hotspot	Number of fire hotspots	Count	Number of fire hotspots, inclusive of all data with confidence level > 20.	Data from NASA MODIS (NASA, 2021)
HD1.1, HD1.2, HD1.3	HDx.y is haze day defined by intensity-x and duration-y. x is PM10 > 50 µg/m ³ and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if PM10 > 50 µg/m ³ for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Phung et al., 2022; Sahani et al., 2014

(continued on next page)

Table 1 (continued)

Variable label	Variable	Unit	Descriptions or equations	Data source or reference
HD2.1, HD2.2, HD2.3	HDx.y is haze day defined by intensity-x and duration-y. x is PM10 > 75 µg/m ³ and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if PM10 > 75 µg/m ³ for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Phung et al., 2022; Sahani et al., 2014
HD3.1, HD3.2, HD3.3	HDx.y is haze day defined by intensity-x and duration-y. x is PM10 > 100 µg/m ³ and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if PM10 > 100 µg/m ³ for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Phung et al., 2022; Sahani et al., 2014
HD4.1, HD4.2, HD4.3	HDx.y is haze day defined by intensity-x and duration-y. x is API >50 and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if API >50 for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Othman et al., 2014
HD5.1, HD5.2, HD5.3	HDx.y is haze day defined by intensity-x and duration-y. x is API >100 and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if API >100 for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Othman et al., 2014
HD6.1, HD6.2, HD6.3	HDx.y is haze day defined by intensity-x and duration-y. x is API >200 and y is 1, 2 and ≥ 3 consecutive days.	Binary	Haze day: Indicated as “1” if API >200 for 1, 2 and 3 days, respectively; and “0” if otherwise	Adapted from Othman et al., 2014
HD7	Burning day index	Category	Indicated as “1” (non-burning day) if number of hotspot is 0; “3” (burning day) if number of hotspot >90th percentile of total hotspot distribution (i.e., 7 counts) and PM10 > 100 µg/m ³ ; and “2” (mixed day) if otherwise.	Adapted from Uttajug et al., 2021
Other Variables				
ONI	Oceanic Niño Index	ONI value	Running 3-month average sea surface temperatures in the east-central tropical Pacific between 120° – 170°W (i.e., Niño 3.4 region)	Data from the National Oceanic and Atmospheric Administration (NOAA, 2021a)
SOI	Southern Oscillation Index	SOI value	A standardized index based on the observed sea level pressure differences between Tahiti and Darwin, Australia	Data from the National Oceanic and Atmospheric Administration (NOAA, 2021b)
FLU	Influenza data	Count	Global web-based tool for influenza virological surveillance at country level.	Data from the World Health Organization (FluNet WHO, 2021)

Note: Data for PM2.5 was not available. The New Ambient Air Quality Standard (NAAQS) in Malaysia was established in 2015 to replace the older standard which has been used since 1989. The new NAAQS included PM2.5 (source: <https://environment.com.my/wp-content/uploads/2016/05/Ambient-Air.pdf>).

the dataset, we also derived some exposure indexes, including temperature variability (Guo et al., 2016), haze days as binary/categorical variables (Liu et al., 2017; Morgan et al., 2010; Othman et al., 2014; Phung et al., 2022; Sahani et al., 2014; Uttajug et al., 2021), and heatwave (MetMalaysia, 2021; Tong et al., 2014; Xu et al., 2018). Fire hotspot data were the Aqua and Terra satellites observations from Moderate Resolution Imaging Spectroradiometer obtained from the Land, Atmosphere Near real-time Capability for EOS Fire Information for Resource Management System of the National Aeronautics and Space Administration (NASA, 2021). Data of ENSO indexes [Oceanic Niño Index, ONI (NOAA, 2021a) and Southern Oscillation Index, SOI (NOAA, 2021b)] were obtained from the National Oceanic and Atmospheric Administration (NOAA), whereas the influenza data were obtained from the FluNet of the World Health Organization (WHO) (FluNet WHO, 2021). The descriptions, detailed definitions, and criteria of each variable are listed in Table 1.

2.2. Main analysis

The main analysis was conducted in two stages (Fig. 1): Stage 1 – Boruta feature selection (Kursa et al., 2010), and Stage 2 – conditional permutation importance via random forest. In Stage 1, we applied the Boruta algorithm (Kursa et al., 2010; Kursa and Rudnicki, 2010) for the preliminary screening. Boruta is a feature selection algorithm, which iteratively compares the variable importance with its randomized copies (Kursa et al., 2010). Subsequently, “highly unimportant” variables were identified and removed. This would allow the main analysis to be more focused and efficient (Chowdhury and Turin, 2020; Wang et al., 2019) due to reduced data dimensionality and improved performance of the random forest (Keller, 2020). The Boruta algorithm is illustrated in Fig. S1. In Stage 2, a conditional permutation for variable importance via random forest was applied on the retained variables from Stage 1. Random forest is an ensemble machine learning model consisting of a group of decision trees. In brief, in the construction of each tree, a part of the data is used for training

while the remaining is called the “out-of-bag” data (OOB data). The OOB data are used to measure the variable importance (i.e., percentage increase in mean square error [%IncMSE]). This value (%IncMSE) is the difference between the mean square error (MSE) from non-permuted OOB and the MSE from permuted OOB. The variable importance value from a random forest is the average value from the ensemble model. In this study, we used an ensemble of 500 trees (number of trees, *ntree* = 500), as we found that this setting would be sufficient, and an increment of the *ntree* value would not further improve the prediction (Fig. S2). Another parameter in random forest is the number of variables considered at each split in a tree, known as “*mtry*.” The number of *mtry* was determined using a grid search method, whereby the *mtry* from the lowest error estimation was used. The *mtry* for each sub-dataset is shown in Table S1. The final value of variable importance was obtained through the average of values from a 10-fold cross validation. The training set to test set ratio was 9:1.

The main analysis was applied to three sub-data stratified by the type of environmental variable: (1) all air pollutant and weather variables, (2) weather variables only, and (3) air pollutant variables only. For each sub-data, we separately examined the variable importance by different data structures as (1) continuous, (2) categorical, and (3) all types (i.e., include all variables of continuous and categorical type). These continuous variables are the measured/monitored data, whereas categorical variables are indicators derived based on previous literatures or environmental standards/guidelines (Table 1). The variables classified by data structure and environmental types are shown in Table S2. The interpretation of a finding from a study would depend on the research question, which relates to the decision of using a continuous or categorical (indicator) variable as the main exposure metric (Tobías and Stafoggia, 2020). Hence, examination by such stratification would facilitate the choice of exposure metric.

For sensitivity analyses, we included the ENSO indexes (i.e., SOI and ONI) and influenza variables. This stage was to examine the importance of these variables for under-five mortality, in addition to the environmental

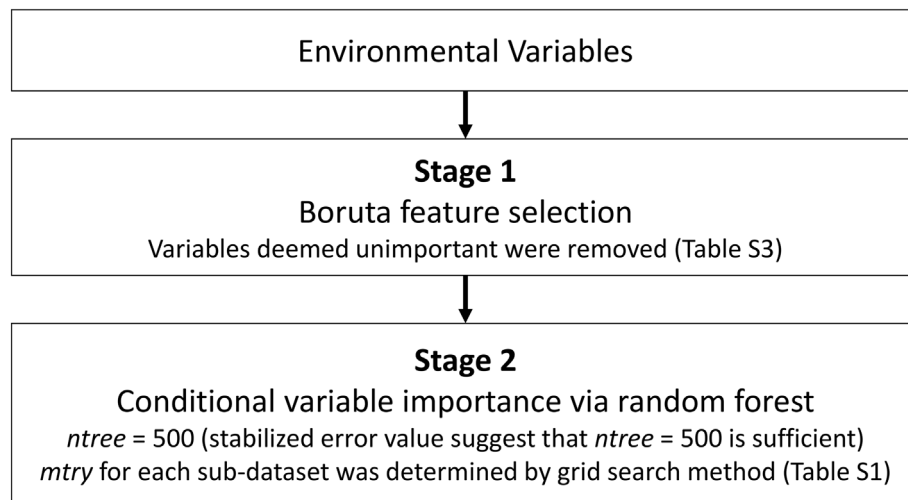


Fig. 1. Flow diagram of analysis

variables which have been evaluated in the main analysis. ENSO is a climatic driver which could persist over several months with irregular pattern, consequently affecting local weather, air pollution, and fire occurrence (Shiogama et al., 2020). The importance of ENSO indexes was examined separately from the main analysis due to two reasons. First, these are monthly-scaled variables, whereas our study focused on short-term effects using daily metrics. The monthly metric may not be the appropriate variable to evaluate a daily pattern, though there could be some relationship. Second, the potential health effects of ENSO may be indirect. ENSO would be related to health impact particularly if the local weather in the region is affected by ENSO; the local weather variables are direct factors of concern considering the plausible biological mechanisms (Heaney et al., 2019; Kovats et al., 2003; Muñoz et al., 2021). The influenza variables were also included in the sensitivity analysis due to its potential confounding effect in the association among weather, air pollution and mortality. It is known that respiratory infection is among the prevalent diseases leading to global under-five mortality (Wang et al., 2016). Due to limited data, we utilized the weekly influenza data from the WHO FluNet (FluNet WHO, 2021) as a proxy for respiratory infections for under-five mortality. Moreover, we repeated the analysis using alternative *dfs* (5 and 10 *df*) for the splines of mortality counts. These *dfs* were examined in accordance with the method used in a previous study (Zhang et al., 2014).

The results were reported based on the averaged value from a 10-fold cross-validation procedure. The findings were discussed for each category: (i) cause of mortality (all-, natural-, and external-cause); (ii) environmental variables (weather, air pollutant, and others (i.e., SOI, ONI, and influenza)); and (iii) data structures (continuous, categorical, and all types). To avoid repetitive iteration, unless otherwise specified, all results are reported for under-five mortality considering all causes of mortality (encompassing all-cause, natural-cause, and external-cause mortalities). The type of sub-data by environmental variables and data structure would be specified. All analyses in this study were performed using R statistical software (R Core Team, 2020). The main functions and R packages used in this study include *Boruta()* in “Boruta” (Kursa et al., 2010), *cforest()* in “party” (Hothorn et al., 2006; Strobl et al., 2007, 2008), *permimp()* in “permimp” (Debeer et al., 2021), and *gam()* in “mgcv” (Wood, 2011).

3. Results

3.1. Descriptive summary

Table 2 shows the descriptive summary of the under-five mortality and all environmental variables. In Malaysia, the under-five mortality rates were 8.3, 8.4, and 8.1, per 1000 live births, in 2014, 2015, and 2016, respectively (Vital Statistics Malaysia 2017) (DOSM, 2017). It was observed

that the under-five mortality may deviate by at least one count from the smoothing spline (minimum = -1; median = 1). The negative value of mortality count indicates lower observed value deviated from the spline. The daily (24-h) mean, minimum, and maximum temperatures ranged from 22.6 to 31.1 °C, 19.9–27.7 °C, and 23.0–43.0 °C, respectively. While most of the air pollutant variables showed low variability over the distribution, there was an extremely high value of PM10 with a maximum value of 315.51 µg/m³. Similar patterns were observed in the air pollutant index, fire-PM10, and fire hotspots.

3.2. Boruta feature selection

In each dataset, the environmental variables were screened using Boruta feature selection to reduce data dimensionality prior to conducting the random forest analysis. The inclusion or exclusion of variables at this stage are shown in Table S3. All continuous variables for both weather and air pollutant were retained for random forest analysis, whereas only a few categorical variables consistently remained: HW2.2, HD1.1, HD1.2, HD1.3, HD4.1, HD4.2, and HD4.3. The burning activity indicator, HD7, was retained when only categorical variables were screened in the “all variables” dataset, but consistently deemed important in the “air pollutant-only” dataset.

3.3. Variable importance based on conditional permutation importance via random forest

Using the retained variables after Boruta screening, the variables which were ranked with the highest importance value for under-five mortality are shown in Table 3. In the sub-data which contained all environmental variables (Table 3), the weather variables, including maximum temperature (maxTemp), heatwave “HW5” (defined by maximum temperature 37–40 °C for three consecutive days) and mean relative humidity (meanRH); and air pollutant variables, including carbon monoxide (CO), haze days [defined by PM10 > 100 µg/m³ for one day (HD3.1)]; and by combination of PM10 and fire hotspot (HD7)], and fire hotspot counts (hotspot) were the prominent variables for the under-five mortality. Fig. 2 shows the importance values of all weather and air pollution variables in all-cause mortality sub-data. The red and black solid circles represent the positive and negative values of environmental variable importance, respectively. The importance values for each sub-data are shown in Fig. S3 (all-cause mortality), Fig. S4 (natural-cause mortality), and Fig. S5 (external-cause mortality).

The results encompassing all mortality categories (i.e., all-, natural-, and external-cause mortalities) are described as follows. The high temperature-related variables (maxTemp and HW5) were more prominent than air pollutant variables when all environmental variables were considered. However, in the sub-data of weather variables, three-day temperature variability (TV03),

Table 2
Descriptive summary of under-five mortality and environmental variables in Malaysia (2014–2016).

Variable	Label ^a	Unit	Mean (SD)	Minimum	Median	Maximum
Under-five mortality^b						
Under-five mortality rate (per 1000 live births): 8.3 (2014), 8.4 (2015), 8.1 (2016) ^c						
All-cause mortality	nall	Deviation count	2 (3)	–1	1	30
Natural-cause mortality	nat	Deviation count	2 (3)	–1	1	25
External-cause mortality	ext	Deviation count	2 (1)	1	2	12
Weather variables						
Daily (24-h) mean temperature	meanTemp	°C	27.6 (1.1)	22.6	27.6	31.1
Daily minimum temperature	minTemp	°C	24.1 (1.1)	19.9	24.1	27.7
Daily maximum temperature	maxTemp	°C	34.4 (1.9)	23.0	34.4	43.0
Daily mean relative humidity	meanRH	%	78.45 (6.08)	54.84	78.99	99.00
Temperature variability (current and 1-previous day)	TV01	°C	5.322 (0.56)	4.249	5.420	6.055
Temperature variability (current and 2-previous days)	TV02	°C	5.322 (0.56)	4.249	5.419	6.055
Temperature variability (current and 3-previous days)	TV03	°C	5.322 (0.56)	4.249	5.419	6.056
Air pollutant variables						
Daily mean concentration of particulate matter with aerodynamic diameter 10 µm	PM10	µg/m ³	44.87 (22.68)	17.64	39.55	315.51
Daily mean concentration of ozone	O3	ppb	17.86 (6.54)	3.79	17.08	47.76
1-h maximum concentration of ozone	O3max1h	ppb	53.58 (22.85)	13.00	49.00	198.00
8-h maximum concentration of ozone	O3max8h	ppb	46.92 (17.00)	15.62	45.12	111.71
Daily mean concentration of nitrogen dioxide	NO2	ppb	8.50 (4.68)	1.88	7.07	28.91
Daily mean concentration of sulfur dioxide	SO2	ppb	1.87 (1.10)	0.00	1.47	8.39
Daily mean concentration of carbon monoxide	CO	ppm	0.543 (0.223)	0.188	0.495	2.610
1-h maximum concentration of carbon monoxide	COmax1h	ppm	1.753 (0.905)	0.400	1.580	15.80
Daily air pollutant index	API	Value	42.11 (14.17)	18.33	39.74	192.89
Daily mean concentration of fire-PM10	firePM10	µg/m ³	6.79 (6.90)	0.00	5.32	27.23
Total count of fire hotspots	hotspot	Count	3 (9)	0	0	227
Other variables						
Oceanic Niño Index	ONI	Value	0.642 (1.01)	–0.700	0.500	2.600
Southern Oscillation Index	SOI	Value	–0.374 (0.843)	–2.200	–0.600	1.400
Influenza cases	FLU	Count	2 (3)	0	1	20

Details and description of each variable are listed in Table 1.

^a Label shows abbreviation for the variables used in the entire context.

^b Under-five mortality counts are shown for the deviation number of mortalities from a baseline derived using a spline on date (7 df per year) in a generalized additive model.

^c Under-five mortality rate for each year are obtained from the Vital Statistics Malaysia 2017, Department of Statistics, Malaysia (DOSM, 2017).

minimum temperature (minTemp), meanRH, and HW5 were ranked as the most important in continuous, categorical, and all types (Table 3). Meanwhile, in the air pollutant-only sub-data, PM10, CO, sulfur dioxide (SO₂), 8-h maximum ozone concentration (O3max8h), HD7, and haze days (defined by PM10 > 100 µg/m³ for ≥ 3 days; HD3.3) were the most prominent in continuous, categorical, and all types (Table 3). HW5 was consistently ranked as the most important for all-cause (Fig. S3-c) and natural-cause (Fig. S4-c) mortality in all environmental variable sub-data, and the most important for all-cause, natural-cause, and external-cause in weather-only sub-data

Table 3
Variables with the highest importance value in the association with under-five mortality in Malaysia.

	All cause	Natural cause	External cause
All environmental variables			
All types ^a	maxTemp	meanRH	HD3.1
Continuous type	maxTemp	CO	hotspot
Categorical type	HW5	HW5	HD7
Weather variables			
All types ^a	TV03	TV03	meanRH
Continuous type	TV03	TV03	minTemp
Categorical type	HW5	HW5	HW5
Air pollutant variables			
All types ^a	PM10	PM10	CO
Continuous type	PM10	SO2	O3max8h
Categorical type	HD7	HD7	HD3.3

Details and description of each variable is listed in Table 1. The variables in each sub-group are listed in Table S2.

^a “All types” denotes all variables of continuous and categorical type, in the respective sub-groups by health outcome and environmental variables.

(Figs. S3-f, S4-f, S5-f); however, this was consistent only for categorical data. The importance of PM10 (Figs. S3-g, h, S4-g, h) and HD7 (Figs. S3-i, S4-i) was prominent for all-cause (Fig. S3) and natural-cause mortality (Fig. S4) in air pollutant-only sub-data, CO (Fig. S5-g, h), O3max8h (Fig. S5-h), and HD3.3 (Fig. S5-i) were prominent for external-cause (Fig. S5) under-five mortality (Table 3).

3.4. Sensitivity analyses

In the sensitivity analyses which considered ENSO and influenza variables, meanRH, hotspot, and haze days “HD3.1” (defined by PM10 > 100 µg/m³ occurring for 1 day) were ranked with the highest importance for all-, natural-, and external-cause mortality, respectively (Table S4, Fig. S6). HD3.1 remained the most prominent variable in external cause. TV03 and PM10 remained prominent, but meanRH and COmax1h (instead of maxTemp) was ranked as the most important for all-cause mortality when the model was altered with 5 and 10 df for the smoothing spline, respectively (Table S4). Although not the highest importance value, maxTemp still ranked as important (positive variable importance value) in all-cause (Fig. S6-a) and natural-cause mortality (Fig. S6-b).

4. Discussion

This study suggested a few environmental variables which were deemed important for the association with under-five mortality in Malaysia. Some of the most prominent variables were maxTemp, TV03, meanRH, PM10, CO, HW5, HD7, HD3.1, HD3.3, O3max8h, hotspot, and minTemp. The consideration of ENSO and influenza variables in the model showed changes in the most prominent variables in certain cases, depending on the types of variables (all, weather, or air pollutant) and causes of mortality (all, natural or external). The variables identified for all- and natural-cause mortalities

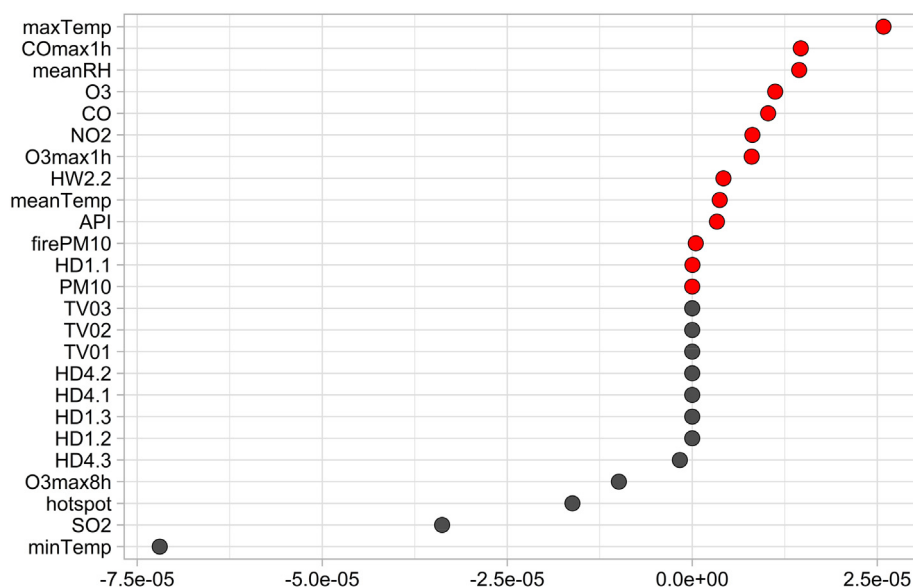


Fig. 2. Permutation importance of weather and air pollution variables in all-cause mortality Red solid circle indicates positive values of permutation importance. Black solid circle indicates negative values of permutation importance.

were considerably consistent, but not for external-cause mortality. However, the relationship between environmental variables and under-five mortality is likely to be weak.

Extreme temperatures (Gasparrini et al., 2015; Hajat et al., 2002; Tong et al., 2014) and temperature variability (Guo et al., 2016) have been related to adverse health effects. Studies from temperate countries consist of both extreme heat and extreme cold weather, but the temperature range in Malaysia is relatively narrower, and falls within higher temperatures (daily average 22–31 °C). Our findings suggest that higher temperatures, temperature variability, and relative humidity were important for the association with under-five mortality. HW5 (i.e., heat wave if the maximum temperature persists for 37–40 °C for ≥ 3 consecutive days) was consistently ranked as the most important indicator weather variable. A previous epidemiological study in Malaysia examined the health effects of temperature using daily mean temperature values as the exposure metric after examining the lowest quasi-Akaike Information Criterion value (Yatim et al., 2021). The study reported higher risks of mortality at higher temperatures in relation to the optimum temperature at 28.2 °C, but it was inclusive of all ages, and no significant risk was reported for children (age ≤ 14 years) (Yatim et al., 2021). The choice of temperature metrics varies between studies and regions, and there is no metric defined as superior to others (Ye et al., 2012). Although the findings of the current study could not suggest any estimates of the health risks in relation to temperature change, it allows exploration of possible techniques in determining the temperature metrics as an exposure variable. Meanwhile, the association between humidity with mortality requires further clarification, although it has been commonly considered as having a confounding effect in temperature-related studies (Armstrong et al., 2019). The association between temperature and under-five mortality remains unclear, such that inconsistent findings have been reported for lower- (Babalola et al., 2018) and higher-temperature effects (Xu et al., 2012).

Among all the air pollutant variables, PM10 was the most prominent variable for under-five mortality in Malaysia, in addition to the PM10-derived haze indexes (HD3.1, HD3.3, HD7). Although our findings suggest the potential of PM10 as a predictor for under-five mortality, which corroborated the results of previous studies (Conceição et al., 2001; Karimi and Shokrinezhad, 2020), it is uncertain whether these were fire or non-fire sourced, or local or transboundary sourced. Nonetheless, our findings suggested that 100 $\mu\text{g}/\text{m}^3$ may be an important PM10 level related to under-five mortality in Malaysia. Increased mortalities have been reported in a previous study using a similar haze definition (HD3.1), though that

study included children aged 0–14 years (Sahani et al., 2014). Smoke haze have been associated with adverse health effects (Delfino et al., 2009; Liu et al., 2017; Morgan et al., 2010; Rappold et al., 2011; Reid et al., 2016; Sahani et al., 2014; Sastry, 2002), whereas previous studies revealed that there were increased child hospital visits related to PM10 on non-burning than on burning days (Uttajug et al., 2021). A study in Malaysia reported null association between smoke haze days and under-five mortality, but informed that the definition of smoke haze days considering different intensity and duration would lead to different lag patterns of health effects (Phung et al., 2022).

The varying importance of the variables identified for all- and natural-cause compared with that of external-cause mortalities may be due to the different pathways or mechanisms. The variables identified for external-cause under-five mortality may be attributed to the child's behavior, thermoregulation, and pathophysiological mechanism. It may also be relevant to the caretaker's psychological and behavior changes. Previous studies have reported the vulnerability of under-fives to ambient temperature (Auger et al., 2015; Knowlton et al., 2009; Kovats et al., 2004; Nitschke et al., 2011; Xu et al., 2014), although some have reported null associations (Huang et al., 2010; Joe et al., 2016). Heat wave has been linked to increased under-five mortality (Nitschke et al., 2011), sudden infant deaths (Auger et al., 2015), hospital admission (Kovats et al., 2004), and total- and electrolyte imbalance- emergency department visits (Knowlton et al., 2009). Some studies have revealed possible associations between extreme temperatures and air pollution with psychological stress and violence (Kim et al., 2019; Kubo et al., 2021; Otrachshenko et al., 2021; Szyszkowicz et al., 2010); however, suicidal and self-harm behavior could not be related to this age group. Meanwhile, ambient temperature might be related to increased external-cause mortality due to falling, drowning, and accidents (Pan et al., 2022). Moreover, our findings showed potential impact of severe smoke haze on under-five external-cause mortality. Carbon monoxide is one of the main air pollutants from smoke haze (Naeher et al., 2007). High level of carbon monoxide could lead to asphyxiation and hypoxia (Blumenthal, 2001; Gozubuyuk et al., 2017). We could not draw firm conclusions toward the association between environmental variables with under-five external-cause mortality; however, the association is likely weak or null, hence the inconsistencies in the importance ranks. As revealed by our results, some variables showed negative variable importance values in each sub-data. This could be attributed to the prediction accuracy after permutation, which turned out to be higher by chance (Debeer and Strobl, 2020). In other words, the variable was interpreted as

a poor predictor, despite the magnitude of the negative values. Thus, interpreting the negative values is not meaningful. This is different from the epidemiological approach, wherein the positive or negative values from epidemiological analysis could be interpreted as directions of association.

The use of different data structures (continuous, categorical, or all types) showed that most of the highest importance were continuous variables. This was mainly consistent for all- and natural-cause mortality, though the variables were not the same for external-cause mortality. However, it is possible to observe some pattern if a variable is strongly related or consist of high importance. For example, a category of heat defined by extremely high temperature (e.g., HW5) was highly related to under-five mortality; however, it contained less information than when using the continuous temperature variable (e.g., maxTemp). Extremely high temperatures might be a highly important variable for under-five mortality; HW5 was defined by a range of maximum temperatures (MetMalaysia, 2021) (Table 1).

We observed that the ranks of variable importance were different in sensitivity analyses, whereby ENSO and influenza variables were included in addition to environmental variables. The relationship between ENSO and under-five mortality has not been clearly established, but these variables are associated with weather changes in Malaysia. There would be a longer period of intensified heat and dry season in El Niño years or more rain in La Niña years. Consequently, it is also linked with the occurrence of vegetation and peat fires, and thus the fire-pollutants in Malaysia (Latif et al., 2018; Wooster et al., 2012). The inclusion of the ENSO variables might have indirectly affected the association between environmental variables and under-five mortality due to its close relationship with environmental variables (Heaney et al., 2019; Kovats et al., 2003; Muñoz et al., 2021; Shiogama et al., 2020). Meanwhile, although influenza is not an environmental variable, it was included in the sensitivity analysis. This was to address the considerable health impact of influenza on children (Sam et al., 2010), and its potential modification on the health effects of air pollution (Wong et al., 2009). However, the impact of influenza on under-five mortality or on the association between smoke haze and under-five mortality in Malaysia (Phung et al., 2022) might be minimal.

There were some limitations in this study. First, the variable importance via random forest approach could not provide information regarding the magnitude of health risks (e.g., relative risk) in relation to exposure to environmental variables. However, this approach may be useful as a preliminary stage of variable selection. It should be further explored for its feasibility to be coupled with epidemiological analyses in future studies. Second, the application of a smoothing spline allowed adjustment for long-term trend and seasonality, and thus the current study only focused on short-term exposures. Studies examining long-term exposures should consider different exposure windows and variables. Third, this study could not infer any baseline importance value to identify an “important” variable due to limited related literature. Rather, this study reported which variables have positive importance values (indicated by red solid circles in Figs. S3–S6), and summarized variables of highest importance level (Table 3). Finally, this study could suggest the important variables for under-five mortality, but not the direction of the health effects. The positive or negative association (if any) should be further examined via other study approaches, such as the epidemiological approach.

Future studies may seek to clarify the associations among the environmental variables suggested in this study, either as a main exposure variable or as a confounding factor. It should be noted that this study focused on under-five mortality in Malaysia. There may be differences in variable importance depending on the local, social or population, and personal characteristics. These include socioeconomic status, characteristics of residential area, personal behavior, lifestyle, and health condition (Chung et al., 2018; Deguen and Zmirou-Navier, 2010; Medina-Ramón et al., 2006; Stafoggia et al., 2006; Zanobetti et al., 2013). For policy implications, the heat and haze indexes should be further examined for their different roles in understanding an association (Tobías and Stafoggia, 2020): (i) as a binary indicator (i.e. haze or non-haze); (ii) as an effect modifier to the main pollutant of interest; or (iii) as an interaction term with the main pollutant of interest. Establishing the associations and identifying the

important indicator would facilitate policy decisions in warning systems or risk communications to the public. Nonetheless, the decision to use either the main variables (continuous) or indicators (categorical) would depend on the purpose of each study.

5. Conclusions

This study suggested a few important environmental variables related to under-five mortality in Malaysia. Among the most prominent variables are heat (maxTemp, meanRH, HW5), temperature variability (TV03, TV02), and haze-related (PM10, CO, SO₂, HD3.1, HD3.3, HD7, hotspot) variables. The importance ranks were mostly consistent for all- and natural-cause under-five mortalities, but not for external-causes.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2022.157312>.

Ethical consideration

The ethical review for this study was approved by the Medical Research and Ethics Committee of Ministry of Health Malaysia [Ethics initial approval: NMRR-18-2945-42784 (IIR)] and Ethics Committee of the Graduate School of Engineering, Kyoto University, Japan (201902).

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CRedit authorship contribution statement

Vera Ling Hui Phung: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Kazutaka Oka:** Conceptualization, Methodology, Writing – review & editing, Funding acquisition, Supervision. **Yasuaki Hijioka:** Funding acquisition, Supervision. **Kayo Ueda:** Data curation, Writing – review & editing. **Mazrura Sahani:** Data curation, Writing – review & editing. **Wan Rozita Wan Mahiyuddin:** Data curation, Writing – review & editing.

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.

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