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Using Bayesian networks for environmental health risk assessment

Sandra Pérez [a,*], Catherine German-Labaume [b], Sébastien Mathiot [c], Sylvaine Goix [d], Philippe Chamaret [d]

[a] University Côte d'Azur, UMR, 7300, Boulevard E. Herriot, Nice, France
[b] Centre Intercommunal de l'Action Sociale du Pays de Martigues, Health and Handicap Department, Avenue Louis Sammut, Martigues, France
[c] AtmoSud, Route de la Vierge, Martigues, France
[d] Institut Ecocitoyen pour la Connaissance des Pollutions, Centre de vie, La Fossette, Fos-sur-Mer, France

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ABSTRACT

The study investigated the potential relationships between air pollution, socio-economy, and proven pathologies (e.g., respiratory, cardiovascular) within an industrial area in Southern France (*Etang de Berre*), gathering steel industries, oil refineries, shipping, road traffic and experiencing a Mediterranean climate. A total of 178 variables were simultaneously integrated within a Bayesian model at intra-urban scale. Various unsupervised and supervised algorithms (maximum spanning tree, tree-augmented naive classifier) as well as sensitivity analyses were used to better understand the links between all variables, and highlighted correlations between population exposure to air pollutants and some pathologies. Adverse health effects (bronchus and lung cancers for 15–65 years old people) were observed for hydrofluoric acid at low background concentration (<0.003 μg m^{-3}) while exposure to particulate cadmium (0.210–0.250 μg m^{-3}) disrupts insulin metabolism for people over 65 years-old leading to diabetes. Bronchus and lung cancers for people over 65 years-old occurred at low background SO_2 concentration (6 μg m^{-3}) below European limit values. When benzo[k]fluoranthene exceeded 0.672 μg m^{-3}, we observed a high number of hospital admissions for respiratory diseases for 15-65 years-old people. The study also revealed the important influence of socio-economy (e.g., single-parent family, people with no qualification at 15 years-old) on pathologies (e.g., cardiovascular diseases). Finally, a diffuse polychlorinated biphenyl (PCB) pollution was observed in the study area and can potentially cause lung cancers.

1. Introduction

Outdoor air pollution is a major public health issue in the world (e.g., Lelieveld et al., 2015; Cohen et al., 2017; Khaniabadi et al., 2018; Sicard et al., 2019; Rovira et al., 2020) leading to half a million premature deaths in the European Union in 2015 (European Environment Agency, 2018). Industrial activities, motor vehicle emissions, transport, and domestic heating are different sources of air pollution in urban areas (European Environment Agency, 2019) releasing air pollutants such as nitrogen oxides (NO_x), volatile organic compounds (VOCs), sulphur oxides (SO_x), black carbon, polycyclic aromatic hydrocarbon (PAH) and particulate matter (PM) in the atmosphere (European Environment Agency, 2019). In Europe, 74% of the population lives in cities (European Union, 2016), and is usually exposed to about 200 air pollutants or classes of air pollutants (Sicard et al., 2012, 2021). Previous studies have reported an association between ambient air pollution exposure and mortality and hospital admissions for respiratory and cardiovascular diseases (e.g., Amoatey et al., 2020; Pascal et al., 2014; Cai et al., 2016; Cohen et al., 2017; Guo et al., 2018; Mannucci et al., 2019; Yang et al., 2020a, 2020b; Khaniabadi et al., 2019; Park et al., 2021). The European Union and the World Health Organization regulate the concentrations of air pollutants by setting limit and target values for the protection of human health (e.g., Directive, 2008/50/EC European Council, WHO, 2006 Air Quality Guidelines 2006).

Martigues conurbation is an urban-industrial area located in Southern France, open onto the Mediterranean Sea, nearby the biggest industrial area in Southern Europe, namely Berre Pond (*Etang de Berre*). The pond is surrounded by major industrial complexes and oil refineries, and experiences high levels of air pollutants impacting the health and well-being of citizens (Allen et al., 2017; Goix et al., 2018; Mantey et al., 2019; Pérez, 2016, 2019). From 2013, epidemiological and scientific studies were carried to investigate the health effects of air pollution on local population (Mantey et al., 2019). The REVELA study (*Rein, VEssie et Leucémie Aigüe)* was conducted by *Santé Publique France* between 2013

* Corresponding author.
E-mail address: sandra.perez@univ-cotedazur.fr (S. Pérez).

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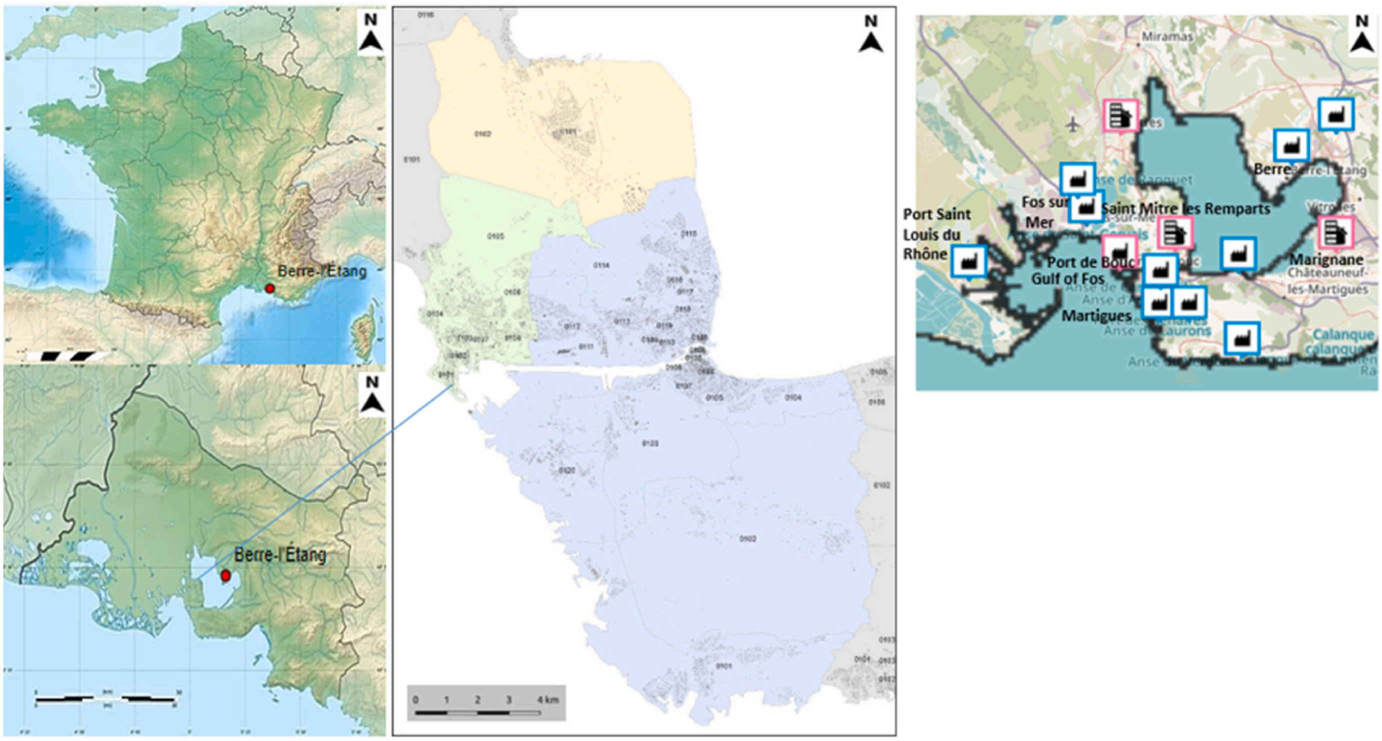


Fig. 1. Location of the study area and air quality monitoring stations (blue/pink: industrial & pre-urban/urban station; square: fixed station. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

and 2016, focussing on kidney and bladder cancers and acute myeloid leukaemia. This study showed that the incidence rate for bladder cancers, among people >20 years-old, was higher than those observed at the national level (Mantey et al., 2019). In 2015, the Fos-EPSEAL study (*Étude Participative en Santé Environnement Ancrée Localement*) was conducted in two urban areas (Fos-sur-Mer and Port-Saint-Louis-du-Rhône) and allowed collecting health data on a random sample of inhabitants through a participatory approach (Allen et al., 2017; Fortin et al., 2017; Jeanjean et al., 2021). Chronic diseases and acute symptoms were often observed in both cities. The prevalence of asthma in adults, of cancers (notably for women) and diabetes (type 1) is significantly higher in both cities than at national level (Allen et al., 2017; Jeanjean et al., 2021). Respiratory ailments (except hayfever) concern almost one in two adults and one in four children (Jeanjean et al., 2021). Then, the INDEX (*Etude d'imprégnation de la population aux polluants atmosphériques de la zone industrialo-portuaire de Fos-sur-Mer*) study was conducted in 2016 in Fos-sur-Mer by the *Institut Ecocitoyen pour la Connaissance des Populations* on blood and urine samples of 138 inhabitants, and revealed an over-impregnation by lead and two heptachlor furans (i.e., 1,2,3,4,6,7, 8-HpCDF and 1,2,3,4,7,8,9 HpCDF), characteristic of industrial emissions, and by benzene for people over 65 years-old (Goix et al., 2018). In this area, gardening was associated with a high impregnation by polychlorinated biphenyl (PCBs), and the consumption of vegetables from garden was associated with a high impregnation by cadmium (Goix et al., 2018). Similarly, the consumption of local seafood (fish, shellfish, and sea fruits) was associated with a high impregnation by PCBs, dioxins/furans, mercury, and chrome (Goix et al., 2018). Finally, the SCENARII (*Simulation de scénarii de pollution atmosphérique pour une Evaluation des Risques Sanitaires - Zone Etang de Berre*) and POLIS (*Plan d'Observation des Polluants d'Intérêt Sanitaire)* studies were conducted in 2010 in 66 cities around the Berre Pond and allowed calculating an excess risk considering 39 substances (AtmoSud, 2016; AtmoSud, 2015). The limit values were exceeded for nitrogen dioxide (NO_2), fine particles with an aerodynamic diameter lower than 2.5 and 10 μm ($PM_{2.5}$ and PM_{10}, respectively), diesel particles, benzene, 1,3-Butadiene and 1, 2-Dichloroetane. Some areas have presented higher level of risk i.e., Gulf of Fos, Martigue, Berre, Marignane and road transport axes.

In Southern France, where air pollution is a major public health issue (Salameh et al., 2018; Khaniabadi and Sicard, 2021), most of published studies focused on the health impacts of exposure to common ambient air pollutants such as PM, NO_2, and tropospheric ozone (e.g., InVS, 2008; Pascal et al., 2014; Sicard et al., 2019). For the first time, a risk assessment was focused on an industrial area in Southern France (Berre Pond as study case). Using Bayesian networks, this study aimed to better understand the relationships between air pollution, biodiversity (lichens), socio-economy, and proven pathologies by age group (i.e., 178 variables in total, Tab. 1S) at intra-urban scale in 2015.

2. Materials and methods

2.1. Study area

Martigues conurbation gathers three municipalities i.e., Martigues, Port-de-Bouc, and Saint-Mître-les-Remparts with a total population of 71,000 inhabitants in 2015 (Fig. 1), and experiences a Mediterranean climate, with an annual mean rainfall and air temperature of 606 mm and 19.5 °C, respectively. Along the French Mediterranean coastline, air pollution is a major public health issue, mainly due to industrial development, oil refineries, road traffic increment, high insolation, and sea/land breeze recirculation (Salameh et al., 2018; Sicard et al., 2019), including tropospheric ozone (O_3) with rising levels in cities in Southern France (on average + 0.31 ppb per year) since the early 2000s (Sicard, 2021).

2.2. Health data

We have selected some pathologies linked to air pollution (e.g., Suissa et al., 2013; Adam et al., 2015; Atkinson et al., 2015; Münzel et al., 2016; Mazenq et al., 2017; Guo et al., 2018; Doiron et al., 2019; Hwang et al., 2020) i.e., corresponding to the following International

Table 1a
Annual mean concentration of each **gaseous air pollutant** (in μg/m^3) for the year 2015 in the study area. M: model, m: measurement, * the background is taken at the level of a point distant from any source (Etang de Rolland area). Limit and target values for air pollutants as given in the European Ambient Air Quality Directive (Directive, 2008/50/EC) for the protection of human health.

Pollutant	Model/ Measurement	Concentration (μg/m^3)	EU limit and target value
Sulphur dioxide - SO_2	M + m	6	Number of exceedance of 24-h mean (125 μg m^{-3}) [a]
Nitrogen dioxide - NO_2	M + m	8.0	Annual mean (40 μg m^{-3}) [b]
Carbon monoxide - CO	M + m	263	
Hydrochloric acid - HCl	M	8.23E-04	
Hydrofluoric acid - HF	M	5.29E-04	
Benzene - C_6H_6	M + m	0.7	Annual mean (5 μg m^{-3})
Benzo [a]pyrene - BaP	M	2.42E-06	
Polycyclic Aromatic Hydrocarbons - PAHs	M	2.11E-3	Annual mean (1.0 ng BaP/m^3)
Dioxins and furans - PCDD and PCDF	M	2.31E-10	
Mercury - Hg	M + m	1.06E-06	
Benzo [a]anthracene - BaA	M	3.42E-06	
Benzo [b]fluoranthene - BbF	M	2.68E-06	
Benzo [k]fluoranthene - BkF	M	1.88E-06	
Indeno [1,2,3-c,d] pyrene - IcdP	M	1.52E-06	
Dibenzo [a,h] anthracene - DahA	M	3.12E-07	
Fluoranthene - Fluoran	M	2.24E-05	
Polychlorobiphenyls - PCB	M	5.663E-07	
1,3-butadiene - CAH_6	M + m	0.13	
Hydrogen sulphide - H_2S	M	5.72E-06	
1,2-dichloroethane - DCE	M + m	0.03	

[a] The 24-h SO_2 mean concentration does not to exceed 125 μg m^{-3} more than 3 times a year.
[b] The annual mean NO_2 concentration does not to exceed 40 μg m^{-3}.

Table 1b
Annual mean concentration of each **particulate air pollutant** (in μg/m^3) for the year 2015 in the study area. M: model, m: measurement, * the background is taken at the level of a point distant from any source (Etang de Rolland area). Limit and target values (threshold in μg m^{-3}) for air pollutants as given in the European Ambient Air Quality Directive (Directive, 2008/50/EC) for the protection of human health.

Pollutant	Model/ Measurement	Concentration (μg/m^3)	EU limit and target value
Particles with an aerodynamic diameter lower than 10 μm - PM_{10}	M + m	16.0	40 [a]
Particles with an aerodynamic diameter lower than 2.5 μm – $PM_{2.5}$	M + m	10.0	25
Benzo-a-pyrene - BaP	M + m	1.63E-04	
Polycyclic Aromatic Hydrocarbons - PAHs	M	1.38E-03	Annual mean (1.0 ng BaP/m^3)
Dioxins and furans - PCDD and PCDF	M + m	2.16E-08	
Lead - Pb	M + m	4.02E-03	Annual mean (0.5)
Arsenic - As	M + m	3.86E-04	Annual mean (0.006 μg m^{-3})
Cadmium - Cd	M + m	1.39E-04	Annual mean (0.005 μg m^{-3})
Nickel - Ni	M	2.03E-04	Annual mean (0.02 μg m^{-3})
Mercury - Hg	M + m	0	
Chromium - Cr	M + m	1.97E-03	
Chromium VI - Cr VI	Cr VI/total Cr	1.40E-04	
Copper - Cu	M + m	3.75E-03	
Selenium - Se	M + m	3.65E-04	
Vanadium - V	M + m	2.51E-03	
Zinc - Zn	M + m	1.93E-02	
Benzo [a]anthracene - BaA	M + m	1.38E-04	
Benzo [b]fluoranthene - BbF	M + m	3.09E-04	
Benzo [k]fluoranthene - BkF	M + m	1.36E-04	
Indeno [1,2,3-c,d]pyrene - IcdP	M + m	2.32E-04	
Dibenzo [a,h]anthracene - DahA	M + m	4.20E-05	
Fluoranthene - Fluoran	M	8.28E-06	
Polychlorobiphenyls - PCB	M	6.30E-07	
Diesel particles - PM_{10} diesel	diesel/PM10	5.00E-01	

[a] For the protection of human health, the annual mean PM_{10} concentration does not to exceed 40 μg m^{-3} (Directive, 2008/50/EC).

Classification of Diseases ICD-10 codes: I00 to I199 all diseases of the circulatory system (e.g., ischemic heart diseases, coronary diseases), J00 to J199 all diseases of the respiratory system (e.g., asthma, bronchitis, bronchiolitis, bronchopulmonary diseases, laryngitis, pharyngitis, sinusitis, tracheitis), E10 to E14 all diabetes types (type 1 insulin-dependent, and type 2 non-insulin-dependent), C34 all types of lung and bronchus cancers, C67 for bladder cancer, and C64 for kidney cancer.

For each pathology, we retrieved the numbers of hospital admissions, classified into three age groups (<15, 15–65, and >65 years-old) for patients having stayed either at the Martigues Centre Hospitalier, the Martigues Clinique, the Paoli Calmettes Institute or in one of the five nearby public hospitals (Hôpital de la Timone, Hôpital de la Conception, Hôpital Nord, Sainte Marguerite and Salvator) in 2015. We did not obtain the "gender" in addition to the "age" because the use of both information mutually was considered as discriminatory by the National Commission on Informatics and Liberty. For statistical studies, the National Institute for Statistics and Economic Studies (INSEE) developed a system for dividing the country into units of equal size, known as IRIS 2000. In French, IRIS is an acronym of "aggregated units for statistical information", and the 2000 refers to the target size of 2000 residents per basic unit. IRIS represented the fundamental unit for dissemination of infra-municipal data. The fact of dealing with a fine territorial scale imposes having enough cases per IRIS and consequently to work by batches of codes (e.g., I00 to I199) rather than by separated codes.

2.3. *Air pollution data*

In risk assessment, exposure is considered equal to air pollutants concentrations at a specific point in space and time (Bogaert et al., 2009). The data for 44 pollutants were provided by the Certified Associations of Air Quality Monitoring in Southeastern France (Atmo Sud) and obtained from January 1, 2015 to December 31, 2015 (Table 1). In the study area, there are 11 industrial and 4 urban monitoring stations (Fig. 1). Only background stations, with more than 90% of validated hourly data in a year, were selected to better represent average exposure (Directive, 2008/50/EC). AtmoSud has developed an Information Technology tool producing maps of annual mean concentrations for air pollutants at 3 × 3 km of spatial resolution from both modelling (Atmospheric Dispersion Modelling System) and *in situ* measurements (AtmoSud, 2016). The air pollution maps were produced for built-up areas on which a 100 m buffer was applied to have a more accurate

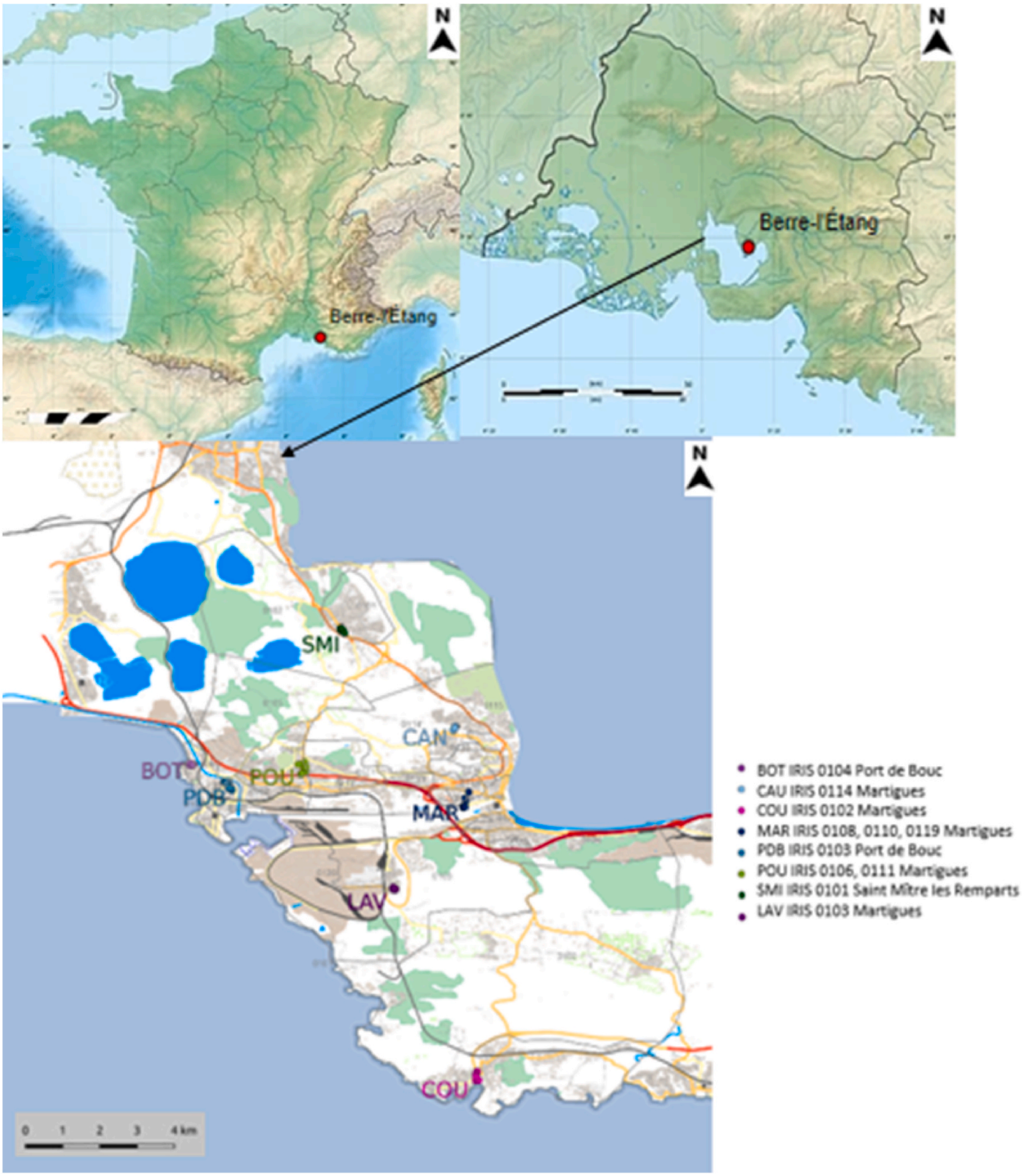


Fig. 2. Location of the lichen sample plots within the study area (source IECP).

measurement of pollution in the population's living spaces (Fig. 1S).

2.4. Lichens: bio-indication and bio-impregnation

In addition to the 44 air pollution variables, 109 chemical analyses (bio-impregnation measurements) were carried out on lichen samples in September 2017 by the *Institut EcoCitoyen pour la Connaissance des Pollution* (IECP) on specific plots (Fig. 2). For spatial representativeness of each plot, a 500 m radius around the bio-impregnation plot was considered, as recommended by the IECP (Ratier et al., 2018). A variability of maximum 35% for metals and 30% for various congenerics PAH has been measured in a plot within a 500 m radius (Ratier et al., 2018). Samples were taken with a knife after humidification and stored at + 39.2 °F for maximum 5 days. The impurities were removed, and the samples were frozen at – 113 °F, then lyophilized at – 131 °F before to be crushed and again frozen at - 113 °F. The chemical analyses were carried out at the laboratory of La Timone (Aix-Marseille University, Faculty of Pharmacy) for PAHs and PCBs, as well as at the "La Drôme Laboratoires" in Valence, for Dioxins and Furans. The impregnation results represent a 6-month integration. These measurements on lichens are useful to limit a confounding factor that could be linked to the residents' way of life more than the effects of air pollution (notably addiction to smoking); most of them are in IRIS area known to be socio-economically disadvantaged.

Looking to the bio-indication, several indicators relating to the biodiversity (Chao et al., 2016) were calculated (abundance of species, lichen diversity value, Index of Atmospheric Purity, and the Shannon's diversity index). The Index of Atmospheric Purity is used for the

Fig. 3. The bio-indication survey (source IECP).

assessment of air quality in polluted urban areas based on phytosociological data of epiphytic lichen communities (Chao et al., 2016). The survey was done on 10 trees per plot, on all four faces of the tree and according to a 5-box observation grid (Fig. 3). The frequency of each species is the ratio of the number of observations of the species per plot divided by 200 (10 trees * 4 faces * 5 boxes).

2.5. Socio-economic data

We have also retrieved seven socio-economic variables, as the air pollution effects will not affect everyone in the same way (Jiao et al., 2018, Næss et al., 2007). The disadvantaged communities might be more exposed to air pollution, but also might have less resources to counter them e.g., by postponing medical consultations by lack of resources, or asthma poorly controlled (Temam, 2017, Fosse-Edorh et al., 2014). These variables were provided by the INSEE from the sub-municipal databases in 2017, including: i) the number of people living in households for more than 10 years (P14_PMEN_ANEM10P), ii) number of unschooled people of at least 15 years-old and without qualification (P14_NSCOL15P_DIPL0), iii) number of people living in single-parent households (C14_PMEN_MENFAMMONO), iv) number of people in main homes occupied by tenants (P14_NPER_RP_LOC), v) number of immigrants (P14_POP_IMM), vi) number of unemployed in the 15-64 years-old age group (P14_CHOM1564), and vii) median income (DEC_MED14).

For comparison between each IRIS area, the above variables were used as percentage of the IRIS total population. All these indicators were used to know the level of precariousness or social disadvantage in each IRIS area. We used disaggregated variables to precisely investigate on which variables differences between IRIS appear. In total, 178 variables (Tab. 1S) were measured within 30 IRIS areas, corresponding to 5340 data. These data were integrated within the same Bayesian model.

2.6. The Bayesian networks

The Bayesian networks allow establishing relations among various variables to analyse their interrelations and combinations by using probabilities (Pearl, 2009a,b; Sottas et al., 2009; Pearl, 2014; Conrady and Jouffe, 2015; Pearl and Mackenzie, 2018). The probabilistic approach is particularly well suited to health risk issues, because relations between variables are not always determinist but rather indirect (Pearl, 2009a; b, 2014). Moreover, Bayesian networks allow at the same time modelling knowledge and producing new knowledge by revealing causal relations until now hidden (causal inference), or latent variables, and this, within the framework of unsupervised analysis (causal knowledge discovery). They bring added value in terms of knowledge and are an interesting tool for quantitative modelling of complex systems in uncertain fields, whether health or others. This is the reason why they are increasingly used worldwide, in fields as diverse as industry, finance, marketing, security, and many others (Weber and Simon, 2016).

A Bayesian network is made up of two elements: a conceptual map and a database (Pearl, 2009a,b). The conceptual map defines the network structure used for knowledge organization and representation. This map is either built from the database, or from expert's knowledge of the investigated subjects. In our case, we decided to extract knowledge included in our database. All processing was carried out using the specific software devoted to Bayesian networks, i.e., BayesiaLab 7.0.1. The conceptual map is visually represented by directed arcs representing the causal relations linking the variables, represented by nodes (Fig. 2S). Between the nodes, causal relationships are drawn using an unsupervised artificial intelligence learning algorithm of the "maximum spanning tree" type. Thereafter, the conceptual map of the 178 variables appears in unsupervised form (Fig. 4).

2.7. Statistical and sensitivity analyses

Data were tested for normal distribution by the Kolmogorov-Smirnov one-sample D test. The correlation analyses were performed using the parametric Pearson test for annual data (Table 2). For health data analysis, we also applied a Hierarchical Cluster Analysis (HCA) to group similar objects into groups called clusters. The distance between two clusters has been computed based on the Euclidean distance. The main output of HCA is a dendrogram showing the hierarchical relationship between the clusters (Govender and Sivakumar, 2020). All health data and number of hospital admissions for each age group and IRIS area were normalized to the total population.

The relations between variables at a finer scale were investigated using sensitivity analyses for each of the 30 IRIS areas, taking simultaneously into account the 44 air pollutants, the 17 variables obtaining from the lichen surveys and acting on pathologies (Chlorobiphenyl CB169, TEQ-2005, CB187, 2,3,4,7,8-PeCDF, As, 2,3,7,8-TeCDF, crustaceans, Lichen diversity value, CB149, CB114, CB157, CB20, CB28, Co, CB194, Lichen abundance, PCB indicators), and the 7 socio-economic variables, i.e. a total of 68 variables (Fig. 5S). Fig. 6S represents all sensitivity analyses per pathology and enabled us to observe the heterogeneity between all IRIS areas.

3. Results and discussion

3.1. Analysis of the correlations

Looking the health variables (Table 2), we found that the number of

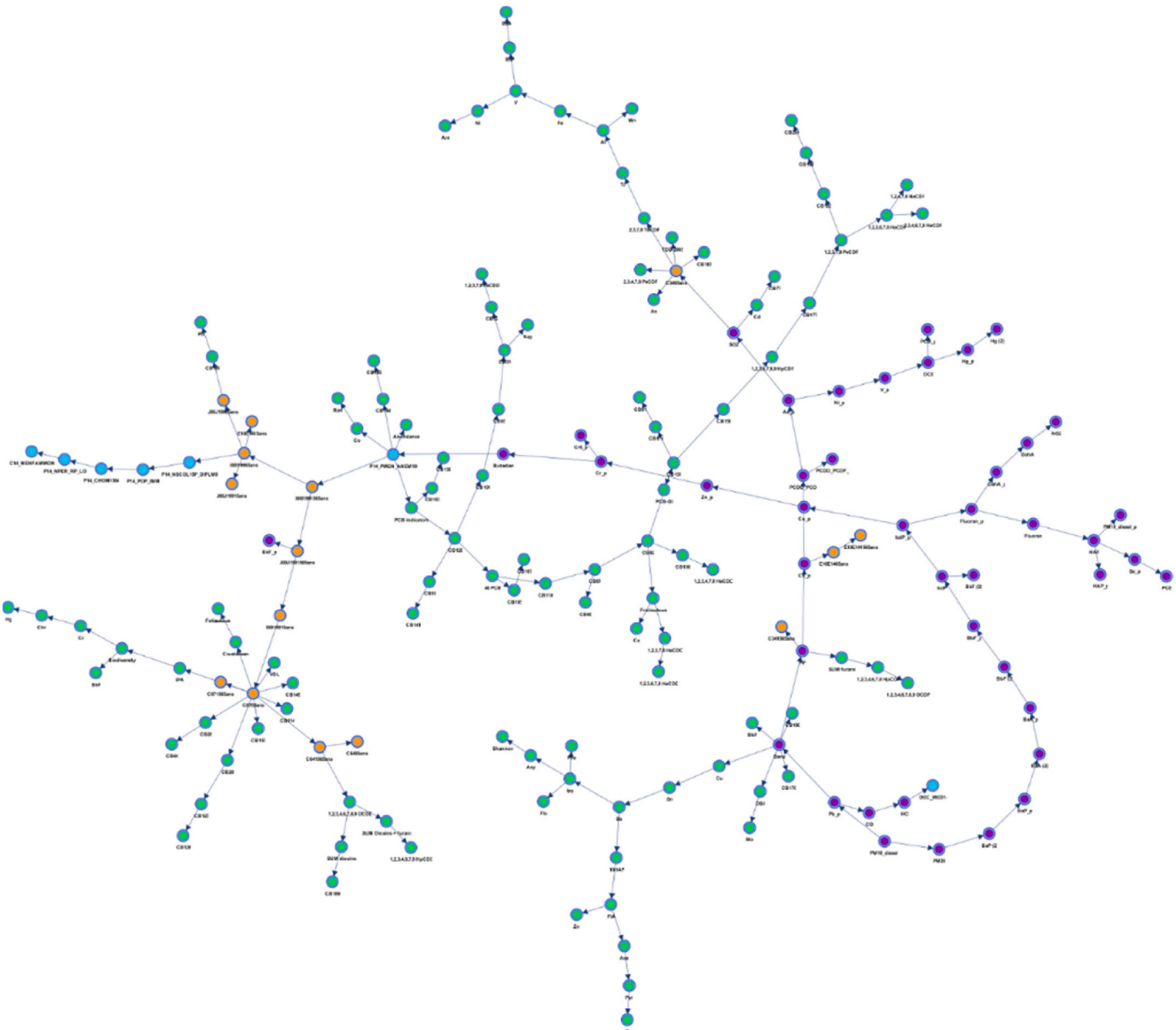


Fig. 4. The Bayesian network - Conceptual map of the 178 variables: orange for pathologies, green for variables resulting from lichens measurements, purple for air pollutants, and blue for socio-economic variables. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

people living the same IRIS area for more than 10 years (P14_PMEN_ANEM10P) is well correlated to the relative abundance of lichen species (r = 0.70). Higher relative abundance of lichen is related to more people living in the same area at long time, and this could be explained by the benefits provided by natural amenities and green infrastructure. Indeed, urban green spaces can reduce air pollution, regulate air temperature, but also reduce noise and provide recreational, social, psychological, and aesthetic benefits (Sicard et al., 2018). We found a negative correlation between the relative abundance of lichen species and Chlorobiphenyl CB194 (r = - 0.70) while a positive correlation was found between the number of people living in the IRIS area for more than 10 years (P14_PMEN_ANEM10P) and carbon monoxide (r = 0.60), and cardiovascular diseases for 15-65 years-old people (r = 0.65). Significant correlations were found between cardiovascular and respiratory diseases (r = 0.70) for patients over 65 years-old, revealing a comorbidity which is well known by doctors (Carter et al., 2019), and also appearing in 15–65 years-old patients (r = 0.52). This is explained by the chronicity of these pathologies as is the case with diabetes (r = 0.73). A strong correlation was observed between respiratory diseases for people >65 years-old and a dioxin-like PCB (r = 0.78) recognized for its toxicity, i.e., CB169 (Van den Berg et al., 2006). A relationship is observed (r = 0.63) between cardiovascular diseases for patients >65 years-old and the socio-economic variable “no qualification”, and between mean income and exposure to the hydrochloric acid (r = - 0.65) meaning that more the households income increases less they are exposed to such pollutant. As regards bronchus and lung cancers for people >65 years-old, we observed positive relationships, in particular with CB187 (r = 0.80), TEQ-2005 (r = 0.83), 2,3,7,8-TeCDF (r = 0.86), 2,3,4,7,8-PeCDF (r = 0.84), As (r = 0.78) and SO_2 (r = 0.62). Concerning bladder cancer, relations appeared between people >65 years-old and Value of Lichen Diversity (r = 0.67), CB20 (r = 0.64), and two dioxin-like PCBs i.e., CB114 (r = 0.85) and CB157 (r = 0.52).

Table 2
Correlation analysis (Pearson test, r value) between the environmental, socio-economic and health variables. We reported here the more significant correlations i.e. with r > 0.50.

versus		r value
P14_PMEN_ANEM10P - Number of people living in the IRIS for more than 10 years	Abundance of lichen species	0.70
	Carbon monoxide - CO	0.60
	Cardiovascular diseases 15–65 years old	0.65
Cardiovascular diseases >65 years old	Respiratory diseases >65 years old	0.70
Cardiovascular diseases 15–65 years old	Respiratory diseases 15–65 years old	0.52
Cardiovascular diseases 15–65 years old	Cardiovascular diseases >65 years old	0.67
Diabetes 15–65 years old	Diabetes >65 years old	0.73
Respiratory diseases >65 years old	CB169: 3,3′,4,4′,5,5′-Hexachlorobiphenyl	0.78
Cardiovascular diseases >65 years-old	No qualification at 15	0.63
Bronchus and lung cancers >65 years old	CB187: 2,2′,3,4′,5,5′,6-Heptachlorobiphenyl	0.80
Bronchus and lung cancers >65 years old	TEQ-2005	0.83
Bronchus and lung cancers >65 years old	2,3,7,8 TeCDF	0.86
Bronchus and lung cancers >65 years old	2,3,4,7,8 PeCDF	0.84
Bronchus and lung cancers >65 years old	Arsenic - As	0.78
Bronchus and lung cancers >65 years old	Sulphur dioxide - SO_2	0.62
Bladder cancers >65 years old	Lichen diversity	0.67
Bladder cancers >65 years old	CB20: 2,3,3′-Trichlorobiphenyl	0.64
Bladder cancers >65 years old	CB114: 2,3,4,4′,5-Pentachlorobiphenyl	0.85
Bladder cancers >65 years old	CB157: 2,3,3′,4,4′,5′-Hexachlorobiphenyl	0.52
Diabetes >65 years old	Cd_p: particulate Cadmium	0.52
Relative abundance of lichen species	CB194: 2,2′,3,3′,4,4′,5,5′-Octachlorobiphenyl	−0.70
Mean income	Hydrochloric acid	−0.65

3.2. Interactions between variables

To deeply investigate the interactions between pathologies, air pollutants and socio-economy, we focussed on relationships between a pathology and a type of variable (either environmental or socio-economic). Here, we focussed on the interactions between respiratory diseases for people >65 years-old and CB169, and the interactions between diabetes for patients >65 years-old and the heavy metal, cadmium (Table 2).

3.2.1. Interactions between respiratory diseases & CB169

We found a significant correlation (r = 0.78) between respiratory diseases for people >65 years-old and CB169 (Table 2). To investigate the interactions between variables, first the relation was spotted in the Bayesian network (Fig. 5a), then we monitored the variables (Fig. 5b), and we saw what happens at the level of their modalities (Fig. 5c). The number of modalities corresponds to the number of classes requested (K-means 5 classes). What is particularly interesting now is to force one of these classes, for example the modality corresponding to the highest number of hospital admissions (here: number of stays >51.75), which then becomes green, and to observe how the associated probabilities of CB169 are then instantly updated. Thus, we observed that if we focus on the highest numbers of stays, the values of CB169 increase, mainly for the two last modalities (e.g., evolution from 16.67 in the initial monitoring to 31.86 in Fig. 5d). Which means that when we consider the highest numbers of hospital stays recorded for respiratory pathologies in the over 65 in this territory, it is in relation with the highest values of CB169 found in the lichen surveys. The most frequent modality (44.38%) has also been forced without showing in that case notable changes in the monitoring.

3.2.2. Interactions between diabetes & Cd

We found a significant correlation (r = 0.52) between diabetic people >65 years-old and particulate Cadmium (Table 2). Cadmium is absorbed in food (dry/wet deposition, air/soil pollution) and can disturb insulin metabolism in the pancreas (Schwartz et al., 2003; Buha et al., 2020). This relation is very strong (Fig. 4S) for the highest modality of diabetes patients (>45.1 number of stays) and concerns a value of Cd_p between 0.214 and 0.250 μg m^{-3} (Fig. 4S). For the most frequent modality, the relation already appears with the lowest values of Cd_p (38.18% under or equal to 0.181 μg m^{-3}).

3.3. Health profiles of the IRIS areas

For instance, in IRIS 130560101 in Martigues, the probability to find people over 65 years-old with respiratory diseases is high, approximatively 50%, followed by 15–65 years-old people with cardiovascular diseases, about 35% (Fig. 6). Based on the HCA, five groups with a similar health profile can be clearly distinguished (Fig. 7). The Group 1 includes atypical IRIS areas with the highest occurrence rates for all pathologies. The second Group differs from the others by less cardiovascular, respiratory and diabetes diseases, but a higher rate of lung cancers for people over 65 years-old (Fig. 7). In Group 3, we can observe high rates of cardiovascular diseases for young people (<15 years-old) and elderly i.e., over 65 years-old (1.21 on average), higher than in the first group (0.81 on average). The same is true for respiratory diseases from the age of 15 years-old with rates almost twice as high as those of Group 1 (1.33 versus 0.70). Diabetes for young people (<15 years-old) also individualises these IRIS areas. Bronchus and lung cancers for people over 65 years-old, without reaching the values of Group 2, are also noteworthy (0.62 on average), just like bladder cancers in the same age group, without nonetheless exceeding Group 1 (0.64 on average). In Group 4, we observed more cardiovascular diseases for people over 65 years-old (1.13 on average), respiratory diseases and a lower cancer rate for people over 65 years-old (1.13, 0.45) and people <15 years-old (0.74). Finally, Group 5 includes IRIS areas with pathology rates comparatively lower than in the other Groups. It can be used as control Group "out-of-area" for model validation with less exposed people to air pollution. However, the endocrine disruptors to which the population can be exposed via pesticides can induce the same pathologies (e.g., diabetes), which could confuse the "control cases" comparisons (Evangelou et al., 2016; Mendes et al., 2021).

3.4. IRIS health profiles and causal factors

The causal factor of health profiles can be either environmental and/or socio-economic, and the combination of both form the pathogenic spaces (Picheral, 1983). Based on the sensitivity analyses, we distinguished the IRIS areas according to the probability of prevalence of environmental and socio-economic factors. First, we have distinguished three IRIS profiles based on a cocktail of air pollutants (Sarigiannis and Hansen, 2012; Svingen and Vinggaard, 2016) with either many HAPs (7 IRIS areas), or many PCBs (8 IRIS areas), or other pollutants (15 IRIS areas).

In the HAPs group, the number of HAPs varied by a factor two (6–12 HAPs) with a direct impact on pathologies. Indeed, the severity of pathology depends on the number of HAPs due to the carcinogenic nature of each HAP (BaP, BaA, BbF, BkF, DahA, Fluoranthene, IcdP) and to their potential noxious mixing (ATSDR, 2012). The favourable socio-economy of the IRIS "Jonquières Foulettes" (income above average) seems to make up for the residents' exposure, similarly to the IRIS "Coudoulière" but to a lesser extent due to less numerous HAPs. Looking the cocktail of PCBs, their health impact is well characterised by e.g., bladder cancers (IRIS Plan de Fossan) even at low doses due to their toxicity (ATSDR, 2012). Finally, the category "Others" refers to air pollutants that cannot be classified in the previous categories. It includes "traditional" air pollutants such as NO_2, SO_2, hydrofluoric acid (HF) and particulate

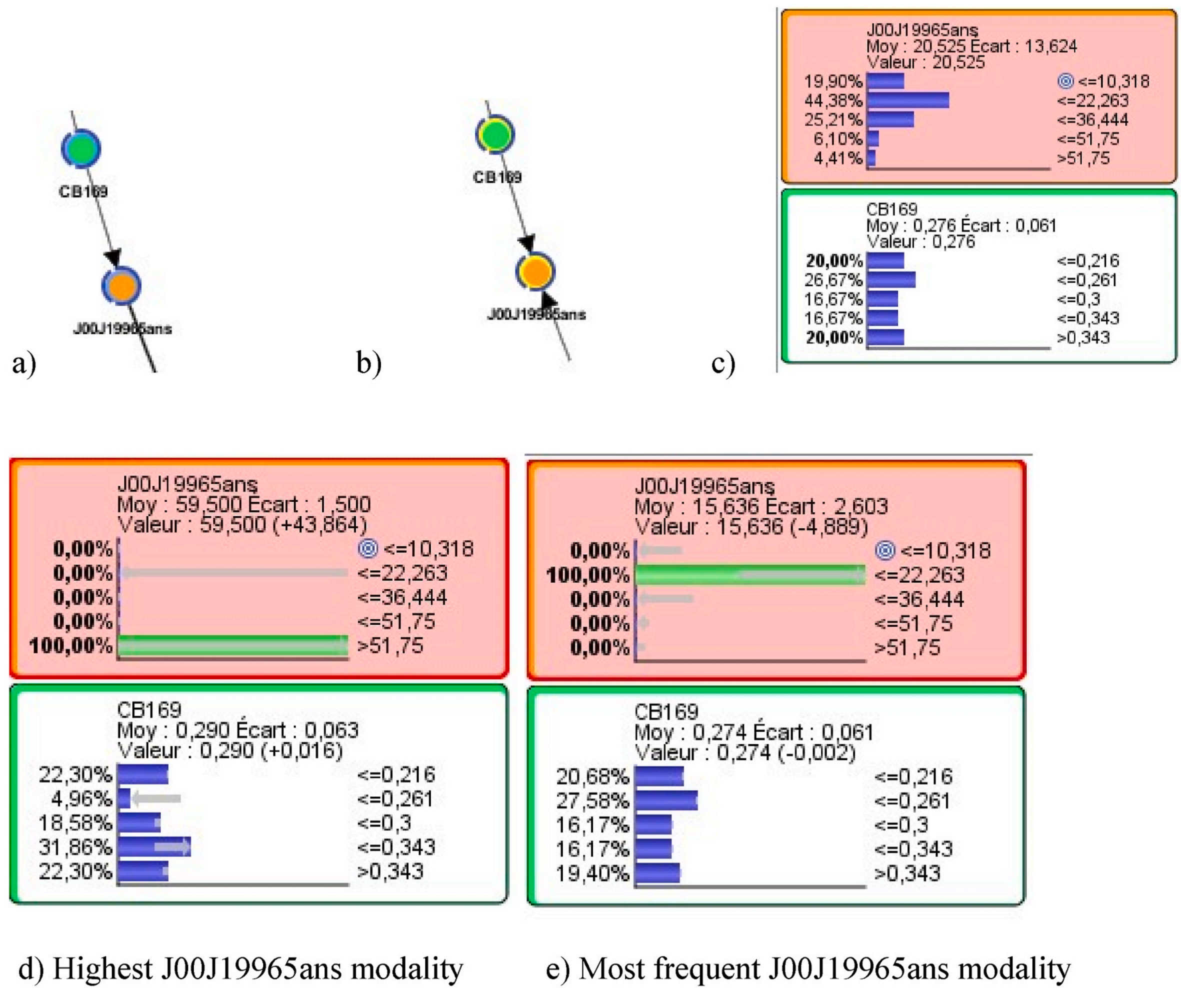


Fig. 5. Interactions between respiratory diseases for people >65 years-old (J00J19965) & CB169.

elements such as Zn, Cd, Cu and the PCDD_PCDF.

Based on the HCA dendrogram, people living in IRIS areas classified as Group 1 (Fig. 7S) was exposed to harmful pollutants: PCDD_PCDF at La Lèque, CB28 at Plan Fossan, Dibenzo (a, h)anthracene at Boudème, HF at PdB Centre and St-Jean Bergerie. In 4 of the 6 IRIS areas, socio-economy combines with air pollutants and corresponds to single-parent families. In fact, it is the prevailing variable for the IRIS "Rayettes". Within IRIS areas of the Group 2 (Fig. 8S), people are exposed to PCBs (Tassy Est, St-Pierre and St-Julien), SO_2 (Tassy Ouest) and to vanadium at much higher levels than in other IRIS areas. The IRIS "Jonquières Est" was exposed to 11 different HAPs while the IRIS "Notre Dame Paradis" was exposed to NO_2. In Group 2, socio-economy (i.e., unschooled at 15 years-old and unemployment) had a pernicious impact. The type of pollutants (PCB, vanadium) and their multiplicity (11 different HAPs) could explain the pathologies found (i.e., bronchus, lung cancers and bladder cancers) in the IRIS areas of this Group 2 (Lees, 1980; ATSDR, 2012). In Group 3 (Fig. 9S), the IRIS "Ferrière" had a similar PCBs profile like the IRIS "St-Mitre Périphérie". This IRIS area is simultaneously exposed to several pollutants (Co, Zn_p, Cr_p, Cr6_p, PCDD_PCDF, HCl, BkF_p) at low concentrations, except from BkF_p leading to respiratory diseases. As regards the IRIS "Gaps", Hg is the most important air pollutant, followed by Co, Cu_p and HF, while the IRIS "Croix Sainte" is rather characterised by the presence of Zn_p, followed by several pollutants of the PCB type, and As. Finally, socio-economic variables seem to have a greater impact on the IRIS "Colline" (immigrant population, single-parent families, unemployment and unschooled 15 years-old, the latter variable having an impact on cardiovascular diseases), and Cd_p, that disrupts insulin metabolism, is the only pollutant in this IRIS area. Starting from this 4th group (Fig. 10S), the number of hospital admissions is relatively low: both IRIS areas "Canto Perdrix" and "Les Comtes Est" stand out in regard to cardiovascular diseases for people over 65 years-old, with a prevalence of BkF_p for the IRIS "Canto Perdrix". Here, we observed a disadvantaged socio-economy and a seemingly deleterious cocktail for "Les Comtes Est" (DCE, V_p, Hg and HF), since the impact is also observed on respiratory diseases for people over 65 years-old. Finally, the control Group (Fig. 11S) was characterised by an overall number of pathologies lower than elsewhere, and less dangerous pollutants and/or in lower quantity than in other IRIS areas of Groups 1–4. Moreover, socio-economy being more favourable (except in the IRIS "Comtes Ouest") tends to offset the pollutants effects. This is particularly true for the IRIS "St-Mitre Centre". Nevertheless, we observed that the presence of SO_2 only had an influence on respiratory diseases in the age range 15–65 years-old within the IRIS "Figuerolles". By gathering all HCA outputs and IRIS profiles (Fig. 8), we observed HAP emissions in the north-east of the study area (Jonquières, Boudème), a vanadium and SO_2 emission in South (Lavéra, Côte Bleue), and a PCB pollution over the whole territory. In study area centre, disadvantaged socio-economy combined with the pollutants.

In this study, we highlighted some limitations. First, here the health data are related to the number of hospital admissions, instead of the number of patients. The number of patients was not available when this study was conducted. Therefore, an overestimation of the number of cases is plausible because some pathologies can necessitate several hospital admissions (in particular for bladder cancers). Likewise, as we

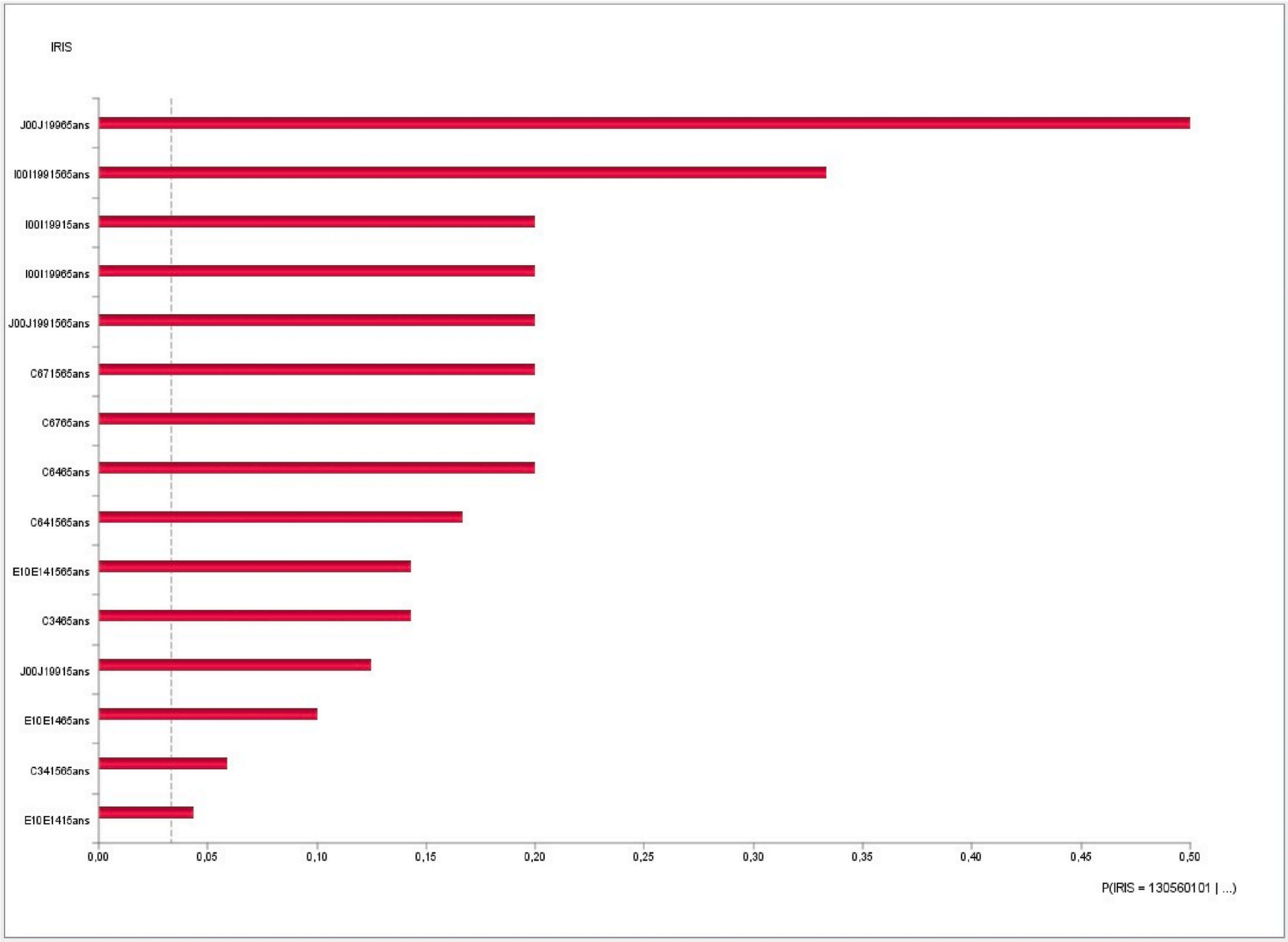
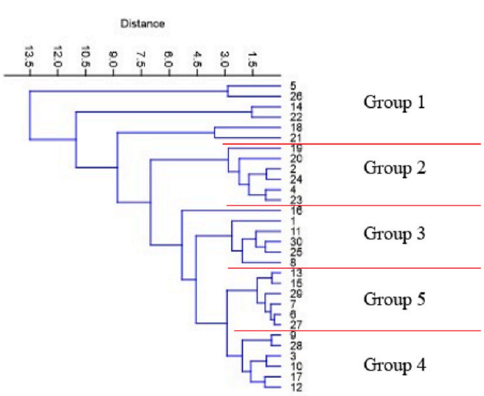


Fig. 6. Sensitivity analysis for all pathologies within the IRIS area "Côte Bleue" (13560101) in Martigues. The probability for respiratory diseases for people over 65 years-old is 0.50.



Group	Pathologies	Environmental factors	Socio-economic factors
1	High number of pathologies	PCDD-PCDF, CB28, dibenzo(a,h)anthracene	Single-parents family
2	Lung cancers (>15 years-old) Bladder cancers (15-65 years-old)	PCBs, SO2, vanadium, 11 HAPs	Unschooled at 15 years old Unemployment
3	Cardiovascular diseases (<15; >65 years-old), Diabetes <15 years-old	BkF_p, Hg, Co, Cu_p, HF, Zn_p, PCBs, As, Cd_p	Immigrant population Single-parent family Unemployment Unschooled 15 years-old
4	Cardiovascular diseases (>65 years-old) Respiratory diseases (<15; >65 years-old)	BkF_p, DCE, v_p, Hg, HF	Unfavorable Socio-economy
5 - Control group	Low number of pathologies	Low exposure to air pollution	Favorable Socio-economy

Fig. 7. Hierarchical Cluster Analysis - Health profiles of the 30 IRIS areas subdivided into 5 Groups.

worked at fine scale, the number of cases for some pathologies in some IRIS areas can be low and induce biases. However, Bayesian networks compare the evolution of proportion between variables, the risk of bias is minimised. By selecting annual averages for air pollutants smooth out the effects of air pollutants. Air pollutant and health data are those of 2015. The estimated effects are erroneous by omitting the lag effect of air pollutants exposure, i.e., by assuming that all effects occur in one day (Schwartz, 2000). In this study, air pollutants concentrations were averaged from air quality monitoring stations, and we assumed that all individuals shared the same air pollution levels in the study area, therefore the individual exposure estimate is erroneous (Park and Kwan, 2017). Human mobility was also ignored by considering residential exposure, and not professional or related to daily commuting. In addition, only the outdoor exposure to air pollutants was considered while people spent about 80–90% of time in indoor environments (Laumbach et al., 2015).

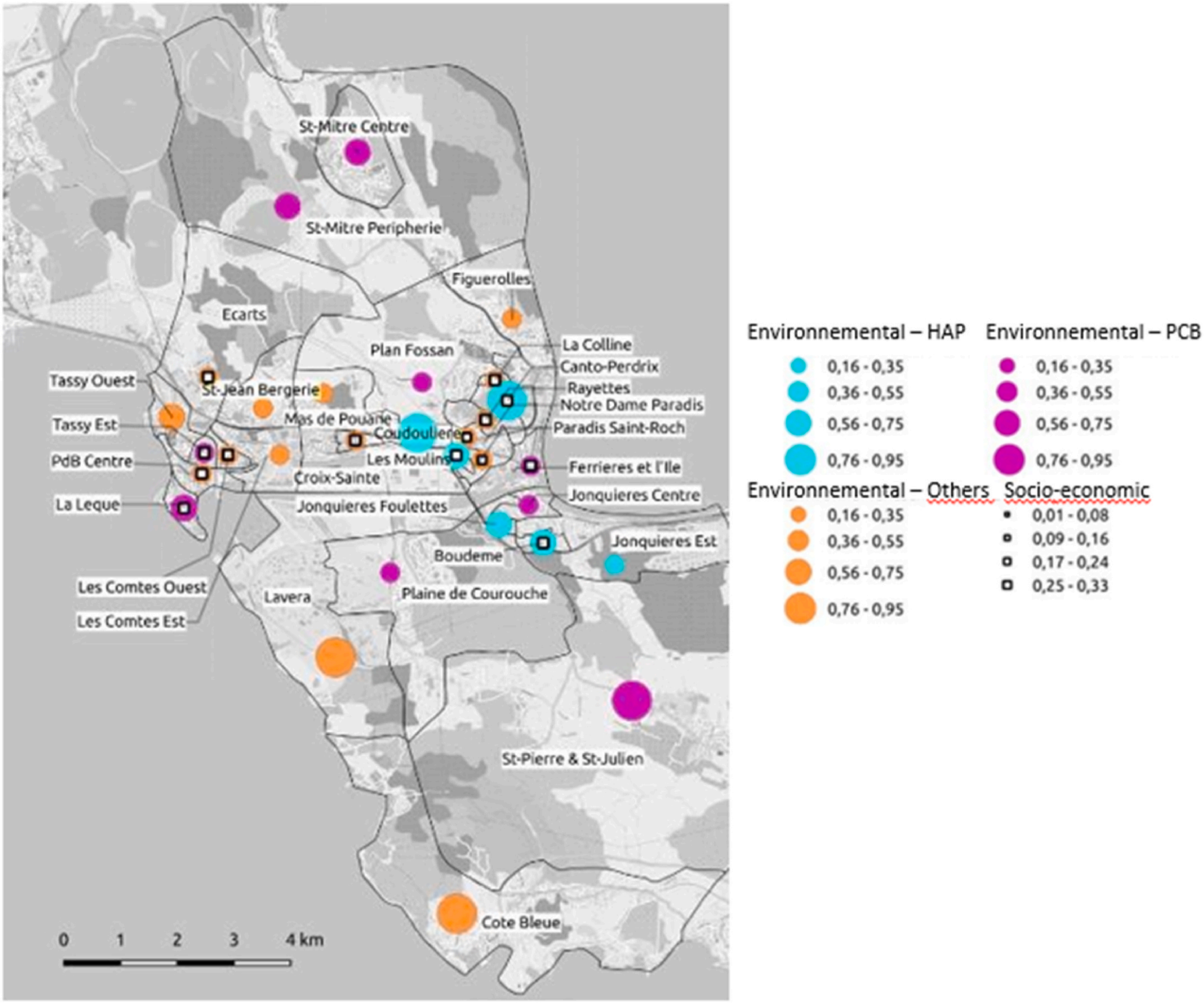


Fig. 8. Profile of IRIS areas according to the prevalence of environmental and/or socio-economic factors. The value indicates the highest probability (scale 0–1) found in the IRIS (sensitivity analyses) according to the type of factor (HAP, PCB, Others and socio-economic). Group 1 – IRIS areas characterised by an increased prevalence of hospital admissions for the whole of the pathologies studied. Group 2 – IRIS areas characterised by an increased prevalence of hospital admissions related to lung cancers (>15 years-old) and bladder cancers (15-65 years-old). Group 3 – IRIS areas characterised by an increased prevalence of hospital stays related to cardiovascular diseases (<15 and > 65 years-old) and diabetes (<15 years-old). Group 4 – IRIS areas characterised by an increased prevalence of hospital stays related to cardiovascular diseases (> 65 years-old) and respiratory diseases (<15 and > 65 years-old). Group 5 – IRIS areas characterised by a lower prevalence of "Control group" pathologies.

Although the lichen plots are scattered over the entire study area and located according to the IRIS areas socioeconomic level, more of them would have enabled us to ascertain our results even better. Studies carried out on environmental health are most of the time criticised because of the difficulty to get to the root causes of pathologies. Another frequently heard argument is the multifactorial character of an individual's health. Furthermore, the design of these studies is most of the time of the ecological kind and can also lead to attribute to individuals the effect of pollutants measured in a space (ecological fallacy), but this argument is itself put into question (Schwartz, 1994). By taking into account a high number of variables (pollutants, pathologies, and socio-economy) which can potentially affect the citizens health and well-being, and by using a robust mathematical formalism at fine city-scale, based on conditional probabilities, we found causal factors. Thus, we have been able to bring forward several relations between exposure to xenobiotics and proven pathologies, sufficient to require an hospital admission in 2015, and which suggest the following recommendations.

Control strategies, and local policy, must focus on reducing SO_2 emissions, as we observed health effects at very low levels, even below European and WHO standards. Companies must continue and ramp up the desulphurisation process of their installations, or, when possible, use a lower-sulphur fuel. However, SO_2 is also emitted by tankers bringing their load to the nearby "Fos-sur-Mer" industrial harbour. The use of a lower-sulphur fuel could contribute to improve the citizens health. In the study area, we observed a diffuse PCB pollution, linked to respiratory diseases for people over 65 years-old, and this major issue should be deeply investigated to take appropriate measures e.g., site remediation by phytomanagement (Aken et al., 2010; Passatore et al., 2014). We can highlight several thresholds above which certain pollutants are particularly noxious, e.g., adverse health effects (bronchus and lung cancers) can be observed for hydrofluoric acid (HF) at 0.0028 μg m^{-3} threshold

(Fig. 12.S), while exposure to particulate cadmium, between 0.214 and 0.250 μg m^{-3} (Fig. 4S) disrupts insulin metabolism for people over 65 years-old. Finally, benzo [k]fluoranthene exceeded the 0.672 μg m^{-3} threshold (Fig. 13.S), and this exceedance was associated to a high number of hospital admissions for respiratory diseases for 15-65 years-old people. Specific pollutants such as chrome, chrome VI, and vanadium in their particle phase, need a continuous monitoring. Therefore, emissions of these pollutants should be reduced, when it is technically and financially possible by e.g., substitute products, less polluting industrial processes, and more effective filters.

4. Conclusions

The study has revealed differentiated health profiles between the different IRIS areas in Martigues conurbation, which should lead to supplying health care that would be better suited to the population needs, from a prevention perspective, and even to promote consultations with certain specialists. For example, with a cardiologist in the IRIS areas where the number of unqualified 15 years-old people is significant, as a relation was found, likely due to more difficult living or working conditions for such people. Likewise, prevention and social support measures should be taken to the benefit of single-parent families. Lastly, present-day pathologies are most of the time the result of former exposures when pollution levels were overall higher. In this study, human mobility, and exposure to indoor air pollutants, where people spend more than 80% of time, were ignored. Therefore, our estimates due to air pollutants exposure were biased. Il would be interesting to obtain older measurements concerning the incriminated pollutants and redo the calculations. The industries in the study area should continue to reduce their emissions concerning the harmful air pollutants. To reduce population's exposure to air pollution, adequate mitigation measures should be implemented to reduce the emissions and concentrations in the air of air pollutants such as an update of national emissions ceilings, an introduction of electric/hybrid cars, green public transportation, regulation of fuel quality, and implementation of green infrastructure to ameliorate urban air quality at city scale (Sicard et al., 2018; Sofia et al., 2020).

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.112059.

Authors' contributions

Project conceptualizing, design of the study, data analysis, writing: SP, Project administration, Funding acquisition, Literature review: GL, Manuscript preparation: SP, SG, Visualization: SG, Participation in the data collection and provided technical input to the data analyses: SM, PC, Validation: SM. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not Applicable.

Consent for publication

This manuscript does not contain any individual person's data in any form.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request, excepting the health data, because the French national commission for Informatics and Freedoms (CNIL) does not allow their sharing.

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