ERC Consolidator Grant 2014
Research proposal [Part B1][1]
(Part B1 is evaluated both in Step 1 and Step 2
Part B2 is evaluated in Step 2 only)

Air pollution and noise exposure related to personal transport behaviour: short-term and longer-term effects on health

MobiliSense

Cover Page:

- Name of the Principal Investigator (PI): **Basile Chaix**
- Name of the PI's host institution for the project: **Inserm (French National Institute of Health and Medical Research)**
- Proposal duration in months: **60 months**
- Commitment of the PI to the project: **75% of working time over 5 years**

Proposal summary

To support policies at the European and national levels, MobiliSense aims to explore the effects of air pollution and noise exposure related to personal transport habits on respiratory and cardiovascular health. Building on methods from Epidemiology, Geography, and Transport sciences, the objectives of MobiliSense are to quantify the contribution of personal transport to the air pollution and noise exposure of individuals; to compare the air pollution and noise exposure in the different transport modes; to investigate whether total and transport-related personal exposure to air pollutants and noise are associated with short-term and two-year changes in respiratory and cardiovascular health; and to examine whether transport-related exposures mediate socioeconomic disparities in health. The MobiliSense project will use passive and active sensors of location, behaviour, environmental nuisances, and health in a representative sample of 1000 participants followed-up over two years. It addresses a gap in knowledge: (i) by assessing transport behaviour over 8 days with GPS receivers and an electronic mobility survey; (ii) by considering the personal exposure to both air pollution and noise and improving its characterisation (inhaled doses, noise frequency components, impulsive noise, and interactions with subjective annoyance); (iii) by measuring a wide range of respiratory and cardiovascular outcomes (smartphone-assessed respiratory symptoms, lung function assessed by spirometry and impedance pneumography, resting blood pressure, ambulatory brachial / central blood pressure, and heart rate variability); and (iv) by investigating short-term and longer-term effects of transport. To assist policy-makers, the final aim is to deliver a simulation tool permitting to determine the extent to which scenarios (i) of changes in personal transport behaviour and (ii) of changes in exposure levels during transport affect individual exposure and respiratory / cardiovascular health.

[1] Instructions for completing Part B1 can be found in the '*Information for Applicants to the Starting and Consolidator Grant 2014 Calls'*.

Section a: ***Extended Synopsis of the scientific proposal (max. 5 pages)***

Air pollution and noise exposure related to personal transport behaviour: short-term and longer-term effects on health

The MobiliSense project will explore the short-term and longer-term effects that air pollution and noise exposures related to personal transport behaviour may have on respiratory health and cardiovascular health. Its final aim is to develop a tool for policy-makers to assess the health impacts of scenarios (i) of changes in personal transport behaviour and (ii) of changes in exposure to air pollutants and noise during transport. The ground-breaking nature of the project is related to the precise assessment of transport behaviour over 8 days with GPS receivers and an electronic mobility survey; to the repeated assessment of transport behaviour at baseline and after two years; to the joint assessment of air pollution and noise through personal sensors; and to the repeated and intensive assessment of health in two 8-day periods with passive and active sensors.

I – SOCIETAL AND SCIENTIFIC BACKGROUND

The MobiliSense project is related to ongoing policy efforts at the European level (i) in the field of Transport (Transport, Health, and Environment Pan-European Programme), (ii) for the regulation of air pollution (December 2013 Clean Air Policy Package), and (iii) for the regulation of noise (European Noise Directive). In a context in which France was urged by the European Commission to implement actions to reduce the concentration of certain air pollutants and noise, our project is also connected to national policies aimed at the reduction of transport-related nuisances (e.g., the 2014–2018 National Health-Environment Plan). Overall, in the context of the insufficient evidence available, it is important to develop innovative research strategies to derive more reliable data on transport-related environmental exposures and their health effects.

We conducted a literature review of studies on the relationships between air pollution and / or noise and respiratory health (respiratory symptoms and lung function) or cardiovascular health (blood pressure and heart rate variability as a determinant of cardiac event incidence and prognosis in heart disease patients[1,2]). This review revealed that a considerable body of research has investigated long-term and short-term effects of air pollution on respiratory symptoms,[3,4] lung function,[5,6] blood pressure,[7,8] and heart rate variability,[9] as well as effects of noise exposure on blood pressure[10] and heart rate variability[11]; but that only few studies established a link between personal transport habits, related environmental exposures, and health.

A Dutch study of 489 adults found that the exposure to black smoke over 24 hours (as an indicator of black carbon emitted by diesel engines) was associated with upper respiratory symptoms, more consistently than the exposure to sulphate and particulate matter with an aerodynamic diameter of 10 µm or less (PM_{10}).[12] Similarly, a US study that relied on repeated measures of blood pressure did not find any association with the concentration of particulate matter with an aerodynamic diameter of 2.5 µm or less ($PM_{2.5}$) but reported that a higher exposure to black carbon over the previous 7 days (as a marker of particulate pollution related to road traffic) was related to an increased blood pressure.[13] Again, a study of 28 elderly subjects reported that a high concentration of $PM_{2.5}$ was associated with reduced heart rate variability, but that the concentration of black carbon resulted in stronger associations.[14] Finally, an experimental study of 60 participants demonstrated that walking for two hours in Oxford Street was associated with more important reductions in forced vital capacity and forced expiratory volume in one second than that observed in the same participants when walking through Hyde Park (as attributable to differences in the exposure to ultrafine particles and black carbon as markers of road traffic with diesel engines).[15] Regarding noise exposure, cross-sectional studies have reported positive associations between road traffic noise,[16] railway noise,[10] or aircraft noise[17] and self-reported hypertension or blood pressure.

Not to mention the small sample sizes, the review allowed us to identify limitations in the assessment of health outcomes: (i) respiratory symptoms were assessed with paper questionnaires referring to relatively long recall periods implying reporting biases rather than with a smartphone survey that also enables to monitor compliance; (ii) studies have relied on spirometry that provides a momentary snapshot of lung function in an artificial setting, but none of them was based on the recently developed assessment of lung function from tidal breathing (in daily lives)[18]; (iii) very few studies have relied on ambulatory monitoring of blood pressure,[19] and none has examined both resting and ambulatory blood pressure (each having its own strengths); (iv) extremely few studies examined pulse pressure, central rather than brachial blood pressure (as more predictive of target organ damage), and aortic pulse wave velocity or the augmentation index (as markers of arterial stiffness[20]) in relation to air pollutants[21]; and (v) too few studies combined indicators of heart rate variability from the time domain and from the frequency domain.

Our review also revealed that a large share of studies have assigned to participants residential estimates of outdoor exposure (from monitoring stations,[22] air dispersion models,[23] or noise maps).[24] Assessing individual exposures with these approaches has a limited validity[25]: (i) because the exposure data either ignore proximity sources or only imperfectly account for these sources; (ii) because people spend a different fraction of their time at their residence rather than at other places visited during daily activities; and (iii) because people spend a different amount of time inside rather than outside buildings. Due to these sources of measurement error, the magnitude of misclassification resulting from the use of residential estimates of exposure likely varies according to individual profiles. There is a large consensus that the use of wearable monitors is key to address these concerns and improve the assessment of personal exposures.[26]

Moreover, most studies captured exposures aggregated for entire periods without discriminating between subperiods of space-time budgets such as the time spent in transport.[27,28] Preliminary evidence suggests that the time spent in traffic contributes significantly to the personal exposure to certain pollutants.[15] The very few studies[27] that compared exposure levels between the transport modes, mostly related to air pollution, were often based on small samples and often compared two predefined itineraries (thus were poorly generalisable) and a limited number of alternative modes. Overall, almost no study assessed altogether the transport behaviour of people (considering alternative transport modes), related environmental exposures, and the resulting health effects. Personal monitoring of exposures will permit to investigate exposures related to personal transport habits, if and only if we are able to accurately apprehend participants' transport behaviour and use of modes using novel methodologies from Transport sciences.

Regarding more specific challenges to address, our review showed that: (i) few studies have performed a *personal* monitoring of black carbon (an excellent marker of road traffic pollution[28] that may be particularly associated with respiratory and cardiovascular outcomes); (ii) few studies of air pollution effects in real-life settings have accounted for estimates of inhaled doses[28]; (iii) few studies were able to consider subjective annoyance as a modifier of objective noise effects[29]; (iv) studies that relied on personal noise dosimeters were unable to distinguish between the different sources of noise[30]; (v) studies have assessed the average overall sound pressure but have not examined impulsive noise or distinguished noise frequency components (e.g., low and high pitch sounds)[31]; and (vi) very few cardiovascular studies considered both air pollutant and noise exposure,[7] and extremely few based on personal monitors (a major limitation because road traffic as a shared source of air pollutants and noise provides potential for reciprocal confounding[11]).

II – OBJECTIVES AND GROUND-BREAKING NATURE OF THE PROJECT

Building on data collection and analytic methods from Epidemiology, Geography, and Transport sciences, the present project aims to develop a comprehensive assessment of the relationships between transport-related exposures and health in a sample of 1000 participants followed over two years (and beyond). Its objectives are to address a gap in knowledge: (i) by focusing on both short-term and longer-term effects of personal transport behaviour; (ii) by considering two distinct environmental exposures (air pollution and noise) related to the transport activity that have often been investigated separately; (iii) by assessing a wide range of health outcomes related to respiratory and cardiovascular health; (iv) by deriving reliable measures of exposures, confounders, and outcomes using passive and active sensors and innovative electronic survey methods; and (v) by using simulations to evaluate the health impacts of scenarios of change of personal transport behaviour and of reduction of exposures during transport, as a tool for decision-makers.

II.A – Main objectives of the project

(i) We will assess the contribution of personal transport behaviour to the overall exposure of individuals to air pollutants [$PM_{2.5}$, black carbon, nitrogen dioxide (NO_2), and ozone (O_3)] and noise; we will compare the air pollution and noise exposure in the different transport modes (walking, biking, 2-wheel or 4-wheel personal motorised vehicle, public transport modes); we will examine the extent to which transport-related exposures contribute to differences in exposure between socioeconomic groups. (ii) We will investigate whether total and transport-related personal exposure to selected air pollutants and noise are associated with short-term respiratory and cardiovascular outcomes and with two-year changes in these outcomes (respiratory symptoms, lung function assessed by spirometry and impedance pneumography, resting and ambulatory blood pressure, and heart rate variability). (iii) We will investigate whether transport behaviour, air pollution exposure, and noise exposure mediate socioeconomic disparities in short-term and longer-term changes in respiratory and cardiovascular outcomes. (iv) We will perform simulations to assess the extent to which scenarios of changes in transport habits or scenarios of changes in exposure levels during transport would affect the time of exposure and respiratory / cardiovascular health, and will deliver a tool for decision-makers.

II.B – Ground-breaking nature of the project

To contribute to strengthen the partnership between Public health and Urban planning decision-makers, our project aims to provide a more comprehensive evaluation of the health effects of exposures related personal transport behaviour than previous studies, by building on innovative data collection and analytic methodologies from Epidemiology, Geography, and Transport sciences.

Regarding measurement, a key strength of the project is that it systematically relies on objective measurement approaches for assessing exposures, confounders, and health outcomes. The protocol will use passive sensors of location, behaviour, environmental conditions, and health (GPS receivers, accelerometers, air pollution and noise sensors, heart rate monitors, ambulatory blood pressure monitors, and impedance pneumography) and active sensors requiring an action of the subject for measurement (blood pressure at rest and spirometry). The use of some of these sensors / monitors is extremely innovative: the TensioMed Arteriograph 24 ambulatory blood pressure monitor measures central blood pressure (more predictive of target organ damage than brachial blood pressure) and aortic pulse wave velocity and the augmentation index as markers of arterial stiffness[20]; the BioPatch that will be worn to assess heart rate variability (and the respiratory rate) has recently received its certification from the US FDA; impedance pneumography has never been used to investigate air pollution effects on respiratory health; and no study has ever relied on a repeated smartphone survey to assess respiratory symptoms as close as possible from their onset.

A second measurement strength, integrating methodologies from Public health / Nutrition and Transport sciences,[32] is related to the precise assessment of personal transport behaviour over 8 days using GPS receivers and a GPS data-based electronic survey of activities and transport modes. Our study is the first ever to combine GPS tracking, such an advanced algorithm-based processing of GPS data, and a full electronic mobility survey over 8 days. This approach allows us to decompose the 8-day period into time spent at the different activity places and trips and trip stages (with a unique mode), permitting to ascribe the data from the behavioural, environmental, and health sensors to each trip or activity place time segment of the mobility survey. Moreover, our methodology to distinguish between *casual* transport behaviour over 8 days and *regular* transport behaviour will permit to investigate short- and longer-term effects of transport on health.

Also, we will perform a simultaneous monitoring of air pollution and noise with personal monitors as few studies have done.[11,33] Moreover, we will compare the exposure to air pollutants and noise as measured by personal sensors, and as estimated by combining the GPS tracks with information from the model-based maps of noise and hourly air pollutant concentrations (Geographic method). Finally, the project will promote ground-breaking strategies to investigate noise health effects, to assess: (i) whether smartphone-evaluated annoyance related to noise modifies noise effects; (ii) the effects of impulsive noise; (iii) whether accounting for noise frequency components in addition to the overall sound pressure permits to better describe health effects; and (iv) whether specific sources of noise are particularly associated with cardiovascular health.

The main analytical innovations of the project are to rely: (i) on Random forest approaches to compare the importance of the multiple versions of the exposure measures[34]; (ii) on a complex regression model to perform a joint analysis of *short-term effects* and *longer-term effects* of exposures; and (iii) on mediation analyses to investigate whether environmental exposures mediate socioeconomic differences in healh.

As important for European and national policies, these ground-breaking innovations will permit (i) to quantify the percentage of exposure to air pollutants and noise that is attributable to the transport activity; (ii) to estimate associations between the use of each transport mode and exposure levels; and (iii) to assess the health impacts of scenarios of changes in transport behaviour and in exposure during transport.

III – DATA COLLECTION, PROCESSING, AND ANALYSIS

III.A – Sampling, recruitment, follow-up, and processing

A Gantt Chart is reported in Extra Annex 6. Participants will be recruited through a three-stage stratified sampling design. In stage 1, we will randomly select neighbourhoods in the Paris city and first crown of counties, stratified by area-level socioeconomic status and road traffic density. To maximise disparities in exposure, within each socioeconomic stratum, we will randomly select five neighbourhoods in each of the two extreme quartiles of traffic density. At the second stage, the real estate property file from the Tax administration will be used to sample dwellings in each neighbourhood. At the third stage, dividing household members between 30 and 64 years of age into three strata (hypertensives, individuals with chronic bronchitis and related symptoms or asthma, and others), eligible individuals within each stratum will be selected for participation according to a stratum-specific sampling rate. Based on the target size of 250 hypertensives, 250 individuals with respiratory problems, and 500 participants free of these conditions (n = 1000), 8000 dwellings will be drawn from the Tax registry, i.e., 200 per neighbourhood (reserve samples will be drawn). There will be no problem of statistical power to assess short-term effects, given the much smaller sample size of previous studies. Regarding effects on two-year health changes, a baseline sample size of 1000 participants will allow us to detect differences in the change in, e.g., systolic blood pressure between baseline and follow-up of slightly less than 1 mmHg between the two contrasted exposure groups. Differences in outdoor residential exposure between these groups is expected to be of more than 30 $\mu g/m^3$ for NO_2 and of more than 25 dB(A) in day-evening-night equivalent sound level. Given the contrasted exposure groups, the reliable health variables (averaging measures over 8 days), and the two-year follow-up (to allow differential changes to occur), the sample size will allow us to detect the expected effects.

Over the 8 days, participants will alternate between a "cardiovascular health" configuration (days 1, 3, 5, and 7) and a "respiratory health" configuration of sensors (days 2, 4, 6, and 8). In both cases, participants will carry a GPS receiver (BT-Q1000XT), an accelerometer (wGT3X+), and an air pollution monitor. On "cardiovascular health" days, they will additionally carry a noise sensor; they will undergo ambulatory blood pressure monitoring for 24 hours (measurement every 20 / 45 minutes during the day / night) using the TensioMed Arteriograph 24 (that assesses central blood pressure, aortic pulse wave velocity, and the augmentation index); they will measure their blood pressure at rest in the morning and evening on days 3, 5, and 7 (self-measurement protocol of the European Society of Hypertension[35] using the Withings blood pressure monitor that permits the real-time transmission of data through the Samsung Galaxy S4 smartphone provided for the study); their heart rate will be measured continuously on days 3, 5, and 7 using the Zephyr BioPatch worn below the pectoral muscle (heart rate variability parameters related to the time and frequency domains will be determined); and they will be surveyed on their noise annoyance with the smartphone (as triggered by the detection of a high noise level). In the "respiratory health" configuration, they will instead have a second air pollution monitor; they will wear the impedance pneumography (IP) recorder[36] that assesses lung function by monitoring breathing during normal daily life and derives indicators reflecting the degree of airway obstruction[18]; they will perform a spirometry test in the morning and evening (using SmartSpiro, which will measure the peak expiratory flow, the forced expiratory volume in one second, the forced vital capacity, etc., and will send the data to the server through the smartphone); and they will be surveyed on their respiratory symptoms by receiving an alert three times per day on the smartphone provided for the study (asthma attack, loose or hacking cough, shortness of breath, wheezing, phlegm, runny nose, and stuffed nose). Participants will receive a gift card of 30 € and a strong support during the follow-up. Our experience in pilot studies (in which participants receiving no gift card wore five sensors) suggests that we will be able to recruit participants. Over 8 days, participants will provide 12000 respiratory questionnaires, 8000 measures of spirometry, 4000 days of follow-up of tidal breathing, 3000 days of follow-up of heart rate, 49500 measures of ambulatory blood pressure, and 8000 measures of resting blood pressure.

Using the most advanced survey strategies in Transport sciences (further developed for the project[32,37]), the GPS data will be analysed with algorithms integrated to the TripBuilder application. These algorithms identify activity places and trips (and their unimodal components), and automatically impute information on trips based on the GPS, survey, and geographic data. Presenting the GPS tracks on an electronic map, this application will allow us to survey participants on their activities and transport modes in each trip and to edit the GPS tracks. The final output over 8 days comprises the cleaned GPS tracks; the location of and the arrival / departure time to / from each activity place; and the location and time of each point of change of mode.

Participants will perform the very same data collection after two years. They will be recruited at baseline only if they intend to participate in the second wave. They will also receive a gift card for the second wave.

III.B – Air pollution and noise exposure

Personal exposure: The metrologists of AIRPARIF (Ile-de-France Air quality monitoring network) will evaluate the following air pollution monitors: Aethalometer AE51 (black carbon), Sidepak AM510 and CairSol ($PM_{2.5}$), and Aeroqual S300 (NO_2). In any case, we will rely on the Aethalometer AE51 (successfully used in few studies[27,28]) in addition to one other air pollutant monitor that the tests will identify. We will estimate the inhaled dose of pollutants by multiplying the inhaled volume of air for each minute of the follow-up [estimated as a function of the one-minute (i) energy expenditure from accelerometry or (ii) respiratory rate from the BioPatch] by the corresponding exposure concentrations.[38] On the "cardiovascular health" days, the Svantek SV 102+ dosimeter fixed at the belt, with a microphone at the collar, will be used for a personal monitoring of noise. Impulsive noise (sound pressure peaks) will be assessed. Frequency spectrum analysis will identify the octave bands that contain the majority of the sound power, allowing us to assess the effects of noise frequency components and noise containing discrete frequencies or marked tones. We will rely on the Orelia ACE-plugin software for the automatic recognition of specific patterns of noise (road, aircraft, or railway traffic; industries; social interactions, music).

Estimation from exposure maps: We will also approximate the exposures with hourly model-based maps of air pollutants from AIRPARIF ($PM_{2.5}$, black carbon, NO_2, and O_3) and noise maps from Bruitparif, both (i) at the residence as commonly done and (ii) along the corrected GPS tracks over 8 days.

We will consider exposure windows of different time sizes[11,13,19] and apply different lags between the end of the exposure window and the health measure. To assess transport-related exposures, we will aggregate the exposure data only for the time slots related to trips within these exposure windows.

Estimation of longer-term exposures: During the mobility survey, participants will be asked for each place visited their frequency of visit to that place over the previous year. For each data collection wave, we will approximate exposure levels over one year by reweighting the average exposure at each activity place and during the trip(s) to that place according to the corresponding frequencies reported over the previous year. This one-year exposure will be calculated by reweighting the exposures measured with the personal sensors, but also from the exposures estimated by combining the GPS tracks with annual exposure maps.

III.C – Data analysis

We will compare the exposure to air pollutants and noise in the different transport modes, both at the trip level and at the trip stage level. We will determine the percentage of exposure that is attributable to transport.

The regression analyses of short-term effects of exposures on health will incorporate a random effect at the individual level (repeated measure framework) and a temporal autocorrelation structure,[39] and will take spatial autocorrelation into account.[40] We will specify random slopes to allow the exposure–health relationships to vary between individuals, to determine whether an observed effect is only documented in few susceptible individuals or among most of the participants.[14] Multi-exposure models will be estimated.

We will take into account – for adjustment or as modifiers: demographic, socioeconomic, and health characteristics; health behaviour; contextual characteristics at the different activity places; meteorological factors; incidence of influenza-like illness[12]; pollen and mould in the air; and hour, day, and season. Quadratic / cubic terms, piecewise regression analyses,[11] or smoothing terms will be used to take humidity or temperature into account and to model nonlinear associations between air pollutants or noise and health.[14] Interactions between the effects of air pollutants and noise will be tested for the cardiovascular outcomes.[33] We will use a Random forest algorithm[34] (a learning approach that constructs decision trees in bootstrap samples) to rank the different versions of the exposure variables according to their predictive contribution.

A two-stage model will be used to analyse longer-term effects of air pollution or noise exposures on changes in respiratory and cardiovascular outcomes. Stage 1 will model the short-term effect of the exposure on the repeated outcome measure. The second stage of the model will estimate the effect of longer-term exposures on the change between waves 1 and 2 in the predicted level of the outcome (predicted from stage 1 for an average level of the short-term exposure). The two stages of the model will be estimated jointly with a Markov chain Monte Carlo approach. A second-stage model will also be estimated to assess the effect of longer-term exposures on a change in the susceptibility to short-term exposures between the two waves.

Beyond average associations, we will investigate the heterogeneity in the estimated health effects of air pollution and noise according: to individual characteristics (interactions); to the geographic location (random effect approach); to the exposure level (interactions); and to the level of the outcome (quantile regression). We will calculate total and direct effects to determine the percentage of socioeconomic differences in respiratory / cardiovascular health that would be eliminated by fixing the exposure at an acceptable level.[41]

Finally, simulations will be performed to test scenarios of pseudo-interventions changing the transport behaviour of individuals and / or the level of environmental exposure during trips. We will test the impact of these probabilistic changes in specific trips on the average individual exposure over 8 days, on the distribution of exposure across individuals, and on the resulting health effects. We will also examine whether each scenario of transport behaviour change and / or of environmental change increases or decreases socioeconomic disparities in exposure and health. The method to perform flexible simulations of scenarios will be packaged in a tool for decision-makers, and will be released as a deliverable of the project.

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