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Health impact pathways related to air quality changes: testing two health risk methodologies over a local traffic case study

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Abstract

Air pollution causes damage and imposes risks on human health, especially in cities, where the pollutant load is a major concern, although the extent of these effects is still largely unknown. Thus, taking the busiest road traffic area in Portugal as a local case study (600 m × 600 m domain, 4 m^2 spatial resolution), the objective of this work was to investigate two health risk methodologies (linear and nonlinear), which were applied for estimating short-term health impacts related to daily variations of high-resolution ambient nitrogen dioxide (NO_2) concentrations modelled for winter and summer periods. Both approaches are based on the same general equation and health input metrics, differing only in the relative risk calculation. Health outcomes, translated into the total number of cases and subsequent damage costs, were compared, and their associated uncertainties and challenges for health impact modelling were addressed. Overall, for the winter and summer periods, health outcomes considering the whole simulation domain were lower using the nonlinear methodology (less 27% and 28%, respectively). Spatially, these differences are more noticeable in locations with higher NO_2 and population values, where the highest health estimates were obtained. When the daily NO_2 exposure was less than 6 $\mu g.m^{-3}$, a fact that occurred in 95% of the domain cells and in both periods, relatively small differences between approaches were found. Analysing the seasonality effect, total health impacts derived from the linear and nonlinear applications were greater in summer (around 18% in both approaches). This happens due to the magnitude and spatial variability of NO_2, as the other health input metrics remained constant. This exploratory research in local scale health impact assessment (HIA) demonstrated that the use of refined input data could contribute to more accurate health estimates and that the nonlinear approach is probably the most suitable for characterising air pollution episodes, thus providing important support in HIA.

Keywords Road traffic · Urban air pollution · Nitrogen dioxide · Linear and nonlinear methodologies · Health impacts · Uncertainties

Introduction

To date, air pollution is a global threat and the biggest environmental risk factor to human health. According to the World Health Organization (WHO), 7 million deaths worldwide every year, mainly from noncommunicable diseases, are attributable to the joint effects of ambient and household air pollution. Regarding the outdoor air pollution problems, responsible for 4.2 million premature deaths, these are more visible in urban areas, where the majority of the population lives and/or works and the main anthropogenic air pollution sources are located (Miranda et al. 2015; WHO 2021a).

These alarming numbers are the result of health impact assessments (HIA) conducted from multiple scales, which report health concerns associated with air pollution. Nevertheless, such HIA are mostly implemented from the country

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to the city level for a broad time horizon and are reasonably systematised. Considering the WHO air quality guidelines, Khomenko et al. (2021) did a quantitative HIA for the year 2015 to estimate the proportion of annual avoidable mortality in adult residents (aged ≥ 20 years) due to fine particulate matter (PM2.5) and nitrogen dioxide (NO_2) pollutant exposure in 969 European cities. In the case of NO_2, a time-series study in 272 major Chinese cities (2013–2015) was carried out to evaluate associations between daily NO_2 and natural-cause mortality and main cardiorespiratory diseases (Chen et al. 2018). Epidemiological evidence revealed almost linear and positive exposure–response curves with no discernible thresholds. A similar conclusion is shared by Meng et al. (2021) and Orellano et al. (2020) when analysing the effects of short-term exposure to NO_2 concentrations. In practice, many key health inputs in large-scale assessments are considered spatially uniform or vary only at a coarse geographic resolution. This assumption could contribute to a low bias, but when moving to a local/urban scale, the bias will likely be more significant given the high levels and variability of both air pollution and population density; hence, spatially refined input data are required (Hubbell et al. 2009; Vlachokostas et al. 2012). However, comprehensive local data may be unavailable or incomplete, requiring a lot of time and resources to obtain and validate them. For these reasons and because the current regulatory and public health framework is based on country-to-city scale human exposure, the design of local-level HIA studies is still limited (Shandas et al. 2016).

Human exposure may result in a variety of physical health impacts, depending on the type of air pollutants, atmospheric concentration levels, duration and frequency of exposure, and stratification of the exposed population (e.g., age, current health status) (Baklanov et al. 2007; WHO 2016a; Burnett et al. 2018). These physical impacts can occur in a short time period after exposure (short-term exposure) and result in acute effects or are a consequence of the cumulative exposure over time (long-term exposure) resulting in chronic effects. They are often expressed through morbidity and mortality indicators derived from epidemiological studies, being mostly related to respiratory and cardiovascular diseases (Seethaler et al. 2003; Rückerl et al. 2011; WHO 2013a; Costa et al. 2014; Héroux et al. 2015). Epidemiological studies combine meta-analyses recorded during air pollution episodes to provide statistical associations by relating ambient concentration changes and different types of health outcomes (WHO 2013b; Costa et al. 2014). The resulting concentration–response functions (CRF) could then be included in linear or nonlinear relative risk (RR) models, which may or may not contain threshold exposure values, and are used to translate unit concentration changes in health impacts. Normally, greater health risks related to ambient air pollution are attributed to linear RR models and certain vulnerable age groups, such as elderly people or children (Pervin et al. 2008; WHO 2013c; Silveira et al. 2016).

In order to quantify the magnitude of these effects, many tools and methodologies have been developed and applied to different spatiotemporal scales. Among them, AirQ+ is a valid and reliable software that was designed by the WHO Regional Office for Europe (WHO), and has been extensively used to estimate health impacts from air pollutants in a wide range of population densities and time periods (Hopke et al. 2018; Rovira et al. 2020; Asgari et al. 2021; Brito et al. 2022; De Marco et al. 2022; Jariwala and Kapadia 2022; Zhu et al. 2022; Kliengchuay et al. 2022; Egerstrom et al. 2023; Arregocés et al. 2023). All AirQ + calculations are based on methodologies and CRF from systematic reviews and well-established meta-analyses of epidemiological studies (Oliveri Conti et al. 2017; Ansari and Ehrampoush 2019; Zhu et al. 2022; Arregocés et al. 2023). Another tool commonly used to calculate health impacts from air pollution is the Environmental Benefits Mapping and Analysis Program – Community Edition (BenMAP-CE) (Bayat et al. 2019; Parvez and Wagstrom 2020). In general, these health risk modelling approaches have been mainly employed considering linear RR models for regulatory and decision-making purposes, as well as for testing air quality improvement scenarios up to the city scale, thus highlighting the potential health and economic benefits.

In view of current scientific developments in HIA arising from air pollution, exploratory research oriented towards the local scale and comparison of linear and nonlinear health methodologies was designed over a busy road traffic area. Thus, the main objective of this work was to investigate the two health risk methodologies and data analytics when estimating short-term health impacts related to daily air quality changes, focusing on a local traffic case study and ambient NO_2 concentrations modelled for winter and summer periods, including an analysis of the underlying uncertainties and limitations. The paper is organized as follows: The "health risk methodologies" section explains the adopted methods for estimating health impacts, i.e., the linear and nonlinear methodologies, whereas the "Application to a local case study" section is devoted to the case study application, where the research design and the health outcomes are presented and discussed. Uncertainties and limitations associated with HIA and emerging challenges are addressed in the "Uncertainties, limitations, and challenges" section. Finally, the main conclusions are drawn in the "Conclusions" section.

Health risk methodologies

The health impacts of air pollution have been estimated using information from epidemiological studies and methods that describe how health can be integrated into air quality assessments. In the present research, two health risk methodologies recommended by WHO, which depict linear and nonlinear RR, were adopted. Figure 1 shows the methodological scheme followed and the input dataset required for the different steps involving HIA from air quality changes.

This HIA scheme is divided into three steps:

- Exposure assessment based on exposed population data and pollutant concentration levels;
- Quantification of physical impacts by applying the linear and nonlinear RR methodologies. These WHO methods can be applied to a wide range of environmental conditions and are seen as the most appropriate at the urban scale;
- Economic evaluation of health losses considering total costs for certain health indicators that are related to pollutant exposure.

A detailed explanation of each step is presented in the following sections.

Exposure assessment

In the first step, exposure assessment is described as a proxy of the estimated pollutant concentration and its spatiotemporal variability to which citizens are or may be exposed. For the area of interest, the population exposure is calculated through the product of the resulting concentrations and the number of residents per age group that could be affected. Pollutant concentrations are usually expressed as daily average or maxima values for designing short-term exposures, whereas annual average concentrations are used for long-term exposure modelling. The examined age groups are based on epidemiological evidence (i.e., CRF) relating to the pollutant, exposure time, and health indicators. This exposure modelling approach has been widely used to study large geographic regions (e.g., city scale) or densely populated areas (APPRAISAL 2013; Brenk 2018), where the elaboration of individual exposure monitoring programmes focused on time-activity patterns is unfeasible. Even if population samples are selected, this sampling might not be representative of the case study. For the same reasons, epidemiological models continue to use ambient concentrations rather than exposure measurements.

Quantifying physical health impacts

When moving from exposure assessment to the quantification of physical health impacts, linear and nonlinear risk methodologies are used to compute the number of unfavourable health cases. Both methodologies are based on the same general equation (Eq. 1), differing only in the RR calculation. Beyond the RR, other input parameters, namely population data and baseline incidence or prevalence rates for the analysed morbidity and mortality indicators, are required. Demographic data are provided from the country's population census, whereas baseline rates, associated with certain health indicators, are usually derived from national statistics or, if not available, using scientific references designed for regions with similar environmental conditions.

$$HI_{(p,i)} = (pop_{(p,i)} \times Inc_{(i)}) \times RR_{(p,i)} \tag{1}$$

Where,

$HI_{(p,i)}$ represents the number of unfavourable implications (cases of disease, deaths) associated with the health indicator *i*, which could be avoided or not due to pollutant p´s short and/or long-term exposure;

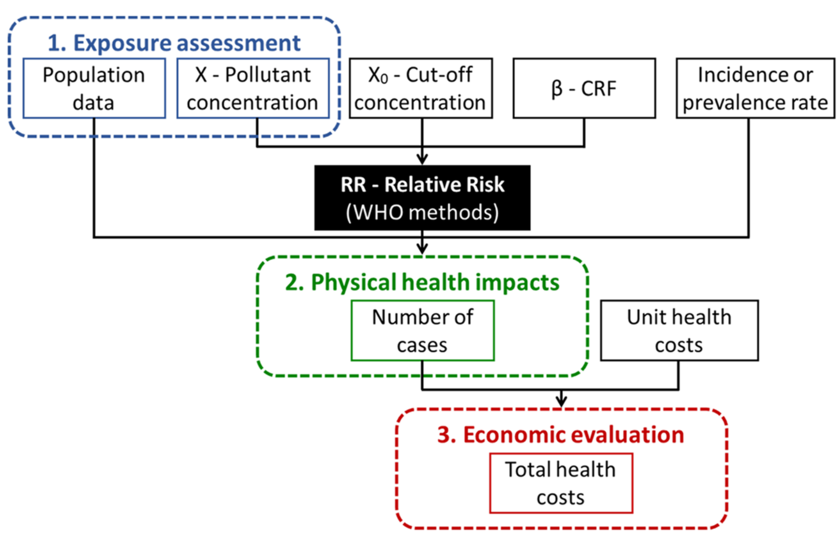


Fig. 1 General structure of the health impact assessment scheme

$pop_{(p,i)}$ is the population at risk (all ages or certain age groups) associated with the RR meta-analysis;

$Inc_{(i)}$ corresponds to the baseline incidence/prevalence rate of a specific health indicator *i* (expressed as the number of new cases per 100,000 individuals per year);

$RR_{(p,i)}$ correlates a pollutant p´s concentration variation with the probability of experiencing or avoiding a specific health indicator i.

To calculate the adjusted RR for a given health indicator, the linear function assumes a positive linearity between concentration and risk (Eq. 2, hereinafter referred to as linear RR). In contrast, the nonlinear method uses a logarithmic RR function in which health risks tend to increase slower with increasing concentrations (Eq. 3, hereinafter referred to as nonlinear RR) (Ostro 2004).

$$RR_{(p,i)} = exp\left[\beta_{(p,i)}\left(X - X_0\right)\right] \tag{2}$$

$$\begin{aligned} RR_{(p,i)} &= [(X+1)/(X_0+1)]^{\beta} \leftrightarrow \\ RR_{(p,i)} &= exp[\beta_{(p,i)}(ln(X+1) - ln(X_0+1))] \end{aligned} \tag{3}$$

Where,

β coefficient denotes the change in the RR for a unit change in concentration X (expressed as the natural logarithm of RR);

X is the pollutant p´s concentration ($\mu g.m^{-3}$). Daily values are used to calculate the short-term exposure risk; or annual averages if long-term RR is required;

X_0 indicates the pollutant p´s cut-off or counterfactual concentration value ($\mu g.m^{-3}$) above which health impacts are calculated.

Standard CRF values (i.e., β coefficients) are often presented with a 95% confidence interval (CI) and result from a systematic review based on published epidemiological studies and their meta-analyses; hence, they are highly recommended rather than single local studies (WHO 2013a, b). Regarding the cut-off concentration values, the WHO air quality guidelines are suggested, as these provide overall guidance on thresholds and limits for key air pollutants harmful to human health (WHO 2021a).

Economic evaluation of health impacts

Economic evaluation of the quantified physical health impacts, at least from the perspective of policymakers, is seen as one of the most important milestones of a comprehensive HIA, as it reflects the societal costs associated with these health damages. Such monetary valuation for the different health indicators, related to the most common air pollutants, is based on economic studies and results from the sum of direct, indirect, and intangible costs. Details about these cost components are described in Hammitt (2005), Pervin et al. (2008), and Silveira et al. (2016).

Thus, for each health indicator, after identifying the economic cost figures (per case, day, or years of life lost) to be considered and determining how to assess them in monetary terms, the overall health damage costs due to air pollutants' exposure, in a particular location, are estimated as follows (Eq. 4):

$$Costs_{(p,i)} = \sum_{i=1}^{n}\left(HI_{(p,i)} \times C_{health(i)}\right) \tag{4}$$

Where,

$Costs_{(p,i)}$ express the overall damage (€), occurred or avoided, on the health indicator *i* due to pollutant p´s short and/or long-term exposure in a specific location;

C_{health} is the monetary value (€) to repair a person´s initial health status or, at least, to remediate the damages of air pollution on the health indicator *i*.

Lastly, as a typical HIA is focused on human exposure to individual air pollutants, the total health costs of each pollutant ($Costs_{(p,i)}$) estimated for the analysed health indicators ($i = 1, \ldots, n$) should be summed up.

Application to a local case study

The linear and nonlinear health risk methodologies described in the previous section were applied to a local traffic case study for estimating health impacts associated with short-term human exposure to ambient NO_2 concentrations. Then, the resulting health estimates are compared and discussed, culminating with an analysis of the associated uncertainties and challenges in the HIA of air pollution.

Research design

This research is in line with the work developed by Silveira et al. (2023), where they present a multiscale air quality and health risk modelling system, referred to as modair4health, and apply it to the same local case study (Fig. 2) considering an input dataset and configurations recommended for testing traffic management strategies. This case study integrates a cascade of nested simulation domains in order to provide chemical boundary and background conditions for the inner ones. To that end, two coupled air quality models able to simulate atmospheric concentrations from regional and urban scales, using the Weather Research and Forecasting model with Chemistry (WRF-Chem), to the local scale, taking advantage of the high-resolution numerical prediction capabilities of the Computational Fluid Dynamics (CFD) model VADIS (pollutant DISpersion in the atmosphere under VAriable wind conditions), were applied. Concerning the health module, the two health risk methodologies tested here were integrated into the modair4health to estimate health impacts and costs due to short and/or long-term exposure to pollutant concentration levels.

In short, the selected case study is one of the busiest road traffic areas of the city of Coimbra in Portugal, and NO_2 was considered the target pollutant, given the largest contribution from road traffic to the current NO_2 levels in urban areas. In addition, it is integrated into a densely built-up and populated zone, where important municipal services are located and a strong commercial activity is known. In this context, frequent and high NO_2 pollution events and the consequent worsening of health conditions are expected. For these reasons, human health impacts resulting from short-term exposure to NO_2 were quantified considering two simulation periods for the year 2015: winter (26th January to 1st February) and summer (15th to 21st June). These periods were selected taking into account the seasonality and the highest NO_2 values measured at the air quality monitoring station (traffic influence)

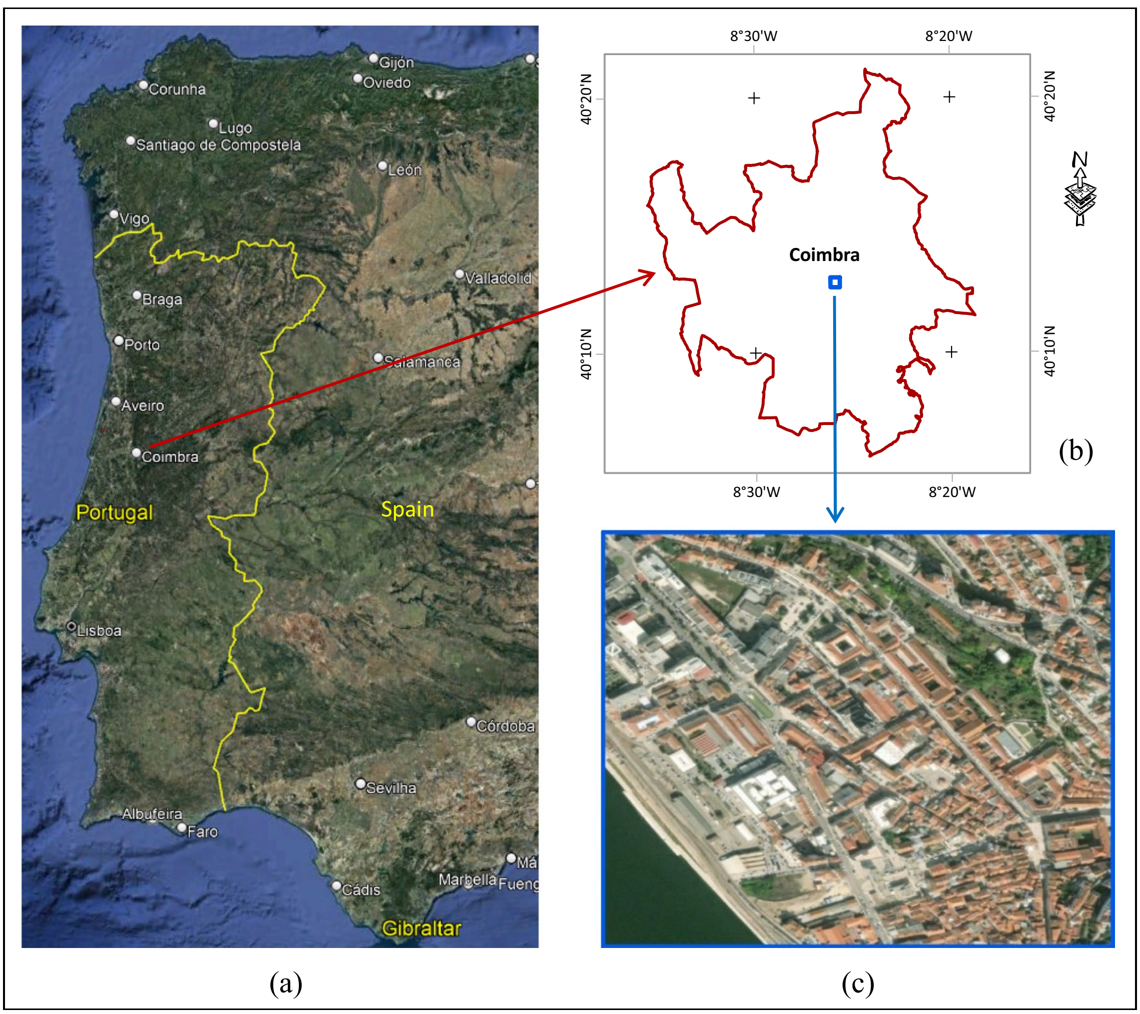


Fig. 2 Geographic location of the case study area: **a** framework, **b** Coimbra municipality, and **c** local case study

located within the case study. NO_2 estimates focused on the local case study (600 m × 600 m) were obtained with the VADIS dispersion model, defining a 3-D uniform grid with an inter-cell spacing of 4 m and hourly resolution, and validated based on the traffic station measurements.

As a last step, which represents the focus of this research, health outcomes, applying the nonlinear risk methodology adopted to evaluate the system operability (reference scenario in Silveira et al. 2023), were compared with health estimates using the linear RR approach. All the other baseline configurations were kept. Table 1 summarizes the health input metrics used for quantifying physical health impacts and underlying damage costs due to short-term NO_2 exposure.

Among these metrics, for each health indicator, the chosen RR function (i.e., CRF) determines that potentially affected age group and reference period for NO_2 concentrations should be analysed. With regard to the RR functions, due to the lack of epidemiological evidence over the targeted geographic region, those recommended by the WHO (central value) were used (WHO 2013b), whereas the baseline mortality and disease incidence rates were obtained from country statistics (WHO 2021b, c). In terms of affected age groups, total resident population data at the subsection (i.e., neighbourhood) level, extracted from the Portuguese National Statistics Institute database – Census 2021 results (INE), were used and disaggregated to the local case study´s grid horizontal resolution (4 m × 4 m) (Fig. 3). In total, 2005 residents were identified.

To estimate the short-term human exposure, daily maximum NO_2 concentrations for the simulation periods and an exposure threshold (i.e., counterfactual concentration value) of 10 $\mu g.m^{-3}$ were considered. The use of this threshold, above which physical health impacts are calculated, is suggested by the AirQ + software tool developers (WHO).

Finally, the overall health damage costs resulting from the estimated number of disease cases or premature deaths were quantified using cost figures (per case and YLL – Years of Life Lost) reported in specialized literature (Maibach et al. 2008; van Essen et al. 2011; Brandt et al. 2013) and updated for the reference year (2015).

Fig. 3 Spatial distribution of the total resident population per grid cell (4 m × 4 m horizontal resolution) for the local case study

Nevertheless, as short-term health impacts are calculated on a daily basis, these costs were converted to the same time scale.

Further information on the modair4health system regarding the adopted models and their connection, tested simulation domains, required input data, recommended configurations, and NO_2 estimates for the case study and selected periods is presented in Silveira et al. (2023).

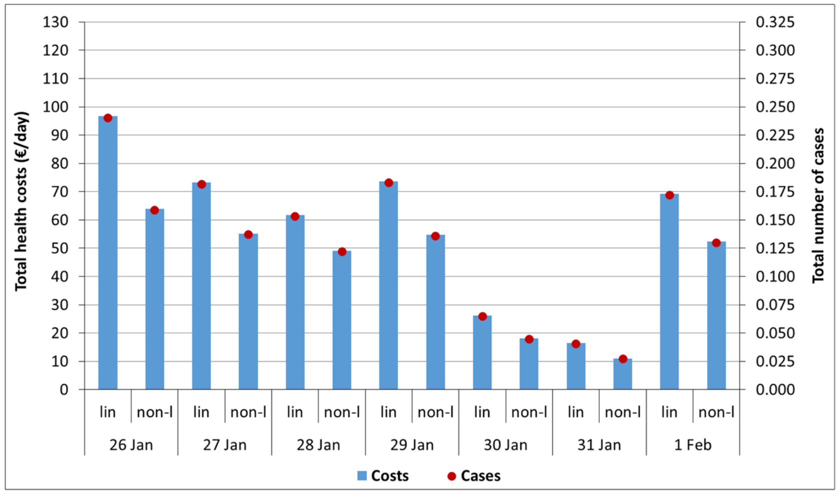
Comparative analysis of health outcomes

Given the inherent uncertainty and high variability embedded in HIA studies, results using different assumptions and methodologies need to be evaluated and communicated. Thus, based on the selected health input metrics, the linear and nonlinear health risk methodologies were applied to the local case study for the winter and summer periods, with the purpose of evaluating the number of unfavourable cases and health costs attributed to the short-term (daily) human exposure to ambient NO_2 concentrations. Figure 4 shows the daily total health impacts for the whole simulation domain, which includes the sum of the two analysed health indicators.

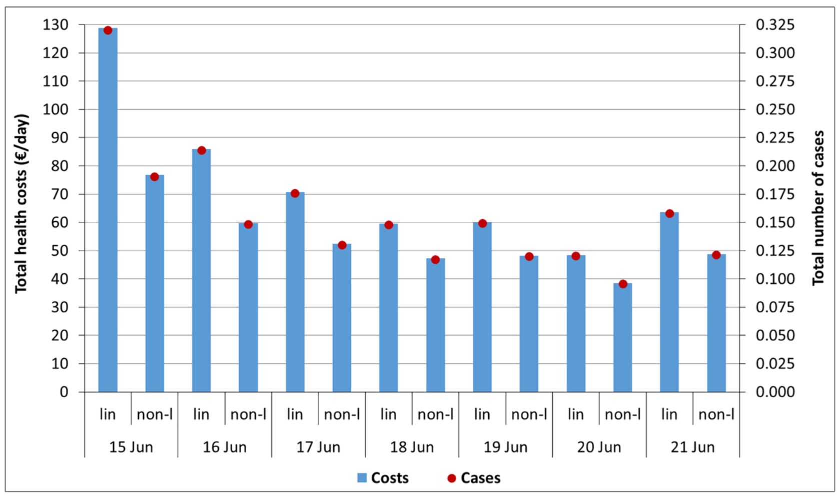
Table 1 Health input metrics used to estimate health impacts and costs from short-term exposure to ambient NO_2 concentrations

Health indicator	Age group	Reference period for NO_2	RR (95% CI per 1 ug.m^{-3})	Baseline rate (%)	Damage cost	
					Price (€)	Unit
Respiratory hospital admissions	All ages	Daily maximum	0.1002 (0.0999–0.1004)	0.05	8960	Case (8-day average duration)
Mortality (all natural causes)	All ages	Daily maximum	0.1003 (0.1002–0.1004)	0.977	1844	YLL

Fig. 4 Daily total health impacts, translated in the number of cases and damage costs due to short-term NO_2 exposure, for the winter (**a**) and summer (**b**) periods using the linear (lin) and nonlinear (non-l) health risk methodologies



(a)



(b)

In general, estimated health impacts are higher using the linear approach, and the daily variability is directly related to the magnitude and spatial distribution of the daily maximum NO_2 concentrations. Therefore, doing a day-to-day analysis, the highest total number of cases and associated costs resulted from the combination of higher values of gridded population data (Fig. 3) with daily maximum NO_2 concentrations. In contrast, the lowest values on 30 and 31 January 2015 occurred because a large part of the simulation domain presented daily maximum NO_2 levels below 10 μg.m^{-3} (i.e., exposure threshold), so no health impacts were calculated for these grid cells. Summing up the health impacts for each simulation period, in winter 415 € total health damage costs (1.04 cases) were estimated using the linear approach, whereas more moderate damages were obtained by applying the nonlinear method (305 € health costs and 0.76 cases). In the summer period, the total health results were slightly higher using the linear and nonlinear approaches: 515 € and 370 € health damages (1.28 and 0.92 cases), respectively. On average, each attributable case has a daily cost of 402 €.

As a support to the information provided in Figs. 4 and 5 gathers daily health outputs for the two simulation periods, with regard to the total number of estimated cases comparing the two health risk methodologies. The range of daily attributable cases varies between 0.03 using the nonlinear approach on 31 January and 0.32 applying the linear method on 15 June. Another aspect to note is the point where the line slope changes (0.16, 0.12), from which larger differences in number of cases tend to increase, leading to linear RR values often overestimated with increasing NO_2 concentrations.

Focusing on the health estimates for the days of each period with higher total differences comparing both approaches, 26 January and 15 June, there is a clear spatial relationship between the ambient NO_2 concentration and the health cost differences (linear – nonlinear) (Fig. 6). Thus, making this connection, the linear methodology presents larger health costs for grid cells with higher daily maximum

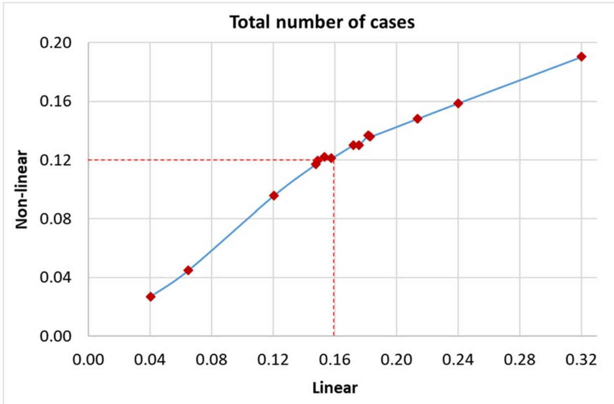


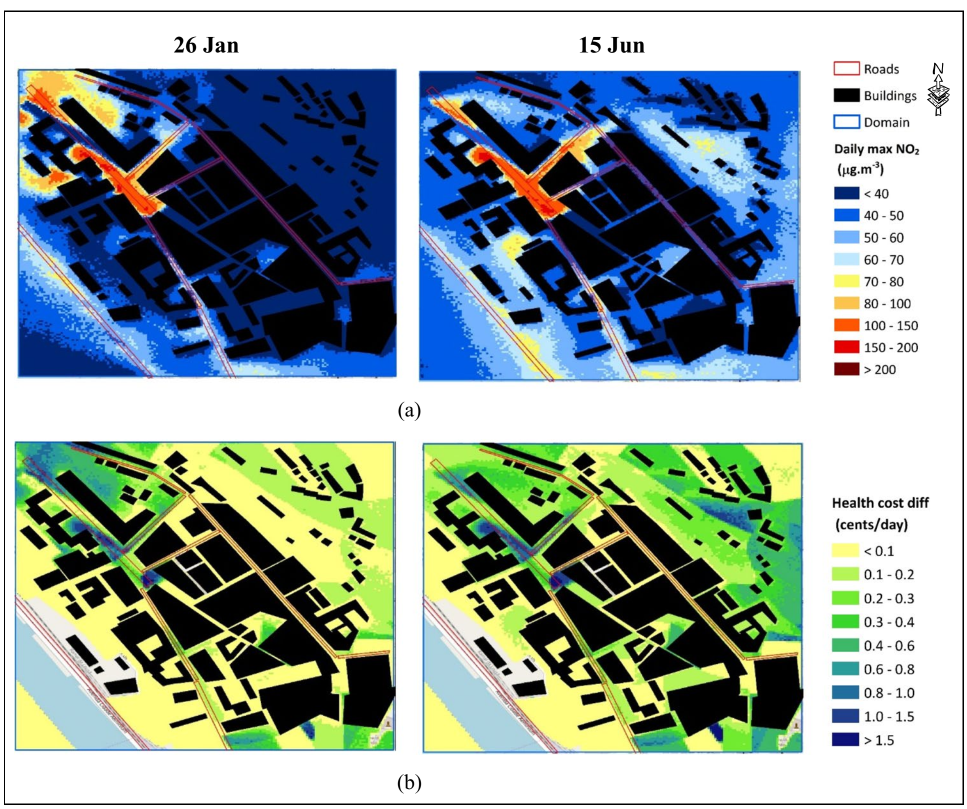
Fig. 5 Total number of cases estimated for the winter and summer periods comparing the linear and nonlinear health risk methodologies

NO_2 concentration values when combined with population data. In turn, the more spatially pronounced cost differences on 15 June reflect the highest total difference among health approaches that was estimated over the simulation domain (Fig. 4).

To complement this analysis, Fig. 7 exhibits the effect of daily NO_2 exposure on the health damage costs for the winter and summer periods and simulation grid cells applying the two tested health risk methodologies. However, it should be noted that 95% of the grid cells in both periods are below 6 μg.m^{-3} for daily NO_2 exposure; thus, relatively small differences are found when comparing the two approaches, although with a slight supremacy of the linear RR-based health outcomes. For higher exposure classes, these differences become more pronounced, and the spatial variability of health costs increases, particularly in winter. Such variability can be explained by the local weather conditions, which influenced the NO_2 estimates, but also due to the combination of these estimated concentrations with population data and the way these variables are included in the formulation of health impacts ("Health risk methodologies" section).

In summary, the lowest health outcomes using the nonlinear methodology (i.e., fewer cases and damage costs) seem to be better adjusted to the local reality, mainly for higher NO_2 concentrations, where the linear RR model is associated with large overestimates of health impacts. This conclusion is shared in epidemiological studies combining meta-analyses recorded during air pollution episodes and different types of health results (Costa et al. 2014; Nasari et al. 2016; Orellano et al. 2020); hence, the nonlinear health risk methodology is recommended, especially when high ambient concentrations of air pollutants are recorded. Otherwise, if the pollutant concentrations are low or if the health indicators are based on average concentration values, the choice between the tested health risk methodologies may be irrelevant to the final outcomes, as

Fig. 6 Spatial representation of the daily maximum NO_2 concentrations (μg.m.$^{-3}$) (**a**); and short-term health cost differences (cents/day) between the health risk methodologies (linear – nonlinear) for the local case study considering 26 January (on the left) and 15 June (on the right) (**b**)



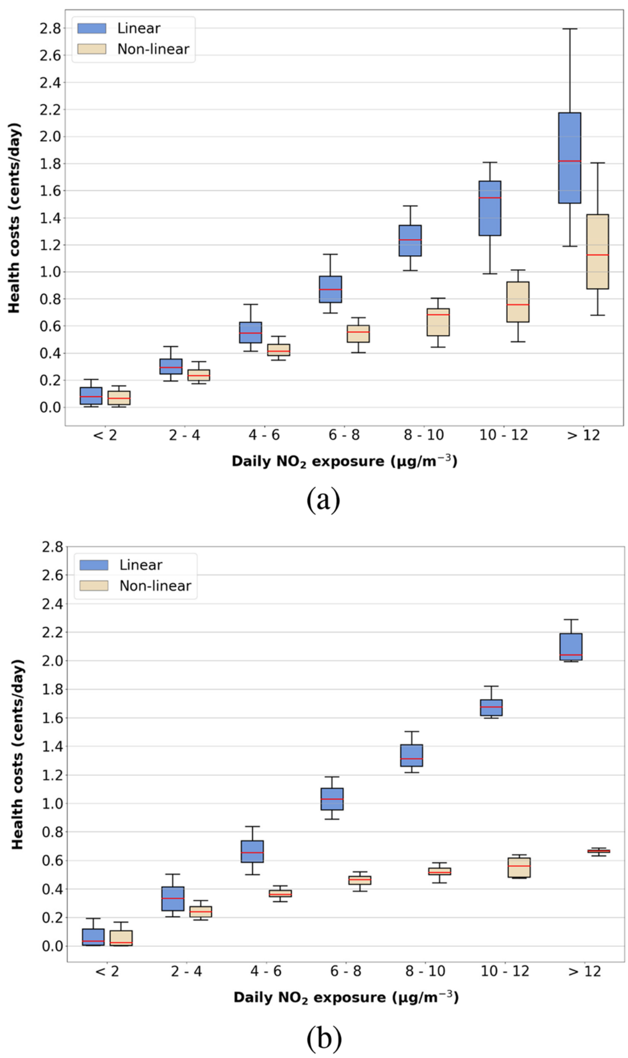


Fig. 7 Daily health costs per simulation grid cell (cents/day) due to the daily maximum NO_2 exposure (µg.m^{-3}) for the winter (**a**) and summer (**b**) periods using the linear and nonlinear health risk methodologies. For each column, the 5th, 25th, 50th, 75th and 95th percentiles are presented

demonstrated in this exploratory study. Nevertheless, if the research design is changed, namely the simulation domain and the health indicators and their CRF, or distinct formulations are applied, significant variations in the HIA could be experienced. These variations tend to be greater and most likely reflect the air pollution-related health status in comparison to the larger-scale HIA commonly carried out because the latter considers health input metrics spatially uniform or that vary only in coarse spatial resolution grid cells. For these reasons, it was not possible to make a direct comparison with the HIA state-of-the-art, but it is hoped that the fine-resolution integrated approach presented here can contribute to promoting the link between different spatial scales.

Methodological aspects related to HIA are analysed in detail in the following section.

Uncertainties, limitations, and challenges

In HIA, the uncertainty analysis should be performed in all stages, from the air pollution exposure assessment to the quantification of physical health impacts and corresponding external costs. Uncertainties result from a simplification or shortcomings of the methodologies used and assumptions for obtaining health input metrics. Their quantification is often based on 95% CI around the mean to provide an estimate of the precision of the HIA outcomes (Rovira et al. 2020; Khomenko et al. 2021).

Regarding the exposure assessment, the major uncertainty sources are related to the air pollutants considered, their measured and/or modelled concentrations over a given location, the estimated number of people exposed, and their current health status (Orru et al. 2009; Martenies et al. 2015; Parvez and Wagstrom 2020; Canha et al. 2021). Usually, only a few pollutants are considered in HIA, as in the case of NO_2, instead of the entire mixture of air pollutants, and it is very likely that this approach does not reflect the real exposure and subsequent health impacts, but it is currently the most acceptable, as the importance of any individual pollutant for the overall mixture is unclear (Ostro 2004; Hopke et al. 2018; DEFRA 2019; Arregocés et al. 2023). Furthermore, the extent of the effects of some pollutants or any combination of different pollutants on human health is not always known, mainly due to the lack of epidemiological evidence (i.e., CRF). Even when there is a reasonable association between a specific type of exposure and a health effect, some doubts about the causality and impact of time lags might still exist (WHO 2008; Rückerl et al. 2011). From the point of view of the concentration-exposure relationship, large uncertainties are associated with the modelling, representativeness of measurements, and assumptions to link them. Thus, when using air quality modelling results to derive exposure, it is not certain that the estimated exposure coincides with the observed ambient concentrations in a given location (WHO 2016a; DEFRA 2019; Canha et al. 2021). In terms of spatial representativeness, HIA assumes that either individual exposure measurements or population-weighted average exposure estimates are representative of the population exposed over a particular area. Even if the population exposure is well estimated, individual exposures can vary substantially as a result of spatial differences in air concentrations and due to the individuals' time-activity patterns (WHO 2016b). As a consequence, an alleged low correlation between personal exposure and ambient concentration contributes to weakening the power of epidemiological studies to detect effects.

Moving from exposure to the quantification of potential health impacts, uncertainties on the number of deaths or cases of disease may be found for a variety of reasons:

- The use of different methodologies to calculate the value of health impacts could result in very significant variations, even if the equations are based on the same input datasets;
- Possible double counting of health effects from several air pollutants, as one health outcome may be captured from different pollutants, or the same effect may be added from two health indicators (e.g., mortality due to a specific cause is a part of all-cause mortality) (Orru et al. 2009; Héroux et al. 2015; WHO 2016b);
- The choice of CRF derived from epidemiological studies inevitably introduces some uncertainty into the results, given the random effects and high variability in the CRF estimates. Moreover, epidemiological experiments on air pollution are often designed using an exposure threshold and are scarce or absent in many regions around the world, thus limiting their reliability and applicability to certain exposure ranges and countries where cohort studies were undertaken. It should be noted that most epidemiological studies have been conducted in developed countries, and the range of studied exposures does not necessarily represent what is observed worldwide (Ostro 2004; Héroux et al. 2015; Martenies et al. 2015; WHO 2016b);
- Baseline incidence and prevalence rates for health indicators of interest may also be highly uncertain with regard to the impact of ambient air pollution. These baseline rates are usually expressed as national average statistics, available for most countries through the following online platforms: Global Health Observatory data repository and European Health for All database (WHO 2021b, c). In the case of mortality rate, the number of premature deaths per a specific cause (e.g., ischaemic heart disease) is estimated from the joint effect of ambient and household air pollution. In addition, when calculating health impacts, this air pollution-related mortality rate should not be combined with CRF linking mortality to all natural causes unless other environmental risk factors (e.g., climate change, contaminated water, waste disposal) are added to the mortality rate. In turn, the largest uncertainties are associated with morbidity indicators because the national health outcomes may come from certain risk factors, not specifying the contribution of air pollution;
- the introduction of a counterfactual level of air pollution, assuming no health impacts below that reference exposure value, raises some doubts about the theoretical minimum concentration that results in minimum population risk. This uncertainty degree becomes more noticeable when different air pollution management policies are tested in order to quantify air quality and health benefits (Martenies et al. 2015; Silveira et al. 2016, 2023; WHO 2016a).

As a last step for analysing uncertainties in HIA comes the economic evaluation of health impacts, which represents the overall estimate of effects, aggregated and converted to monetary values based on the pollutant-health outcome pairs (Holland et al. 2005; Héroux et al. 2015). In most economic studies, the total health costs of air pollution were probably underestimated for two main reasons:

- Several known health effects related to the targeted air pollutant are often neglected due to the lack of epidemiological evidence, so they are not monetized;
- Certain health damage costs, namely intangible costs, have not been quantified, or their evaluation is clearly biased. Within this cost component, the quality-adjusted life year (QALY) and willingness-to-pay (WTP) values vary greatly and are sensitive to how the studies are conducted, usually through personal interviews reporting the individual's willingness to spend money aiming an expected health improvement or avoiding a particular health risk. Moreover, these values might depend on additional variables, such as income and age, and probably differ between health effects (WHO 2008).

These uncertainties pose several challenges to the scientific community that investigates the relationships between air quality, health impacts, and their economic evaluation. The key issues are broadly related to the following concerns: (i) how to identify and quantify all the health impacts of air pollution; (ii) how these impacts can be converted into a monetary value; and (iii) how to increase the accuracy of the resulting estimates.

Accurate estimates imply the use of appropriate HIA methodologies and input data that is as refined as possible. In most cases, developed HIA approaches are applied up to the city scale with acceptable results for regulatory and decision-making purposes. However, the predictions are most likely underestimated because they do not take into account the influence of the volumetry of buildings or other obstacles on the dispersion and distribution of air pollutants, nor account for health impacts associated with steep concentration gradients in near-road environments. In this aspect, various improvements were promoted by the present research, namely, the fact of selecting a local case study where an intense road traffic activity is visible, as well as the option for a CFD model to reproduce the pollutant dispersion around the main roads and obstacles ("Research design" section), thus obtaining high-resolution and accurate air quality estimates. Even if HIA are conducted at the regional or urban scales, fine-resolution spatial data should also be used, as long as they are available, in order to reduce the health effect estimation bias, which normally leads to underestimated predictions (Lobdell et al. 2011; Parvez and Wagstrom 2020; Niepsch et al. 2022).

To evaluate human exposure, some advances were also achieved due to the use of official resident population data at the subsection (i.e., neighbourhood) level, which were spatially disaggregated per age group to the case study´s grid cells (4 m × 4 m horizontal resolution, Fig. 3). Nevertheless, additional efforts for characterising the people affected (e.g., health status, daily activity patterns) and exposure degree to pollutant concentrations are required.

When moving from human exposure to health impacts, the challenges involve identifying all the health indicators associated with the targeted pollutant, selecting the most appropriate CRF and health risk methodologies, developing new single and multi-pollutant epidemiological studies whose health effects are widely recognised, and refining their baseline incidence and prevalence rates and minimum exposure thresholds. Once the physical impacts are quantified, their monetization for the health indicators analysed should be based on records from regional hospital units, considering damage costs with the treatment, medication, and loss of productivity (i.e., inability to work).

Regardless of the methodologies and health input metrics used, sensitivity analyses to evaluate the effect of changes in inputs and models on the magnitude of final health estimates are recommended. These analyses can help to minimize uncertainties and reduce the potential for biased outcomes.

Conclusions

Health impacts of air pollution are increasingly being addressed and documented due to the joint collaboration of experts in different scientific fields, namely, air pollution, public health, sociology and economy. Based on the shared knowledge and identification of key aspects aimed at integrating these thematic areas, a set of HIA tools has been developed. These tools have been applied in world cities to assess their suitability when testing multiple health effects from different air pollutants and input parameters (e.g., CRF, baseline morbidity and mortality rates, exposure thresholds). As a result, a widespread consensus that the current levels of urban air pollution contribute to the worsening of morbidity and premature mortality has emerged. Among the main pollution sources of anthropogenic origin, road traffic and its contribution to high ambient NO_2 concentrations in urban areas have received particular importance, given the frequent occurrence of NO_2 pollution hotspots that trigger significant short-term health effects. However, this concentration–response relationship has been poorly explored due to the difficulty in obtaining local scale inputs with very high resolutions. Accordingly, the present study aimed to investigate a local traffic case study in Portugal, applying two health risk methodologies (linear and nonlinear) for estimating short-term health impacts due to changes in daily NO_2 concentrations. To that end, two particular periods, one week in winter and another one in summer, were simulated considering refined concentration and population data to assess health outcomes from the linear and nonlinear RR approaches. In both periods, lower health impacts considering the whole simulation domain were obtained from the nonlinear methodology (less 27% and 28% in winter and summer, respectively). Spatially, these differences were more significant in areas that combine higher NO_2 concentrations and population data and, consequently, aggravated health impacts were estimated. In these cases, the nonlinear approach probably produces more realistic results; hence, its use is recommended for portraying local case studies with strong gradients of air pollution. When the human exposure to daily maximum NO_2 concentrations fell to values below 6 $\mu g.m^{-3}$, a fact that occurred in 95% of the domain cells and in both periods, relatively small differences between the tested RR approaches were observed. Lastly, when assessing the total health impacts for each simulation period, the highest estimates were achieved in summer (around 18% in both approaches), being directly related to the NO_2 magnitude and its spatial variability, as the other input health metrics remained constant.

Notwithstanding the relevance of HIA arising from air pollution, the results should be interpreted with caution, taking into account the associated uncertainties so that they can provide meaningful support for policymakers, who must make decisions to prevent and control air pollution at different scales. However, in the case of NO_2, the reported adverse effects on human health have been controversial, as different limits for NO_2 in air quality guidelines have been adopted by various intergovernmental institutions. From another perspective, HIA results are also extremely useful to analyse the cost-effectiveness of potential interventions, as well as to select the best policies that lead to air quality improvement in accordance with the 2030 Agenda, by establishing clean air as an integral element of the principle of sustainable development.

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