Milestone M11 (M2.7)
Best practice document for roadmap upscaling

RI-URBANS
Research Infrastructures Services Reinforcing Air Quality Monitoring Capacities in European Urban & Industrial AreaS (GA n. 101036245)

By

ISGlobal
Barcelona
Institute for
Global Health

28/10/2024

RI-URBANS (www.RIURBANS.eu) is supported by the European Commission under the Horizon 2020 – Research and Innovation Framework Programme, H2020-GD-2020, Grant Agreement number: 101036245

Milestone M11 (M2.7): Best practice document for roadmap upscaling

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Work package (WP)	WP2 / Health effect assessment of PM, PM components, nanoparticles, and their source contributions
Milestone	M11 (M2.7)
Lead beneficiary	ISGlobal
Means of verification	Document available
Estimated delivery deadline	M37 (31/10/2024)
Actual delivery deadline	28/10/2024
Version	Final
Reviewed by	WP2 Leaders and Project Coordinators
Accepted by	Project Coordination Team
Comments	This document is a product of WP2, which aims to provide stakeholders at municipal or regional level with tools and instructions on how to quantify the health impact of monitored air pollutants in their areas.

RI-URBANS (www.RIURBANS.eu) is supported by the European Commission under the Horizon 2020 – Research and Innovation Framework Programme, H2020-GD-2020, Grant Agreement number: 101036245

Table of Contents

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1. About this document

RI-URBAN's WP2 focuses on evaluating the use of measurements of new air quality (AQ) metrics, especially nanoparticles, for improved health impact assessment and epidemiological health studies.

This document aims to provide stakeholders at municipal or regional level with tools and instructions on how to quantify the health impact of monitored air pollutants in their areas.

This is a public document, available at the RI-URBANS website, https://riurbans.eu/work-package-2/#milestones-wp2, and distributed to all RI-URBANS partners for their use as well as submitted to the European Commission as an RI-URBANS Milestone M11 (M2.7).

2. Introduction

Air pollution is the leading environmental contributor to the global burden of disease and ranks among the top preventable causes of disease over time (Cohen et al., 2017). Evidence from epidemiology and toxicology indicates that short- and long-term exposure to particulate matter (PM) impacts negatively on human health (WHO, 2013), with 237,000 premature deaths (in 2021) in Europe and 4.2 million worldwide (in 2019) attributed to exposure to outdoor air pollution (EEA, 2023; WHO, 2024).

Regionals and local authorities have a crucial role in protecting and promoting the health of residents and visitors. Local governments in areas with air quality monitoring stations or where long-term measurements of air pollution have been conducted can take advantage of existing statistical tools from epidemiology to evaluate the impact of air pollutants in their region (i.e. using time series analyses, as explained below) and to assess the benefits or costs associated with a specific policy (e.g. Health Impact Assessments, also detailed in this document). All these tools can be utilised to design informed policies aimed at reducing air pollution levels.

3. Types of studies to link air pollution concentrations and health at a city/regional level

Different types of studies can be used to link short-term exposure to air pollution with health effects. Here, we will focus on two main types of studies that effectively use data from Air Quality Monitoring infrastructures in cities to draw conclusions on the health effects of different air pollutants, thus, they can be done at a low cost based on existing infrastructures, and the results of these studies can provide timely and useful information on the harmfulness of different air pollutants. The studies on short-term effects usually detect the effects of air pollution on the most vulnerable groups while studying the full population.

Both types of studies address the estimation of the short-term health effects of air pollution, i.e. those health effects that occur on the same day or a few days after an air pollution episode occurs. It is important to note that this methodology does not only estimate the effects of extreme episodes (i.e. days with very high levels of air pollution), but it also estimates effects of small changes in air pollution. These methods do not address, however, the estimation of effects of long-term exposure to air pollution, i.e. the effects of being chronically exposed (over years) to polluted air which are generally more important than the short-term effects (but these designs are more costly regarding the resources needed).

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Two main studies on short-term exposure effects will be described:

- **Time series studies (TSS)**. Such studies compare data from two time series: one of daily air pollution concentrations, and another of daily health indicators such as the daily number of deaths or the daily number of hospital admissions. If air pollution has an effect on mortality, one would expect to see a higher number of deaths on polluted days in comparison with clean days. Such studies are based on a single location, e.g. a city. TSS are used to investigate if an association exists and to quantify its magnitude. The data analysis requires complex methods that control for temporal and seasonal trends and time-varying potential confounders. In order to produce trustful estimates, TSS require a large number of cases, which can be achieved by conducting the study in large cities, by having long daily time series for several years, or by pooling data across cities.

- **Health impact assessment (HIA).** This technique uses existing knowledge on the relationship between air pollution and health to predict what is the expected effect in a target population, or to predict the health benefits in the target population under realistic assumptions (e.g. what would be the health benefits of reducing the levels of a certain air pollutant by 10%, or by not exceeding some recommended limits). Thus, HIA is not used to investigate if a relationship between pollution and health exists, but to predict the local health burden.

4. How to perform a time series analysis (TSS)

In order to perform an assessment of short-term effects of air pollution on mortality and hospital admissions, one should obtain data of the exposure (air pollutant) and health outcome (death counts, hospital admissions counts, visits to emergency room, or similar) at the same level of time-resolution, most commonly, daily average of air pollutant concentrations from an urban monitoring station and daily counts of deaths and hospital admissions. Detailed information on this task is available in Deliverable D9 (D2.1) 'Best practices for evaluation of nanoparticles and health for application in pilots' as well as in the ST14 'Evaluation of health effects of novel air quality parameters' of the RI-URBANS project. Other tutorials are also available elsewhere (Dominici and Peng, 2008; Tobias et al., 2024).

4.1 Required sample size

In order to generate robust and reliable results, this analysis should only be applied if there is a minimum sample size (in this case, it refers to the total number of deaths or hospital admissions) to ensure the detection of the small changes, usually increments in mortality and morbidity, attributed to the exposure to air pollutants.

In order to detect such small increases in mortality or hospital admissions, which are much smaller than the day-to-day variation in these variables, one needs big studies. Otherwise, studies do not have statistical power to detect such changes. Thus, one should not embark in conducting a time series study with small datasets, as they will likely not detect the associations, even if they really exist, and are also at higher risk of finding false positive associations. The statistical power of time series studies and the required sample sizes to conduct them, have been explored recently (Armstrong et al., 2020), indicating the total number of cases as the most important factor. They found that, in order to have 80% power to detect an increase of 1% in the health outcome (e.g. death or hospital admissions counts) associated to an increase of 1 usable standard deviation (this may be close to the 10 $\mu g/m^3$ increase often reported, e.g., in London, UK it was 8.5 $\mu g/m^3$), one would need around 100,000 deaths. For example, the city of Barcelona (Spain), with a population of around 1.5 million, has a daily average mortality count of around 50 deaths per day. These represent around 18,250 deaths per year. Thus, a time series study would require at least 5.5 years of data to have enough power. One can achieve the required number of deaths by studying large cities,

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by studying long time periods or by combining data from different cities. In order to detect an increase in the health outcome of around 2%, the required number of events goes down to around 25,000.

4.2 Health data collection

Estimates of the short-term associations between air pollution and health are usually based on studying the relationship between daily variations of air pollutant concentrations and daily variations of health outcomes such as number of mortality and/or morbidity cases (e.g.: hospital admissions or hospital visits by various causes). Common mortality and morbidity outcomes that are often associated with short-term air pollution changes are respiratory and cardiovascular diseases. Such studies are usually conducted at the city level.

Mortality causes and hospital admissions diagnosis are usually classified according to the International Classification of Diseases (ICD), developed by the World Health Organization (WHO) (https://icd.who.int/en). Daily mortality and hospitalisation data (visits, emergency admissions, etc.) often originate from official registries and hospital reports and may include information such as cause of death, age, sex and the patient´s place of residence. While this information can be used to evaluate the impacts of air pollution on sensitive groups of population, the presence of personal information in the data, may lead to data suppression or complications in the data release by health providers. For this reason, it is recommended to request the aggregated health outcomes by age, sex or cause of death/admission. In general, the aggregated hospitalisation data may be more difficult to obtain than the mortality data.

The most recommended sources for health data are national statistics offices and national/regional health agencies as these are official sources. Data from statistics offices and health agencies are often released with a lag time of months or years after collection. If recent mortality data is needed, burial services may provide a faster alternative source for mortality data, although may lack cause of death, sex or age information.

An important issue commonly found in health time series is data suppression. Some health data providers may suppress small numbers of cases of a certain outcome to minimise the risk of patient identification, that is, privacy protection. Decreasing the number of personal details requested (e.g., requesting two large age groups instead of four smaller ones) or increasing the geographic coverage are examples of ways to avoid health data suppression. Although these could result in decreased level of analytical details. Alternatively, techniques like multiple imputation and models for left-censored data may provide a solution to analyse suppressed data, as long as the percentage of data suppression is kept to a minimum.

It is good practice to keep a catalogue of each health data set including details of the health data request and data use limitations. An example of such a catalogue is provided in Deliverable D9 (D2.1).

When collecting health data for epidemiological analysis, one should be aware of issues that may compromise health data quality. Some of them are:

- *Errors in diagnosis* due to changes in ICD-code classifications: Diagnosis record errors may arise from the transition among ICD code revisions.
- *Outdated information* in the health care system: patients may be either wrongly included or excluded in the researched area due to outdated information in the health care system, e.g., outdated place of residence.
- *Misdiagnosis*: Misdiagnosis of the cause of death/hospitalisation will result in inaccurate cause-specific daily counts (Baker and Nieuwenhuijsen, 2008).
- *Multiple hospital admissions with the same diagnosis in a short time interval* (e.g., days or weeks). Patients may return to the emergency room a few days or weeks after the first incident. While this emergency

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admission will be recorded twice by the hospital, the second hospitalisation may be caused by the same diagnosis as the first, and could be seen as a continuation of the same event. One may avoid this "double counting" by excluding repeated hospitalizations with the same diagnosis within for instance one month apart from each other. This is only feasible when data on individuals can be accessed.

- *Misinterpretation of the data request*: To avoid misunderstandings, one should create a clear health data request, making sure to state any patient inclusion/exclusion rules adopted by the study.

For more detailed information on health data collection please refer to Deliverable D9 (D2.1).

Finally, please remember that collecting health data may be time consuming and expensive, therefore it is important to allocate enough time and financial resources for health data collection during the study design phase.

4.3. Air quality variables and complementary data

Time series analysis to associate short-term air pollutant variations with health outcomes is often based on daily air pollution measurements in order to match the resolution of the health data, which is often recorded as daily counts. Although most time series are based on daily data, other resolutions like hourly (Vivanco-Hidalgo et al., 2018) or yearly (Andersen et al., 2022) are also found in the literature.

In terms of exposure, regulated air pollutants such as particulate matter with a diameter <= 2.5 ($PM_{2.5}$) µm or <= 10 µm (PM_{10}), NO_2, SO_2 and O_3 are commonly used as exposure variables in epidemiological time series studies. However, in recent years, an increasing number of studies have focused on novel unregulated exposure metrics including particle number (a proxy for ultrafine particles), black carbon and lung deposition surface area, due to the potential threat these metrics pose to public health.

Air quality measurements should preferably be based on one or more urban background stations known to represent the outdoor air of the geographical area under evaluation and should follow standardised measurement protocols whenever possible. If more than one urban background station is used, one should calculate the average concentration across stations. Alternatively, air quality data may be obtained from official air quality databases with well documented Quality Assurance protocols.

In general, the air quality data should have the highest quality, avoiding large gaps of missing data. One way to deal with missing data in epidemiology is using interpolation techniques.

Statistical models used for epidemiological time series studies should be adjusted to account for potential confounding variables and consequently reduce uncertainties from the modelled results. The model may be adjusted for measured and unmeasured variables like long-term trends and seasonality, temperature and relative humidity, bank holidays, days of the week, influenza season and the effects of co-pollutants of low to moderate correlation. A short description of how these variables affect the the air pollution-health associations is provided below:

- ***Long-term time trends and seasonality***: researchers often adjust models with flexible functions of time (e.g. splines), to control for seasonal and long-term trends. These trends can act as noise to the air pollution-health associations. The inclusion of splines of time in the model is a way to control for unobserved confounders that vary slowly over time and is an essential step in the analysis in order to obtain unbiased results.

- ***Weather variables***: temperature and relative humidity are known confounders for air pollution-health associations, and therefore must be accounted for in epidemiological models. Temperature affects health outcomes in a non-linear manner, for instance increasing mortality during cold days in the winter and very

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warm days during summers (Gasparrini et al., 2015), and often temperature covaries with time. Meteorological data is often readily available from meteorological or air quality monitoring networks.

- ***Bank holidays and day of the week***: holidays influence air pollutant concentrations as people travel outside the city boundaries, decreasing vehicular emissions inside the city. Similarly, health outcomes may also show a weekdays/weekend dependence (e.g., (Bates et al., 1990; Bell and Redelmeier, 2001)), which may be caused by lower pollution levels in the city, or other weekend/holiday related factors like decreased number of health care workers resulting in increased mortality (Bell and Redelmeier, 2001; Huang et al., 2019; Jahromi et al., 2019).
- ***Influenza***: Influenza and respiratory infections are associated with mortality and explain a significant part of the mortality peak in winter months (Peng et al. 2006). These influenza peaks may coincide with peaks of air pollution. Therefore, one needs to control for that in the analysis, either by using hospital records or by calculating a proxy based on peaks of respiratory disease admissions/mortality.
- ***Other air pollutants***: other air pollutants may bias the time series analysis results as they often impact health, come from common sources and are affected by the same factors (e.g., weather), which increase correlation. Disentangling the health effects of different pollutants is a great challenge, and therefore must be taken into account in time series epidemiological models.

5. How to perform a health impact assessment (HIA)

Health impact assessment is a tool that can be used to predict the potential health benefits and health impacts from a policy, program, activity or situation in a given population. In the case of short-term effects of air pollution, it could be used to assess, for example, how many premature deaths could be prevented if air pollution levels in a city did not exceed the limits recommended by WHO (or any other limit) any day of the year. Note that this technique can be used to illustrate the effects of air pollution in an area even when one does not have access to the time series of health data (e.g. the daily mortality series), or when the time series is too short to draw valid conclusions. This can be done provided that there is good evidence in the literature of the health effects of the particular pollutant for which one wants to do the study. In particular, one needs an estimation of the relative risk of the pollutant, ideally coming from a meta-analysis of many studies, so that the relative risk is estimated with good precision and can be trusted. For example, the recent WHO systematic reviews (Chen and Hoek, 2020; Huangfu and Atkinson, 2020; Lee et al., 2020; Orellano et al., 2021, 2020; Zheng et al., 2021) provided the best available exposure–response functions (ERF) for health impact assessment of the effects of PM, O_3, NO_2 and SO_2 (WHO, Regional Office for Europe, 2013). They provided ERF estimates for both short-term and long-term exposure associations with health. In most HIAs, long-term exposure dominates the HIA outcome.

5.1 Required data

For the case of short-term associations, the health impact assessment calculates the number of cases (e.g. mortality or hospital admission cases) attributable to air pollution in the baseline scenario, and compares it to the attributable number of cases in a counterfactual scenario. The data needed to conduct the health impact assessment is the following:

- **Baseline exposure**. This is usually the present or past exposure, and one can use a daily time series of the specific pollutant under investigation to represent current exposure.
- **Air pollution levels in the counterfactual scenario**. The available time series can be modified to obtain that. For example, if the counterfactual scenario is one in which a certain threshold is never exceeded, all days

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that exceed the threshold in the real series are replaced by the threshold. This way, the threshold is never exceeded in the modified series. Other types of scenarios could be envisioned, e.g. one in which the concentration of all days is reduced by 10%.

- **Size and profile demographics of the population exposed**. This may just be the population (total number) living in the particular area under study. In some cases, the population by sex and age ranges can also be used. The population can be considered to be the same in the current and counterfactual scenario, or it can be assumed to change.
- **Incidence rate of the health effect being studied**. For example, the underlying mortality rate in the population, in deaths per thousand people, or the hospital admissions from cardiovascular or respiratory diseases.
- **The risk estimate from exposure-response functions relating air pollution to the health effect** (e.g. mortality). This estimate comes from the epidemiological literature and ideally it should be an estimate based on the meta-analysis of several studies that appropriately summarises the best available evidence for the association. There exist very good estimates of exposure-response functions for PM, NO_2 or O_3. For the case of nanoparticles or PM constituents, there is less evidence and the estimates available will be considered of less quality. In 2014, a WHO expert meeting concluded that it was premature to derive specific exposure-response functions for any PM component (World Health Organization, Regional Office for Europe, 2014). However, estimates are available, and HIA exercises could be done as long as the limitations of the data are acknowledged.

5.2 Calculation of attributable cases

The predicted number of attributable cases (attributable number, AN) for a certain air pollutant (Poll), assuming the association is linear, can be calculated as $AN(Poll) = P*B*(1-1/RR(Poll))$, where P is the exposed population (number of subject), B is the baseline population incidence of the given health effect, RR(Poll) = exp(β*Poll), Poll are the levels of the pollutant and β is obtained from the exposure response functions. Then, one can do the calculations for the baseline and counterfactual scenario to obtain the difference in the number of cases. In the context of a time series study, one can do the calculations for every day in the series and sum the number of cases throughout the study period. The following references provide examples of such HIA calculations (Holland et al., 2005; Izquierdo et al., 2020) .

Uncertainty analysis is a key part of health impact assessment. One can use different estimates of the exposure response functions, and use the confidence intervals of the exposure-response function estimates in simulation procedures to incorporate the uncertainty in the final estimates. Uncertainties in the disease burden, the pollution exposure level, response to the pollution and the counterfactual level of air pollution should also be incorporated. More details on the implementation of HIA studies can be found in the following reference (Holland et al., 2005).

6. Recommendations

In terms of methodology for assessing the short-term health effects of air quality parameters, including novel metrics, we recommend:

- Use daily data and long time series to evaluate the health effects of air pollution, as the size of the effect is small and large sample sizes are needed to capture them with precision. Combining results from multiple cities is also a good strategy, especially if small cities are involved, although one then may need to consider differences between cities, e.g. in terms of pollutant mixtures.

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- Models should control for seasonality to avoid biases, and different lags should be explored to detect delayed effects.
- When examining novel metrics, fitting two-pollutant models that include a more established health-damaging pollutant (e.g. $PM_{2.5}$) is recommended, to identify if the novel metric captures an independent effect.
- When studying nanoparticles in multi-city studies, the size range should be restricted so that all cities include the same range, particularly for the lower size limit.
- HIA recommendations: include ERF from an authoritative body such as WHO
- Include equity in the analysis

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