

Construction, optimization and interpretation of exposome databases for the study of the impact of air pollution on COPD and cystic fibrosis patient cohorts

Scientific background and ongoing projects

With global warming leading to an increase in the frequency of extreme weather events, but also urban lifestyles that force daily proximity between individuals and sources of air pollutants, the question of the consequences of exposure to air pollution on people with chronic diseases is increasingly raised. Indeed, numerous studies show that acute and chronic exposure to air pollution is accompanied by a decrease in respiratory function in healthy adults. Deleterious effects on lung growth and lung function in children exposed to high levels of air pollution have been demonstrated, as well as in people with chronic respiratory disease. Among non-communicable respiratory diseases, chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF) appear to be two very debilitating diseases that are of particular interest to be examined in parallel studies on human exposure. The roots of these two diseases are opposite: COPD is currently considered to be mainly related to the external exposome¹ (smoking, ambient particulate matter, household air pollution, occupational particulate matter, ozone...). On the other hand, CF is the consequence of a genetic defect in the *CFTR* gene, which gives an essential role to factors outside of the exposome. However, modifying genes are now considered to play part in CF disease, therefore also implying a role for internal components of the exposome in this disease. Importantly, COPD and CF share common characteristics such as high phenotypic variability of unknown origin, and similar progressive loss of lung function with small bronchi alterations. Given this high phenotypic variability, which prevents good therapeutic efficacy for these two diseases, as well as the high diversity of exposome composition, it is clear that the overall picture must be supplemented by taking into account additional components of the exposome than those currently considered in COPD and CF diseases.

In this context, the IMRB, CHIC and LISA have been involved in studying the role of pollution peaks on the occurrence of exacerbations and lung function in patients, in order to extend the understanding of the contribution of the exposome to COPD and CF diseases. Deciphering the impact of atmospheric components throughout the lifespan on the phenotypic variability of COPD and CF could represent a major step forward in reducing the morbidity and mortality associated with these two non-curable diseases, and could identify modifiable risk factors on which preventive action could be implemented.

Objectives of the thesis

This PhD project is part of a broader perspective that consists in retrospectively studying the impact of air pollution on the course of COPD and CF diseases.

The objective of the PhD is to build and interpret exposome databases for cohorts of patients spread over different French and European territories. They include for France the Paris region (Créteil, Suresnes, Trousseau) and the cities of Limoges, Lille, Marseille, Rennes, Toulouse, Lyon and Bordeaux, as well as the Danish Cancer Health cohort (DCH), the Norwegian Women and Cancer Cohort (NOWAC) and the ALSPAC cohort (UK) for abroad. The ambition is to gather data and then identify the most relevant pollution markers (fine particles, oxidizing capacity, combustion tracers...) to trace their potential health impacts on patients. The data will come from operational air quality

¹ The exposome includes all health problems that are not of genetic origin and this over the entire lifespan, integrating not only the environment but also the psychological and socio-economic causes.

monitoring conducted by approved networks, but also from modelling data produced or to be produced. In addition, data from individual portable mini-sensors will supplement the information available. These mini-sensors will be implemented during the PhD for a subset of patients and will measure in particular the fine particles present in the indoor and outdoor environments visited. The candidate will contribute to the implementation of the campaign with pollutant portable sensors. The processing of the data collected will consist in studying the statistical signals (correlation or causality) linking the concentrations of pollutants measured in the atmosphere and the occurrence of exacerbations in the patients included and in finding the best statistical parameters representative of the chronic or point pollution suffered, and its spatial and temporal evolution.

This work will require an ongoing dialogue between the PhD student, the IMRB and CHIC teams in charge of the medical data of the cohorts, and the LISA researchers in charge of the environmental component of the projects. The PhD student will be welcomed in Pr Ralph Epaud's team, in daily contact with the LISA modelling team.

Profile required

- Master 2 in sciences: biology, chemistry, environment, health
- Excellent scientific, medical and/or environmental skills. Awareness of health issues is expected. Knowledge of epidemiology will also be a strong asset.
- Proficiency in statistics, data analysis
- Openness to multidisciplinary and societal issues (socio-environmental inequalities, vulnerable populations, etc.).

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