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ORIGINAL RESEARCH ARTICLE

Impact of environmental factors on heart failure decompensations

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Abstract

Aims Heart failure (HF) is a clinical syndrome caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress. This disease often causes decompensations, which may lead to hospital admissions, deteriorating patients' quality of life and causing an increment on the healthcare cost. Environmental exposure is an important but underappreciated risk factor contributing to the development and severity of cardiovascular diseases, such as HF.

Methods and results We used two different sets of data (January 2012 to August 2017): one related to the number of hospital admissions and the other one related to the environmental factors (weather and air quality). Admissions related data were grouped in weeks, and then two different studies were performed: (i) a univariate regression to determine whether the admissions may influence future hospitalizations prediction and (ii) a multivariate regression to determine the impact of environmental factors on admission rates. A total number of 8338 hospitalizations of 5343 different patients are available in this dataset, with a mean of 4.02 admissions per day. In European warm period (from June to October), there are significant less admissions than that in the cold period (from December to March), with a clear seasonality of admissions, because there is a similar pattern every year. Air temperature is the most significant environmental factor ($r = -0.3794$, $P < 0.001$) related to HF hospital admissions, showing an inversed correlation. Some other attributes, such as precipitation ($r = 0.0795$, $P = 0.05$), along with SO_2 (precursor of acid rain) ($r = 0.2692$, $P < 0.001$) and NOX air (major air pollutant formed by combustion systems and motor vehicles) ($r = 0.2196$, $P < 0.001$) quality parameters, are also relevant. Humidity and PM10 parameters do not have significant correlations in this study ($r = 0.0469$ and $r = -0.0485$ respectively), neither relevant *P*-values ($P = 0.238$ and $P = 0.324$, respectively).

Conclusions Several environmental factors, such as weather temperature and precipitation, and major air pollutants, such as SO_2 and NOX air, have an impact on the HF-related hospital admissions rate and, hence, on HF decompensations and patient's quality of life.

Keywords Heart failure; Environmental factors; Decompensations

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Introduction

Several investigations about the impact of environmental factors in public health are already published. For example, in 2004, the first American Heart Association scientific statement on "Air Pollution and Cardiovascular Disease" concluded that exposure to particulate matter (PM) air pollution contributes to cardiovascular morbidity and mortality.[1] This study was updated later giving new evidence of the impact of PM exposure with cardiovascular diseases.[2] Moreover, in

D'Amato's study,[3] urban air pollution and climate change were demonstrated to be environmental risk factors of respiratory diseases. A similar research indicates that air pollution is a major preventable cause of increased incidence and exacerbation of respiratory diseases.[4]

Data from the World Health Organization[5] are clear: air pollution is responsible for about 7 million deaths a year in the world, 2.5 million of which are because of heart disease (25%) and 1.4 million due to stroke (24%). The polluting products with the greatest environmental impact are particles of suspended matter, both solid and liquid, the most dangerous being those measuring 2.5 micrometres (μm) (PM2.5) or less: ozone, carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), and volatile organic compounds. Although most of the activities carried out in contemporary societies generate polluting products, road traffic is one of the main culprits in the deterioration of air quality in cities.

Nevertheless, few studies in the field of HF have been carried out. For instance, an article published in the American Journal of Public Health investigated the association between hospital admissions for congestive HF and air pollutants, where ambient carbon monoxide levels were positively associated with the admissions.[6] In addition, another Canadian study examined the role that ambient air pollution plays in exacerbating cardiac disease.[7] They found a positive association between daily admissions fluctuations of congestive elderly HF patients and variations in ambient concentrations of carbon monoxide, nitrogen dioxide, sulphur dioxide, ozone, and the coefficient of haze.

Additionally, other investigations about the effect of meteorology in HF health status have been developed with dissimilar results. To start with, the International Journal of Cardiology published a text where the relationships between meteorological events and acute HF were globally explored. [8] The results showed that meteorological fluctuations appear most relevant in the 3 days prior to the HF hospitalization with temperature, demonstrating a relationship with HF. In contrast, some authors demonstrated that the number of hospitalizations for HF increases during winter.[9] Others concluded that there is a substantial seasonal variation in HF hospitalizations and deaths.[10]

However, to the best of our knowledge, there are not studies that determine the impact of a set of several environmental factors on HF decompensations, being the field where our work is focused on.

Material

This study makes use of two different sets of data: one related to the number of hospital admissions and the other one related to the environmental factors to determine whether they have an impact on HF-related decompensations.

Hospital admissions

The way to study HF decompensations is by means of hospital admissions. Therefore, the first dataset compiles the daily hospitalizations related to HF in the public hospital OSI Bilbao-Basurto (Osakidetza), located in the Basque Country (Spain). The usable admissions dataset is from January 2012 to August 2017. A total number of 8338 hospitalizations of 5343 different patients are available in this dataset, with a mean of 4.02 admissions per day.

We have relied on discharge coding, being HF in the principal position (highest degree of accuracy), withdrawing cases with codes related to respiratory infections.

Environmental data

This environmental dataset is separated in weather information and air quality information. This information was selected due to their demonstrated impact on HF decompensations in previous studies.[7–9,6.10]

Weather

Bilbao and its metropolitan area have an oceanic climate with mild winters and warm summers. The climate of Bilbao and the rest of the north-western part of Spain is characterized by a high amount of rainfall and precipitation days, few sunshine hours, and mild temperatures in winter while in summer it is comparable to northern half of Europe with temperate climate.

The Basque Agency of Meteorology (Euskalmet) enables the possibility to access weather data recorded since 2003, from the Open Data Euskadi website.[11] This information is collected every 10 min by each station of Euskalmet distributed in Euskadi. The different attributes that can be found in these datasets are listed in the succeeding texts: mean direction of wind (°), mean velocity of the wind (km/h), maximum velocity of the wind (km/h), sigma of the velocity of the wind (km/h), sigma of the direction of the wind (°), air temperature (°C), humidity (%), precipitation (mm = L/m^2), atmospheric pressure (mb), water plate (m), and irradiation (w/m^2).

We selected the station located in Deusto (Bilbao) because it is the closest one to our reference area (2 km from the station to the OSI Bilbao-Basurto Hospital. Location of the meteorological station: high 3 m, longitude −2.96°, latitude 43.3°).

The preprocessing of this dataset consisted in three steps. First, the selection of the attributes for obtaining a complete dataset was performed, because not all the variables were measured in all the years between 2012 and 2017 (some of them started to be measured later). In order to obtain a complete dataset, only the attributes measured in those years were taken into account. Thus, the parameters of air temperature, humidity, precipitation, and irradiation are the ones used for this experiment. Second, each parameter was grouped per day (data were recorded every 10 min), calculating their mean value. In addition, as the literature suggests,[8] in case of temperature, the minimum and maximum values for each day were also added to the dataset. Finally, an imputation of missing values (0.33% of the data) was performed, which may be caused by technical problems in the station. The imputation by Structural Model & Kalman Smoothing was used for this, as it is the one that best performs for time series with a strong seasonality.[12] In summary, the dataset corresponding to weather consists of humidity (%), precipitation (L/m^2), irradiation (w/m^2), mean temperature (°C), minimum temperature (°C), and maximum temperature (°C).

Air quality

The Open Data Euskadi website also gives the opportunity to recover information about the air quality.[13] The dataset is formed by air quality specific parameters, such as carbon monoxide (CO) (μg/m^3), nitric oxide (NO) (μg/m^3), nitrogen dioxide (NO_2) (μg/m^3), nitrogen oxides (NOX) (μg/m^3), tropospheric ozone (O3) (μg/m^3), sulphur dioxide (SO_2) (μg/m^3), particulate matter 10 (PM10) (μg/m^3), benzene (μg/m^3), orthoxylene (μg/m^3), toluene (μg/m^3).

After selecting the parameters that had a complete dataset between 2012 and 2017, the final dataset is containing the attributes nitric oxide (NO), nitrogen dioxide (NO_2), nitrogen oxides (NOX), particulate matter 10 (PM10), and sulphur dioxide (SO_2).

For the preprocessing part of this dataset, the missing values that corresponded to an 11% of the data were imputed using the same method as for the previous dataset, the imputation by Structural Model & Kalman Smoothing.[12]

Methods

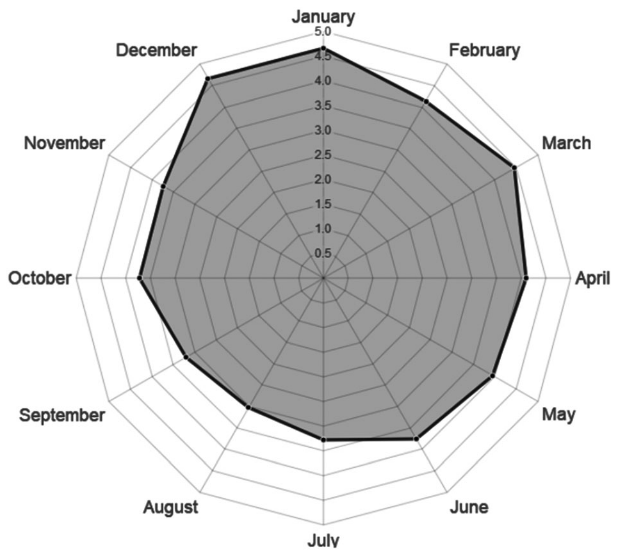
Before starting the analysis to support our hypothesis that environmental factors may contribute to HF patients' health status, a pre-analysis was performed by illustrating the number of admissions per day (*Figure 1*).

Grouping

The number of hospitalizations per day is 4.02. As this is not a sufficient number to analyse the data within each day, each attribute of the study was grouped by weeks. On the one hand, admissions related data are grouped by the total number of admissions in each week. On the other hand, the mean, maximum, minimum, and the standard deviation of each week are used to group the environmental attributes.

Once the data were grouped by weeks, two different studies were performed: (i) a univariate regression to determine whether the admissions may influence future hospitalizations prediction and (ii) a multivariate regression to determine the impact of environmental factors on admission rates.

Figure 1 Daily number of admissions per month.



Univariate regression

In order to study the effect of admissions in future hospitalizations rate, first time series decomposition is performed to later choose the best auto-regressive integrated moving average (ARIMA) model.

Decomposition

The hospitalization rate may vary on time depending on several factors. In order to determine how these variations behave, a decomposition process was conducted. This is a mathematical procedure that transforms a time series into three components, each of them depicting one of the underlying categories of patterns.[14] In *Figure 2*, the decomposition of admissions on these components is shown. The first graph represents the original admissions data series, and below the seasonality of it is illustrated. Seasonality represents patterns that are repeated in a fixed period of time (e.g. repeating pattern over years).

Univariate auto-regressive integrated moving average

Once the decomposition was performed, the hospitalizations dataset was analysed as time series to determine the impact of admissions on following week's hospitalizations. For that, the ARIMA model was implemented.

Auto-regressive integrated moving average (ARIMA) is a class of statistical models for analysing and forecasting time series data. [15]

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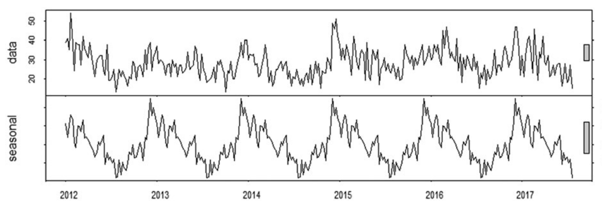
Figure 2 Decomposition of admission data series.



Multivariate regression

The next step was to analyse the regression taking also into account the environmental information. First of all, we calculated the correlations between all environmental factors and admission rates. This way we could select the most significant factors for the experiment. Following, the multivariate ARIMA was implemented to determine their impact all together.

Selection of attributes

As mentioned before, the variables were grouped by weeks. The correlation was estimated using the non-parametric test of Kendall, which measures the strength of dependence between two numeric variables[16] and is one of the most used tests for this type of non-parametric data. In addition, this analysis was performed relating all the attributes with the number of admissions of the following week.

Note that, because the mean, maximum, and minimum values of the environmental factors were closely related, only the one with the highest correlation was taken into account per attribute. In *Table 1*, we summarize the selected ones.

Multivariate auto-regressive integrated moving average

After the study of the univariate ARIMA and the selection of the most correlated environmental attributes, a multivariate ARIMA model was carried out.

For that, first, we employed all attributes and tested the Akaike information criterion (AIC) value; this criterion states that the one that presents the minimum AIC value is considered the optimal.[17] If the *P*-value of an attribute was too high, this value was discarded, and the AIC value was checked again. If the value improved (AIC decreased), we kept that value out of our model. Otherwise, we put it back. This process was performed iteratively until AIC did not decrease anymore.

Table 1 Selected attributes for the experiment and their correlation with heart failure admissions

Attribute	Selected	Correlation	*P*-value
Humidity	Max	0.0469	0.238
Precipitation	Mean	0.0795	0.05
Temperature	Mean	−0.3794	<0.001
Irradiation	Mean	−0.2629	<0.001
NO	Max	0.1733	<0.001
NO_2	Mean	0.1876	<0.001
NOX	Max	0.2196	<0.001
PM10	Min	−0.0485	0.324
SO_2	Max	0.2692	<0.001

Results

In *Figure 1*, we present the number of admissions per day. In each axis, the daily mean value of the number of hospitalizations per day is shown within each month. This figure illustrates that in European warm period (from June to October), there are significant less admissions than that in the cold period (from December to March).

In *Figure 2*, the decomposition of admissions on seasonality is shown. The first graph represents the original admissions data series, and below the seasonality of it is illustrated. Overall, it shows a clear seasonality of admissions, because there is a similar pattern every year. Moreover, as shown in *Figure 3*, there is a correlation between the number of admissions in a week with the adjoining weeks and with the week of the previous year.

Table 1 analyses the correlations between all environmental factors and admission rates using a multivariate analysis and demonstrates that the most correlated attribute is the temperature, with the highest (inversed) correlation value (multivariate analysis). That is, the lower the temperature, the larger is next week admission rate. On the other hand, humidity and PM10 parameters do not have significant correlations with this method, neither relevant *P*-values.

Table 2 shows the impact of the optimal attributes in the multivariate ARIMA model. As can be seen, the attribute with most impact on the number of admissions is the admissions itself. This is reflected in the variables called ‘ma1’ and ‘sma1’, which are the moving average and the seasonal moving average (season of a year), respectively. Nevertheless, environmental factors also have a considerable influence. For example, the model predicts that when the mean temperature raises 1°C, the estimated number of hospitalizations will decrease by 0.6 (when the rest of attributes remain constant). Moreover, the maximum value for SO_2 within a week also has an effect (P = 0.007). Additionally, the variability of air quality parameter (NOX) also presents an impact on admissions predictions. Finally, the results also present that the more it rains, the smaller number of hospitalizations occur the following week.

Figure 3 Correlation between the number of admissions in a week with the adjoining weeks.

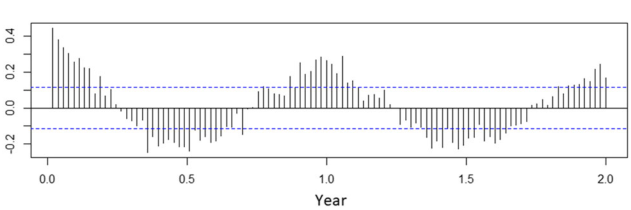


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Table 2 Results of the multivariate auto-regressive integrated moving average model study

Variable	Estimate	Std. error	*P*-value
ma1[a]	−0.9230	0.0258	<0.001
sma1[b]	−0.7075	0.1192	<0.001
Mean precip.	−0.2935	0.1189	0.014
Mean temp.	−0.6056	0.1865	0.001
Max. SO_2	0.3171	0.1176	0.007
Std. NOX	−0.0797	0.0342	0.02

[a]Moving average order 1 of admissions.
[b]Seasonal moving order 1 of admissions.

The mean air temperature, which has high impact on admission rate prediction (*Table 1*), is represented in a more visual way by comparing the number of admissions per weeks with the mean temperature, using a line graph (*Figure 4*).

Discussion

In this paper, the impact of previous HF decompensations and different environmental factors on hospital admissions due to worsening HF is studied. For that, a regression model for time series was built, and the external attributes that most affect the number of hospitalizations were tested. The attribute with most impact on the number of admissions is a previous HF admission. It also has a cyclical distribution with a similar pattern repeated every year: the period with most decompensations is the cold one, and this number depends on the number of admissions in the previous weeks. Regarding the external attributes that most affect the number of hospitalizations, air temperature is concluded to be the most significant environmental factor (negative correlation), although some other attributes, such as precipitation, are also relevant. So a significant winter peak in HF-related hospitalizations has been identified. These population-based findings are in accord with the results of other studies examining this topic,[7,8,10] which found a similar seasonal variation in discharges.

These results may not be applicable to other regions with different climates, as temperature variations and rain rate differ from our study. One might think that these effects would be more striking in countries with colder climates, while they would be more moderate in tropical regions.

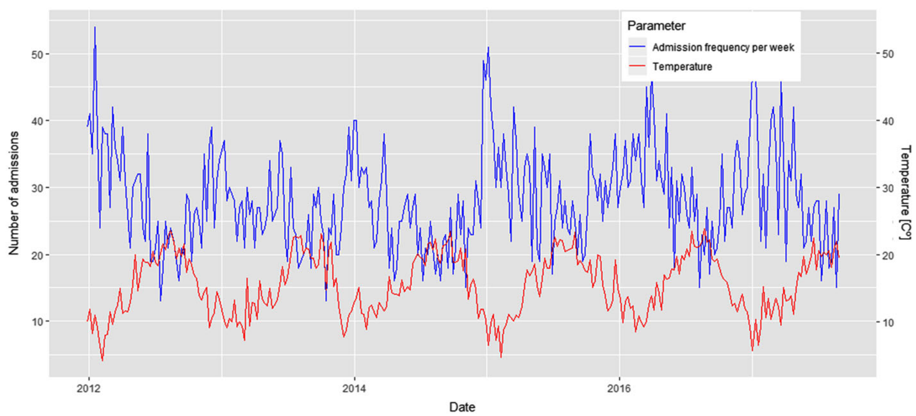
The haemodynamic stresses and neurohumoral activation that accompany a reduction in temperature may exacerbate HF, induce myocardial ischaemia, and precipitate arrhythmias, which in turn could further increase the risk of HF decompensation. Other mechanisms could also underlie the seasonal variation in HF-related morbidity and mortality. Respiratory infections, especially those related to influenza, are more frequent in winter and could precipitate HF[10] so a significant percentage of HF hospitalizations could be accounted for by this seasonal increment in respiratory diseases.

Moreover, this analysis shows a consistent association between increasing levels of some ambient pollutants, such as SO_2 (precursor of acid rain) and NOX air (major air pollutant formed by combustion systems and motor vehicles).

These results contrast to those obtained by Burnet[7] and Morris,[6] in which concentrations of carbon monoxide in big cities of the USA and Canada displayed the strongest and most consistent association with hospitalization rates among the pollutants. This association was independent of season, temperature, and other major gaseous pollutants. Nevertheless, it is possible that the observed association represented the impact of some other, unmeasured pollutant or group of pollutants covarying in time with carbon monoxide.

However, the climate in Bilbao, the environmental aspects and the socio-economic conditions are different to those described in other cities included in this kind of studies. As explained before, Bilbao has an oceanic climate, the rain rate is high, and traffic is restricted to certain areas of the city,

Figure 4 Comparison between the number of admissions (blue line) and the mean temperature (red line) per week over time.



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so the dispersion of pollutants is higher and that may explain the distribution and effect on health of air pollutants.

In fact, carbon monoxide exposure leads to elevations in the systolic blood pressure and, to a lesser extent, the heart rate and respiratory quotient, altering the ability of haemoglobin to transport oxygen to a degree enough to induce cardiac disease. Nitrogen oxides (NOX) and sulphur dioxide (SO_2) are other important ambient air pollutants. NOX exposure increases the risk of respiratory tract infections through the pollutant's interaction with the immune system. Sulphur dioxide (SO_2) contributes to respiratory symptoms in both healthy patients and those with underlying pulmonary disease. An alternative mechanism for the induction of congestive heart failure by air pollutants involves direct myocardial toxicity. Moreover, direct toxicities of these pollutants to the heart are very well demonstrated,[18] as for the brain more recently, increasing risk of stroke.[19]

These data support the warning issued by the World Health Organization: air pollution is responsible for about 7 million deaths a year in the world, 2.5 million of which correspond to heart diseases (25%) and 1.4 million to stroke (24%). In this regard, there are several Spanish studies indicating that 93% of the Spanish population breathes air that exceeds the limits considered dangerous to health.

Our study has several limitations. First, this is an observational study, and despite statistical adjustments, a causal and definite relationship between seasonality, environmental pollutants, and hospital admissions for HF cannot be determined. Second, we analysed data only from Bilbao city (single centre study), so results may not be extrapolated to other regions with different climate or pollution levels. Third, our dataset does not contain information on clinical characteristics. Lastly, we have relied on discharge coding, which has high accuracy in the principal position but is lower in secondary positions. As differentiating an exacerbation of respiratory disease, respiratory infection and decompensated HF is clinically difficult, particularly in the elderly, miscoding of pulmonary infection as HF may be as likely as HF miscoded as pulmonary infection.

Despite these limitations, our analysis of data demonstrates the impact of pollutant agents and the seasonality of hospital admissions for HF. Our findings have potentially important management implications. First, increased vigilance in winter is important in patients with HF in order to detect and correct decompensation at an early stage. Second, pneumococcal and influenza immunization should be encouraged, not just to avoid these infections, but also for their potential role in winter exacerbations of HF. Finally, this document warns about new effects of these pollutants and opens the way for a more exhaustive study of theses parameters and how to improve the quality of our environment.

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Conflict of interest

None declared.

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References

1. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, Luepker R, Mittleman M, Samet J, Smith SC Jr, Tager I. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation* 2004; **109**: 2655–2671.
2. Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation* 2010; **121**: 2331–2378.
3. D'Amato G, Cecchi L, D'amato M, Liccardi G. Urban air pollution and climate change as environmental risk factors of respiratory allergy: an update. *J Investig Allergol Clin Immunol* 2010; **20**: 95–102.
4. Laumbach RJ, Kipen HM. Respiratory health effects of air pollution: update on biomass smoke and traffic pollution. *J Allergy Clin Immunol* 2012; **129**: 3–11.
5. World Health Organization, 2018. Burden of disease from the joint effects of household and ambient air pollution https://www.who.int/airpollution/data/cities/en/
6. Morris RD, Naumova EN, Munasinghe RL. Ambient air pollution and hospitalization for congestive heart failure among elderly people in seven large US cities. *Am J Public Health* 1995; **85**: 1361–1365.
7. Burnett RT, Dales RE, Brook JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide

levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. *Epidemiology* 1997; **8**: 162–167.
8. Das D, Bakal JA, Westerhout CM, Hernandez AF, O'Connor CM, Atar D, McMurray JJV, Armstrong PW, Ezekowitz JA. The association between meteorological events and acute heart failure: new insights from ASCEND-HF. *Int J Cardiol* 2014; **177**: 819–824.
9. Levin RK, Katz M, Saldiva PHN, Caixeta A, Franken M, Pereira C, Coslovsky SV, Pesaro AE. Increased hospitalizations for decompensated heart failure and acute myocardial infarction during mild winters: a seven-year experience in the public health system of the largest city in Latin America. *PLoS One* 2018; **13**: e0190733.
10. Stewart S, McIntyre K, Capewell S, McMurray JJV. Heart failure in a cold climate: seasonal variation in heart failure-related morbidity and mortality. *J Am Coll Cardiol* 2002; **39**: 760–766.
11. Basque Government, B.G., 2009. Open Data Euskadi, datos abiertos del Gobierno Vasco - Euskadi.eus. URL http://opendata.euskadi.eus/inicio/ (18 September 2018).
12. Moritz S, Bartz-Beielstein T. imputeTS: time series missing value imputation in R. *R J* 2017; **9**: 207–218.
13. Gobierno Vasco, E.J., 2017. Calidad del aire en Euskadi durante el 2017. URL http://www.geo.euskadi.eus/calidad-aire-en-euskadi-2017/s69-geodir/es/ (17 May 2018).
14. Jebb AT, Tay L. Introduction to time series analysis for organizational research: methods for longitudinal analyses. *Organ Res Methods* 2017; **20**: 61–94.
15. Brownlee, J., 2017. *Introduction to time series forecasting with python: how to prepare data and develop models to predict the future*. Machine Learning Mastery, PDF format Ebook. Edition: v1.7. https://machinelearningmastery.com/introduction-to-time-series-forecasting-with-python/ (18 November 2018).
16. Rui S, Vera C. *Comparative approaches to using R and python for statistical data analysis*. Pensilvania, USA: IGI Global; 2017. http://dx.doi.org/10.4018/978-1-68318-016-6
17. Akaike H. A new look at the statistical model identification. *IEEE Trans Autom Control* 1974; **19**: 716–723.
18. Mustafic H, Jabre P, Caussin C, Murad MH, Escolano S, Tafflet M, Périer MC, Marijon E, Vernerey D, Empana JP, Jouven X. Main air pollutants and myocardial infarction. A systematic review and meta-analysis. *JAMA* 2012; **307**: 713.
19. Hadley MB, Baumgartner J, Vedanthan R. 2018. Developing a clinical approach to air pollution and cardiovascular health. *Circulation* 2018; **137**: 725–742.