Environmental Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

# Impact of different exposure models and spatial resolution on the long-term effects of air pollution

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ARTICLE INFO

*Keywords:*
Urban area
Buildings
Particulate matter
Cause-specific mortality
Nitrogen dioxide

ABSTRACT

Long-term exposure to air pollution has been related to mortality in several epidemiological studies. The investigations have assessed exposure using various methods achieving different accuracy in predicting air pollutants concentrations. The comparison of the health effects estimates are therefore challenging. This paper aims to compare the effect estimates of the long-term effects of air pollutants (particulate matter with aerodynamic diameter less than 10 μm, $PM_{10}$, and nitrogen dioxide, $NO_2$) on cause-specific mortality in the Rome Longitudinal Study, using exposure estimates obtained with different models and spatial resolutions. Annual averages of $NO_2$ and $PM_{10}$ were estimated for the year 2015 in a large portion of the Rome urban area ($12 \times 12$ km$^2$) applying three modelling techniques available at increasing spatial resolution: 1) a chemical transport model (CTM) at 1km resolution; 2) a land-use random forest (LURF) approach at 200m resolution; 3) a micro-scale Lagrangian particle dispersion model (PMSS) taking into account the effect of buildings structure at 4 m resolution with results post processed at different buffer sizes (12, 24, 52, 100 and 200 m). All the exposures were assigned at the residential addresses of 482,259 citizens of Rome 30+ years of age who were enrolled on 2001 and followed-up till 2015. The association between annual exposures and natural-cause, cardiovascular (CVD) and respiratory (RESP) mortality were estimated using Cox proportional hazards models adjusted for individual and area-level confounders. We found different distributions of both $NO_2$ and $PM_{10}$ concentrations, across models and spatial resolutions. Natural cause and CVD mortality outcomes were all positively associated with $NO_2$ and $PM_{10}$ regardless of the model and spatial resolution when using a relative scale of the exposure such as the interquartile range (IQR): adjusted Hazard Ratios (HR), and 95% confidence intervals (CI), of natural cause mortality, per IQR increments in the two pollutants, ranged between 1.012 (1.004, 1.021) and 1.018 (1.007, 1.028) for the different $NO_2$ estimates, and between 1.010 (1.000, 1.020) and 1.020 (1.008, 1.031) for $PM_{10}$, with a tendency of larger effect for lower resolution exposures. The latter was even stronger when a fixed value of 10 μg/m$^3$ is used to calculate HRs. Long-term effects of air pollution on mortality in Rome were consistent across different models for exposure assessment, and different spatial resolutions.

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https://doi.org/10.1016/j.envres.2020.110351
Received 6 August 2020; Received in revised form 21 September 2020; Accepted 13 October 2020
Available online 31 October 2020

## 1. Introduction

Several epidemiological studies have shown a clear association between long-term ambient air pollution exposure and adverse health effects (Pope et al., 2020; Vodons et al., 2018; Hoek et al., 2013; Chen and Hoek, 2020; WHO, 2013). Most of them have relied on existing cohort studies, with exposure assessment made at the residential address (Cesaroni et al., 2013; Lipsett et al., 2011; Lepeule et al., 2012; Gan et al., 2011).

Alternative modelling approaches have historically been used to assess exposure. Land use regression (LUR) (Hoek, 2017; Hoek et al., 2008; Cesaroni et al., 2012) is an empirical model which establishes a relationship between observed concentrations (dependent variable) and land-use predictors (independent variables) to better describe the spatial variability of atmospheric pollution. Once the relationship is established, the model predicts air quality levels at external receptor points, such as residential addresses of a longitudinal study. More recently, machine-learning (ML) approaches, such as the Random Forest, have been used thanks to their flexibility and capability to capture complex relationships and non-linearities between predictors and observations (Stafoggia et al., 2019; Gariazzo et al., 2020).

Dispersion and chemical transport models (CTM) are a valid alternative: they consider the major processes affecting air pollution formation and dispersion, such as emissions, dispersion, chemical reactions in gaseous and aerosol phases, and deposition (Gariazzo et al., 2007; Silibello et al., 2008; Zhang et al., 2012).

Ensemble models, i.e. weighted averages of different model outputs, have been recently proposed to exploit the relative benefits of individual base learners (Shtein et al., 2020).

In urban areas, the effect of urban structures, like buildings, is not considered or dealt with a simplified form using either land use data or urban features parametrizations considered by meteorological models (e.g. roughness length). Indeed, the presence of buildings produces low dispersion conditions, accumulation of pollutants and large spatial inhomogeneity in their concentrations. Since the simulation of such effects can be performed by complex numerical models, e.g. computational fluid dynamic (CFD) or large eddy simulation (LES) techniques, whose application is possible only on small domains and for limited period (hours to days), epidemiological studies do not include such building effects on exposure estimations.

As there is no consensus on the best approach for estimating exposure, methods are often compared with controversial results (Chen et al., 2019; Beverland et al., 2012; Wang et al., 2015; de Hoogh et al., 2014; Yu et al., 2018; Butland et al., 2020). In addition, there are few studies comparing the impact of different exposure models on the assessment of long-term health effects (Sellier et al., 2014; Yap et al., 2012; McGuinn et al., 2017; Wang et al., 2015). Results depend on models used, spatial resolution, pollutants, study areas and health outcomes. More research is needed to understand to what extent the accuracy in estimating small-scale spatial variability of air pollution and the related intra-urban differences, affects the estimation of health effects.

The research activities available from the BEEP project (Big data in Environmental and occupational EPidemiology) have been used. BEEP main goals were to improve exposure assessment and to support environmental epidemiological studies in Italy at both national (Stafoggia et al., 2019; Shtein et al., 2020; Marinaccio et al., 2019) and urban (Gariazzo et al., 2020; Fasola et al., 2020) scales. This paper aims to compare long-term effects of air pollutants (particulate matter with aerodynamic size less than 10 μm, $PM_{10}$, and nitrogen dioxide, $NO_2$) on cause-specific mortality from exposure estimates available in the BEEP project and obtained by different models and spatial resolutions. We took advantage of the existence of a consolidated longitudinal study in Rome (Cesaroni et al., 2010, 2013) in order to investigate differences across models in estimating pollutants exposures, and to analyse to what extent different methods and resolution in air pollution exposure assessment might influence estimates on mortality from natural, cardiovascular and respiratory causes.

Section 2 presents the study area, the population under study, the exposure models herein used and the statistical model applied to assess the association of health outcomes with exposures. The incidence of health outcomes in the population under study, the model's exposure and the estimated long-term health effects are presented in section 3. A discussion of main findings follows in section 4.

**Abbreviations:**

| | |
|---|---|
| CI | Confidence Interval |
| CFD | Computational Fluid Dynamic |
| CTM | Chemical Transport Model |
| CVD | Cardiovascular disease |
| FARM | Flexible Air quality Regional Model |
| HR | Hazard Ratio |
| IQR | Interquartile Range |
| LPDM | Lagrangian Particle Dispersion Model |
| LUR | Land Use Regression model |
| ML | Machine Learning |
| PMSS | Parallel Micro-Swift-Spray model |
| RESP | Respiratory disease |
| RoLS | Rome Longitudinal Study |
| SEP | Socioeconomic position |
| WRF | Weather Research and Forecasting model |

## 2. Material and methods

### 2.1. Study area and study population

Rome is the largest Italian city, with a population of about 2.5 million inhabitants in a 1,290 $km^2$ area, mostly living within the large urban area (Fig. 1). The Rome's air quality has been described in scientific articles (Gariazzo et al., 2007, 2015, 2016, 2020; Cattani et al., 2017) and in local reports (ARPA Lazio, 2018). The related health effects have been also assessed (Cesaroni et al., 2012, 2013, 2014; Renzi et al., 2018; Cerza et al., 2018).

Most of studies are based on the Rome Longitudinal Study (RoLS) (Cesaroni et al., 2010, 2013; Paglione et al., 2020). RoLS is an administrative cohort enrolled at Census 2001 and followed up until 2015. Population records have been linked to health information systems, such as mortality registry, hospital discharge files, and drugs prescriptions. All residents above 30 years of age at baseline, and who had resided in the same address since at least 5 years before the enrolment, have been included. Baseline information is available on sex, age, place of birth, education level, marital status, occupation (general statistical categories, without data on occupational exposures) and residential history. A small-area (census block) composite index of socioeconomic position (SEP) (Cesaroni et al., 2006) is also added to better characterize residential social deprivation. A follow-up to determine vital status using the Rome Municipal Register during the period October 2001–December 2015 has been carried out. RoLS is part of the National Statistical Program and was approved by the Italian Data Protection Authority.

For computational reasons (see par. 2.2.3), we could only include a portion of the whole study area, encompassing only 12 × 12-km and 482,259 (38%) of the original 1,263,715 subjects.

The study area is shown in Fig. 1 (red box). This area includes a portion of the city's centre with residential, commercial and touristic districts, as well as outskirts neighbourhoods. High, medium and low urbanization levels, with different building heights, can be found in this area, as well as open urban parks. A statistical analysis of some urbanization parameters of the studied area is shown in table S1 of the Supplementary Materials (SM).

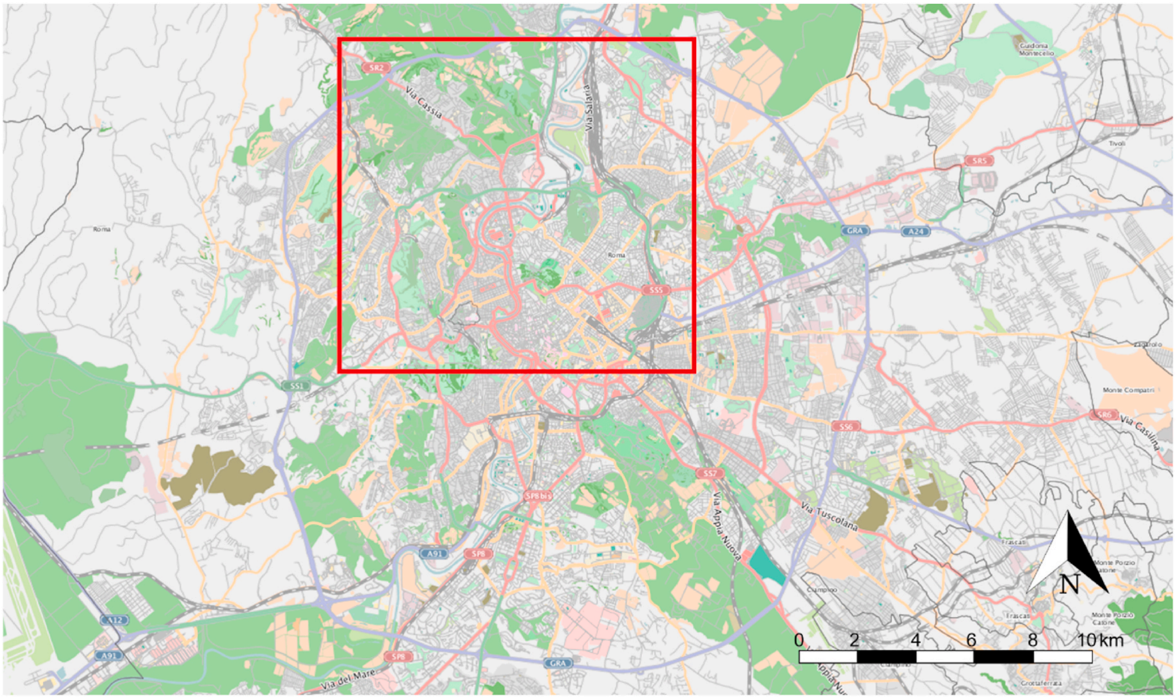


**Fig. 1.** Map of the city of Rome, Italy, with the study area (in red) ($12 \times 12$ $Km^2$). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

The size of the area was selected on the basis of computational/ budget constraints for yearly simulation; on an High Performance Computer (HPC) platform with 180 cores, the computational time was 4.5 h per simulated day for the selected domain with detailed traffic sources considered. The position of the area was chosen to maximise the number of underlying resident population and, at the same time, to optimize the contrast in exposure according to former studies (eg. Cesaroni et al., 2013).

### 2.2. Exposure assessment to air pollutants

Exposure assessment studies were carried out using three modelling techniques applied at different temporal and spatial resolutions: 1) a CTM; 2) a ML model; 3) a micro-scale Lagrangian particle dispersion model (LPDM). A description of the above model techniques is following in the next subsections.

#### 2.2.1. The chemical transport model FARM

As a first step, an air quality modelling system (AQMS) was used to provide air pollution concentration fields at urban scale. The AQMS is based on the CTM FARM (Flexible Air quality Regional Model: Gariazzo et al., 2007; Silibello et al., 2008).

Air pollutants emissions were derived from a local emission inventory, integrated with detailed vehicles emissions estimated from traffic flow data. Meteorological data were provided by the prognostic non-hydrostatic model WRF (Skamarock et al., 2008) applied with the so-called Building Environment Parameterization (BEP, Martilli et al., 2002).

Boundary conditions to WRF and FARM models were provided by previous national scale simulations, performed by same models and described elsewhere (Silibello et al., 2019). Details about the CTM and WRF models and their use in predicting air pollutants concentrations in the main metropolitan areas of Italy carried out within the BEEP project are reported by Gariazzo et al. (2020).

In brief, the simulations with the above modelling systems have been performed for the year 2015 over the Metropolitan area of Rome ($60 \times 60$ $km^2$), on an hourly basis, with a horizontal resolution of 1 km. Annual values were derived for this study. Although FARM provided concentrations for many gaseous pollutants and aerosol fraction and components, only $NO_2$ and $PM_{10}$ were considered since they can be simulated by the micro-scale model. For the reference year, FARM was able to achieve an $R^2$ of 0.49 for both $NO_2$ and $PM_{10}$ (see Table S2 SM).

#### 2.2.2. The random forest models

A second step, based on a Random Forest (RF) ML technique, was performed to downscale FARM model concentration fields, on a daily basis, at a higher spatial resolution of 200 m. RF models consist of an ensemble of decision trees (forest), suitable for both classification and regression problems (Liaw and Wiener, 2002).

In our application, the RF model used a set of spatial and spatial-temporal predictors to predict daily concentrations of air pollutants over the whole metropolitan area at a spatial resolution of 200m. Some of these predictors were the FARM model results, the imperviousness surface areas (a Copernicus satellite data), the Corine land cover, the length and distance from types of roads, and the traffic data derived from the Open Transport Map open data. Details about the RF application can be found in Gariazzo et al. (2020).

In this study, we used the RF $NO_2$ and $PM_{10}$ daily predictions obtained for the city of Rome for the reference year (2015), averaged over an annual base. The 10-fold cross-validated RF model results were able to achieve an $R^2$ of 0.62 and 0.76 for $NO_2$ and $PM_{10}$, respectively (see Table S2 SM).

#### 2.2.3. The micro-scale Lagrangian particle dispersion model

The third step was based on the PMSS (Parallel Micro-Swift-Spray) modelling system (Oldrini et al., 2017) to provide air pollution concentration fields on a $12 \times 12$ $km^2$ domain (see red box in Fig. 1) covering a large portion of the city of Rome, at the horizontal resolution of 4 m. This limited size domain was caused by the high computational needs required by such modelling system. PMSS is constituted by the parallel microscale versions of MSS modelling system, composed by the SWIFT diagnostic flow model and the SPRAY Lagrangian particle dispersion model.

SWIFT is a terrain-following 3D diagnostic mass-consistent model providing wind, turbulence, and temperature fields, taking into account building effects (Tinarelli et al., 2007; Hanna et al., 2011; Trini Castelli et al., 2017).

SPRAY (Tinarelli et al., 2012) is a 3D Lagrangian Particle Dispersion Model, where the dispersion of an atmospheric primary pollutant is simulated following the trajectories of a suitably large number of numerical particles. The trajectories are determined integrating in time a 3D form of the Langevin equation or the random velocity, following Thomson (1987).

PMSS is suitable for applications in built-up areas over relatively large domains (up to the dimension of entire cities) using a domain decomposition into squared tiles, allowing a parallel computation over large HPC systems and simulations at microscale over large periods such an entire year. Hourly averaged ground level concentration of $NO_x$ and $PM_{10}$ emitted by the road traffic have been computed by PMSS using detailed vehicular traffic information provided by the mobility agency of Rome. The first guess flow was the same provided to the FARM model by the WRF prognostic meteorological model. The effect of buildings on flow was then estimated by SWIFT component of PMSS. As PMSS provided pollutants concentration for the traffic source only, a further no-traffic FARM simulation for the year 2015 has been performed excluding traffic emissions within the microscale domain. We refer to this simulation as "no-traffic FARM". The latter includes other sources contributions coming from both outside the micro-scale domain, and inside it, not directly considered by PMSS (such as the heating systems during the winter season). Then, the traffic contributions estimated by PMSS and those estimated by the "no-traffic FARM" run were summed up. This approach intrinsically avoids the double counting of traffic emissions within the micro-scale domain, preserving physical and chemical consistency between the two models in a simple way, as the two simulations take in account different emission sources. According to this approach, the "no-traffic FARM" simulation reproduces the pollution levels inside the city (the "urban concentration"), while PMSS captures the dispersion processes within street-canyons (the "street increment"). To calculate the $NO_2$ contribution from the $NO_x$ directly simulated, hourly results provided by the full sources FARM simulation have been used in a polynomial regression analysis, which provided a function for $NO_x/NO_2$ concentration ratio to be applied in the urban area of Rome. For the year 2015, the combination of PMSS and "no-traffic FARM" results was able to achieve an $R^2$ of 0.44 for $NO_2$ and 0.5 for $PM_{10}$ (see Table S2 SM). Examples of a $NO_2$ concentration field at micro-scale and a time series comparison of modelled vs observed daily $NO_2$ concentration are shown in figures S1 and S2 of SM respectively. The $NO_2$ and $PM_{10}$ hourly results were then averaged on an annual base to be used for health effect estimations. In the following sections, we refer to PMSS simulation as to the sum of PMSS and "no-traffic FARM" runs.

#### 2.2.4. Assessment of the exposure for the individuals in the cohort

The $NO_2$ and $PM_{10}$ concentration fields, provided by the above models, together with the cohort addresses of the studied population, were processed using a common spatial reference system to extract mean annual exposures at each residential address. While FARM and RF model results provided the exposure at their own spatial resolution, 1 km and 200 m respectively, for the micro-scale model PMSS we took advantage from the extremely high spatial resolution (4 m) to calculate the mean exposure also at following buffer sizes: 12, 24, 52, 100 and 200 m. Table 1 shows a list of available models results and related exposure data used for this study. Finally, individual exposure was assigned from models' exposures available at each residential address (about 49K).

**Table 1**
List of available models results and related exposure estimation data.

| Model | Model characteristics | Model resolution | Exposure data | Exposure spatial representativeness |
|---|---|---|---|---|
| PMSS | LPDM with obstacles effect treatment | 4 m | PMSS_4m | 4 m |
| | | | PMSS_12m | 12 m |
| | | | PMSS_24m | 24 m |
| | | | PMSS_52m | 52 m |
| | | | PMSS_100m | 100 m |
| | | | PMSS_200m | 200 m |
| RF | ML model | 200 m | RF_200m | 200 m |
| FARM | CTM | 1 km | FARM_1km | 1 km |

### 2.3. Outcomes and statistical analyses

We analysed mortality for natural non-accidental causes (International Classification of diseases, 9th revision - ICD-9: codes < 1–799), cardiovascular (CVD) (ICD-9: codes 390–459) and respiratory (RESP) (ICD-9: codes 460–519) causes. Age was used as underlying time axis in the Cox proportional hazards model. We further adjusted for individual-level covariates (sex as a stratification variable, place of birth, education level, occupation) and area-level covariates (census-block SES and income, unemployment rate, % of low or very high education in the neighbourhood).

Each exposure variable ($NO_2$ or $PM_{10}$ from different models/resolution) was analysed separately and included in the Cox model as a linear term. The association estimates are reported as adjusted Hazard Ratios (HR) and corresponding 95% Confidence Intervals (95% CI) per interquartile range (IQR) increment and per 10 μg/m$^3$ (see SM) in the exposure.

## 3. Results

### 3.1. Population under study and incidence of mortality

Table 2 summarizes the relevant data of the cohort under study. A total of 482,259 residents were included with a mean age of 56 years (SD = 15.8, IQR = 25.9). Most of the subjects had a high school educational level (34.4%) or a university degree (23.5%). Retired persons were 25%, followed by housewives (19.9%), while people employed were 33% in non-manual and 12.9% in manual/other activities, respectively. As for social economic position, 28.5% of the population was in the very high category, whereas 8.8% was in the very low category. During the follow-up there were 98,480, 39,393 and 6,558 deaths from natural, CVD and RESP causes, respectively.

### 3.2. Exposure assessment by model and their correlations

Fig. 2 shows maps of mean annual $NO_2$ and $PM_{10}$ concentrations estimated by FARM, RF and PMSS models for the year 2015. The improvement in the details of the estimated concentration is clearly detectable going from the model with the lowest resolution (FARM) to that with the highest one (PMSS). The larger pollutants' concentrations produced by roads emissions are clearly visible in more spatially resolved models (RF and PMSS), as expected. The micro-scale model PMSS shows the highest concentrations, especially in the high-urbanized districts, due to lower dispersion conditions induced by the presence of buildings.

Table 3 shows the values of the main statistical parameters for $NO_2$ and $PM_{10}$ exposure data for the individuals in the cohort, estimated for each considered model and related resolution. All models show very close mean values for both pollutants (43.0 and 32.0 μg/m$^3$ for $NO_2$ and $PM_{10}$, respectively), except for the FARM ones, which exhibits lower values (29.2 and 25.5 μg/m$^3$ for $NO_2$ and $PM_{10}$, respectively) due to its lower spatial resolution that does not permit to capture the levels commonly observed at kerb-side monitoring stations. There are larger differences in the models for the standard deviations (SDs), the highest percentiles and maximum values. The higher the spatial resolution, the higher are the SDs, 95th percentiles and maximum values. As for exposures provided by PMSS model, estimates in lower buffer sizes have

**Table 2**
Characteristics of population cohort and incidence of natural, cardiovascular and respiratory mortalities.

| Continuous covariates | | n | mean | sd | min | median | max | IQR |
|---|---|---|---|---|---|---|---|---|
| Age (baseline) | Years | 482,259 | 56.5 | 15.8 | 30.0 | 55.9 | 107.3 | 25.9 |
| High education | % (by neighbourhood) | 482,259 | 19.0 | 9.09 | 2.51 | 18.52 | 37.24 | 17.17 |
| Very low education | % (by neighbourhood) | 482,259 | 22.1 | 6.32 | 12.69 | 20.93 | 37.78 | 10.56 |
| Unemployment rate | % (by neighbourhood) | 482,259 | 12.9 | 3.39 | 7.38 | 11.98 | 24.37 | 4.62 |

| **Categorical covariates** | | **Total population** | | | **Natural mortality** | | **CVD mortality** | | **RESP mortality** | |
|---|---|---|---|---|---|---|---|---|---|---|
| **variable** | **Category** | **n** | **%** | **P.YEARS** | **n** | **rate*1000** | **n** | **rate*1000** | **n** | **rate*1000** |
| sex | Male | 213,102 | 44.2 | 2,501,644 | 45,147 | 18.0 | 16,581 | 6.6 | 3,132 | 1.3 |
| | Female | 269,157 | 55.8 | 3,244,277 | 53,333 | 16.4 | 22,812 | 7.0 | 3,426 | 1.1 |
| marital status | Married | 298,340 | 61.9 | 3,651,709 | 51,541 | 14.1 | 18,015 | 4.9 | 3,228 | 0.9 |
| | Single | 86,112 | 17.9 | 1,060,418 | 10,648 | 10.0 | 4,218 | 4.0 | 724 | 0.7 |
| | Separated | 36,334 | 7.5 | 447,520 | 4,377 | 9.8 | 1,370 | 3.1 | 242 | 0.5 |
| | Widow | 61,473 | 12.7 | 586,275 | 31,914 | 54.4 | 15,790 | 26.9 | 2,364 | 4.0 |
| Education level | University | 113,190 | 23.5 | 1,416,752 | 15,653 | 11.0 | 5,904 | 4.2 | 1,028 | 0.7 |
| | High school | 165,934 | 34.4 | 2,057,601 | 22,398 | 10.9 | 8,337 | 4.1 | 1,371 | 0.7 |
| | Junior school | 103,752 | 21.5 | 1,224,467 | 21,516 | 17.6 | 8,392 | 6.9 | 1,405 | 1.1 |
| | <=Primary | 99,383 | 20.6 | 1,047,101 | 38,913 | 37.2 | 16,760 | 16.0 | 2,754 | 2.6 |
| Occupational status | 1 = Employed, non-manual I | 83,505 | 17.3 | 1,091,890 | 4,788 | 4.4 | 1,275 | 1.2 | 208 | 0.2 |
| | 2 = Employed, non-manual II | 75,481 | 15.7 | 990,599 | 2,959 | 3.0 | 653 | 0.7 | 104 | 0.1 |
| | 3 = Employed, manual | 35,750 | 7.4 | 452,680 | 2,193 | 4.8 | 610 | 1.3 | 68 | 0.2 |
| | 4 = Employed, other | 26,652 | 5.5 | 342,398 | 1,372 | 4.0 | 343 | 1.0 | 57 | 0.2 |
| | 5 = Housewives | 95,815 | 19.9 | 1,117,780 | 24,936 | 22.3 | 10,881 | 9.7 | 1,616 | 1.4 |
| | 6 = Unemployed | 19,921 | 4.1 | 252,582 | 1,147 | 4.5 | 256 | 1.0 | 45 | 0.2 |
| | 7 = Retired | 122,024 | 25.3 | 1,261,259 | 52,429 | 41.6 | 21,577 | 17.1 | 3,844 | 3.0 |
| | 8 = Other condition | 23,111 | 4.8 | 236,734 | 8,656 | 36.6 | 3,798 | 16.0 | 616 | 2.6 |
| Socio economic position | 1 = Very high | 137,675 | 28.5 | 1,644,463 | 28,616 | 17.4 | 11,824 | 7.2 | 1,917 | 1.2 |
| | 2 = High | 134,528 | 27.9 | 1,600,409 | 27,366 | 17.1 | 10,984 | 6.9 | 1,822 | 1.1 |
| | 3 = Medium | 103,552 | 21.5 | 1,234,409 | 20,562 | 16.7 | 8,104 | 6.6 | 1,393 | 1.1 |
| | 4 = Low | 64,070 | 13.3 | 760,599 | 13,080 | 17.2 | 5,148 | 6.8 | 842 | 1.1 |
| | 5 = Very low | 42,434 | 8.8 | 506,042 | 8,856 | 17.5 | 3,333 | 6.6 | 584 | 1.2 |
| Income98 | 1 = Very low | 8,799 | 1.8 | 102,127 | 2,406 | 23.6 | 976 | 9.6 | 189 | 1.9 |
| | 2 | 10,771 | 2.2 | 131,980 | 1,815 | 13.8 | 682 | 5.2 | 105 | 0.8 |
| | 3 | 15,534 | 3.2 | 184,602 | 3,056 | 16.6 | 1,263 | 6.8 | 191 | 1.0 |
| | 4 | 86,392 | 17.9 | 1,040,793 | 16,755 | 16.1 | 6,362 | 6.1 | 1,040 | 1.0 |
| | 5 | 14,158 | 2.9 | 171,478 | 2,565 | 15.0 | 992 | 5.8 | 172 | 1.0 |
| | 6 | 70,916 | 14.7 | 840,267 | 14,897 | 17.7 | 6,123 | 7.3 | 906 | 1.1 |
| | 7 | 85,916 | 17.8 | 1,027,953 | 16,986 | 16.5 | 6,796 | 6.6 | 1,133 | 1.1 |
| | 8 | 103,417 | 21.4 | 1,227,052 | 21,238 | 17.3 | 8,546 | 7.0 | 1,490 | 1.2 |
| | 9 | 46,806 | 9.7 | 549,195 | 10,501 | 19.1 | 4,386 | 8.0 | 728 | 1.3 |
| | 10 = Very high | 39,550 | 8.2 | 470,475 | 8,261 | 17.6 | 3,267 | 6.9 | 604 | 1.3 |

Source: data retrieved from the Latium regional health information system.

the highest percentiles and maximum values distribution due to spatial heterogeneities of the concentration fields produced by the dispersion around buildings. The $NO_2$ 95th percentile estimated by RF and PMSS agree at lower resolution (200 m), while the maximum values significantly differ. The ubiquitous nature of $PM_{10}$ shows minor differences from higher to lower spatial resolutions. The $NO_2$ and $PM_{10}$ statistical distributions (5th - 95th percentiles) exhibit lower exposure values estimated by FARM than those computed by PMSS and RF models. To better visualize these results, boxplots and density plots of cohort population pollutants exposure by model are presented in the SM (Figure S3).

Table 4 shows the correlation coefficients among models. As expected, the correlation among the exposure estimations based on PMSS model at different buffer sizes are very good for both pollutants ($r = 0.99$–$0.80$). As for $NO_2$, PMSS model is well correlated with both RF and FARM models ($r = 0.6$) while, RF is well correlated with FARM ($r = 0.58$). Similar results are obtained for $PM_{10}$. Scatter plots between model results are presented in SM for both $NO_2$ and $PM_{10}$ (Figure S4). Although the modelling approaches are different (Lagrangian -PMSS-, statistical -RF- and Eulerian -FARM-), they share most of the input data, like emissions, flow and territorial data. Consequently, these degrees of correlation among models are partially expected.

### *3.3. Long term health effects according to different exposure models*

Table 5 shows the adjusted HR and 95% CI for increments corresponding to the IQR of pollutants for natural non-accidental, cardiovascular and respiratory mortality obtained using the different exposure models and resolutions. Forest plots of HRs for fixed increment of 10 $\mu g/m^3$ are presented in the SM (Figure S5). Overall, all exposure models show significant associations for natural non-accidental and cardiovascular mortality for both pollutants. Respiratory mortality showed positive association with $NO_2$ and $PM_{10}$ in all models, but without reaching statistical significance. HR values span from 1.012 to 1.018 (mean = 1.016; SD = 0.002) and from 1.022 to 1.042 (mean = 1.033; SD = 0.006) for $NO_2$ natural and cardiovascular mortality, respectively, using the different exposure models. The corresponding HR values for $PM_{10}$ span from 1.010 to 1.020 (mean = 1.015; SD = 0.003) and from 1.027 to 1.042 (mean = 1.035; SD = 0.006) for natural and cardiovascular mortality, respectively.

The HRs results obtained from the PMSS exposure model at different buffer sizes (from 4 to 200 m) for natural and cardiovascular mortality show an increasing trend with decreasing model resolution for both pollutants. The HR value at the lowest PMSS resolution (PMSS_200m) agrees with the FARM results obtained at 1 km of spatial resolution. Conversely, a small drop in HR values is observed for RF results at 200m resolution, particularly for cardiovascular mortality. However, according to confidence intervals of each HRs prediction, those differences in HRs values are not statistically significant. Fig. 3 summarizes HRs results of natural mortality for different model and resolution.

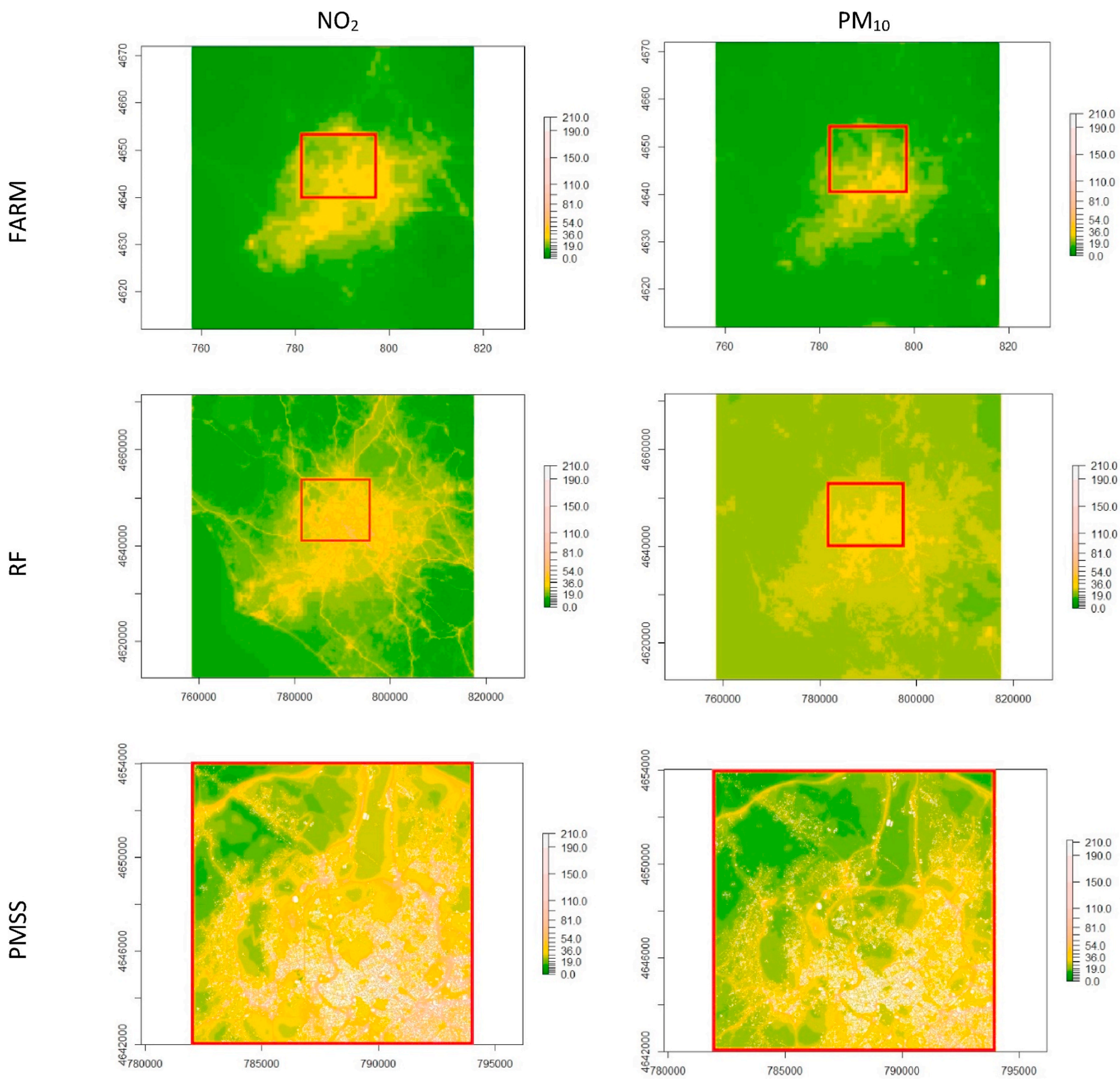


**Fig. 2.** Mean annual (2015) concentration (μg/m$^3$) of $NO_2$ and $PM_{10}$ estimated for the whole city by the CTM FARM and the Random Forest (RF) models, and for a portion (12 × 12km$^2$) of it by the micro-scale Lagrangian particles with building effects (PMSS) model. The red box shows the studied area. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

**Table 3**
Main statistics of mean annual (2015) $NO_2$ and $PM_{10}$ exposure (μg m$^{-3}$) of cohort population estimated by the CTM FARM (FARM), the Random Forest (RF) and the micro-scale Lagrangian particles with building effects (PMSS) models.

| Pollutant | Model | Res (m) | n. data | min | mean | SD | percentile | | | | | IQR | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 5 | 25 | 50 | 75 | 95 | max | |
| $NO_2$ | PMSS | 4 | 416,766 | 9.8 | 43.6 | 13.5 | 25.5 | 34.1 | 41.9 | 50.9 | 67.2 | 204.5 | 16.7 |
| | PMSS | 12 | 480,197 | 9.9 | 44.1 | 13.1 | 26.2 | 34.9 | 42.7 | 51.3 | 66.7 | 190.9 | 16.4 |
| | PMSS | 24 | 482,259 | 10.0 | 44.3 | 12.9 | 26.4 | 35.1 | 43.2 | 51.6 | 66.3 | 162.0 | 16.5 |
| | PMSS | 52 | 482,259 | 10.4 | 43.6 | 12.1 | 26.4 | 34.8 | 42.7 | 50.8 | 64.3 | 119.6 | 16.0 |
| | PMSS | 100 | 482,259 | 10.6 | 43.2 | 11.3 | 26.4 | 34.9 | 42.7 | 50.7 | 63.0 | 102.0 | 15.8 |
| | PMSS | 200 | 482,259 | 11.1 | 42.8 | 10.5 | 26.3 | 35.0 | 42.8 | 49.9 | 60.9 | 84.6 | 14.9 |
| | RF | 200 | 482,259 | 20.5 | 43.8 | 9.7 | 29.6 | 36.6 | 41.7 | 51.1 | 61.7 | 67.6 | 14.4 |
| | FARM | 1000 | 482,259 | 15.7 | 29.2 | 3.7 | 22.0 | 26.7 | 29.2 | 31.8 | 35.7 | 35.9 | 5.1 |
| $PM_{10}$ | PMSS | 4 | 416,766 | 11.1 | 32.9 | 10.8 | 19.6 | 25.3 | 31.2 | 38.4 | 52.2 | 186.5 | 13.1 |
| | PMSS | 12 | 480,197 | 11.1 | 33.3 | 10.6 | 19.9 | 25.8 | 32.0 | 39.0 | 51.6 | 171.4 | 13.2 |
| | PMSS | 24 | 482,259 | 11.2 | 33.5 | 10.6 | 20.0 | 25.8 | 32.3 | 39.4 | 51.8 | 139.3 | 13.5 |
| | PMSS | 52 | 482,259 | 11.2 | 33.2 | 9.9 | 20.0 | 25.7 | 32.1 | 39.2 | 50.3 | 106.8 | 13.6 |
| | PMSS | 100 | 482,259 | 11.2 | 33.0 | 9.3 | 19.9 | 25.7 | 32.2 | 39.3 | 49.4 | 87.7 | 13.6 |
| | PMSS | 200 | 482,259 | 11.4 | 32.7 | 8.7 | 19.8 | 25.7 | 32.7 | 38.8 | 48.1 | 67.8 | 13.1 |
| | RF | 200 | 482,259 | 24.0 | 30.9 | 1.9 | 27.4 | 29.7 | 31.1 | 32.2 | 33.9 | 38.2 | 2.5 |
| | FARM | 1000 | 482,259 | 12.9 | 25.5 | 5.2 | 16.3 | 21.8 | 25.2 | 28.6 | 35.6 | 38.2 | 6.8 |

**Table 4**
Correlation between pairs of exposure models[a] estimating mean annual (2015) $NO_2$ and $PM_{10}$.

| Pollutant | exposure model | | overall | |
|---|---|---|---|---|
| | | | n. data | r |
| **$NO_2$** | PMSS_4m | PMSS_12m | 416,766 | 0.99 |
| | | PMSS_24m | 416,766 | 0.97 |
| | | PMSS_52m | 416,766 | 0.92 |
| | | PMSS_100m | 416,766 | 0.87 |
| | | PMSS_200m | 416,766 | 0.79 |
| | | RF_200m | 416,766 | 0.59 |
| | | FARM_1km | 416,766 | 0.56 |
| | RF_200m | FARM_1km | 482,259 | 0.58 |
| **$PM_{10}$** | PMSS_4m | PMSS_12m | 416,766 | 0.99 |
| | | PMSS_24m | 416,766 | 0.97 |
| | | PMSS_52m | 416,766 | 0.93 |
| | | PMSS_100m | 416,766 | 0.88 |
| | | PMSS_200m | 416,766 | 0.81 |
| | | RF_200m | 416,766 | 0.56 |
| | | FARM_1km | 416,766 | 0.65 |
| | RF_200m | FARM_1km | 482,259 | 0.70 |

[a] CTM FARM (FARM_1km), Random Forest (RF_200m) and micro-scale Lagrangian with building effects (PMSS_4-200m).

## 4. Discussion

This study aimed at evaluating whether estimates of association between long-term exposure to air pollutants and mortality differed by exposure assessment method and spatial resolution. We found consistent results across exposure models when estimates were expressed per IQR. When we used a fixed increment (10μg/m$^3$), the effects were generally larger for larger buffer size (PMSS model, maximum effect at 200 m resolution) and using RF and FARM models.

In this work, a detailed exposure assessment study for the metropolitan area of Rome, Italy has been carried out using state-of-art modelling techniques. Exposure were available at different resolution, from 4m to 1 km, depending on the model used. The models were also different in terms of underlying paradigm (deterministic versus statistical), chemical-physical processes considered, data used, computational requirements.

As an example, CTM models need emissions to be spatially and temporally disaggregated over the model domain, as well as boundary and initial conditions determined and provided for the urban analysis.

The main efforts in machine learning modelling approach is the identification of a coherent set of spatial-temporal predictors, supposed to be related to the investigated phenomena, and their integration in a GIS environment.

Lagrangian particles models with obstacles treatment, in addition to data required by CTM models, need a detailed description of urban structure that must be provided at the target resolution of the model (4 m in this case). Furthermore, as these micro-scale models consider the buildings effect on flow and consequently on concentrations, we expect high spatial heterogeneities in the predicted pollutants concentration, particularly in highly built urban districts. Consequently, assigning the exposure at the residential address using the highest spatial PMSS resolution, might produce a misclassification of the actual neighbourhood exposure, with possible bias. For this reason, we considered different buffer sizes for PMSS results to consider the mean effect of surroundings areas at different distances from the residential address.

The above modelling techniques require also different computation resources and have different running time (from 11 min for FARM to 4.5 h for PMSS to run a single day).

Although the models provide exposure estimates at different spatial resolution leading to differences in the IQRs values, particularly between PMSS and FARM models, the differences in terms of HRs values for non-accidental and cardiovascular mortalities due to either $NO_2$ or $PM_{10}$ exposures were not statistically significant. These results imply that computational efforts required to estimate exposure at very fine resolution, using sophisticated model techniques like PMSS, do not provide significant differences in either HRs or their CI of long term health effects assessment with respect to simpler, less resolved and computational intensive modelling approaches like CTM or machine learning methods. Possibly, the annual averaging could have reduced the spatial-temporal inhomogeneity existing at hourly and daily resolution.

The models were highly correlated in estimating population exposures (r = 0.6–0.9) and differed only for the extreme values (above 95th percentile). Similar results in exposure analysis were obtained by Chen et al. (2019) comparing 16 algorithms driven by satellite, CTM, land use and traffic data, to predict annual average $PM_{2.5}$ and $NO_2$ concentrations across Europe.

All models predict mean HRs of 1.015 (SD = 0.002) and 1.032 (SD = 0.006) for non-accidental and cardiovascular mortalities respectively due to $NO_2$ exposure, while the corresponding HRs mean values for $PM_{10}$ exposure are 1.015 (SD = 0.003) and 1.034 (SD = 0.006). Respiratory mortality was found to be positively associated with the considered pollutants, but without reaching statistical significance. The statistical power was lower for respiratory mortality (number of cases 6,558) than for the other conditions.

In a study involving the whole population cohort of Rome, Cesaroni et al. (2013) found HRs of 1.03 (CI 1.02–1.04) for both non-accidental and cardiovascular mortalities for increments of IQR of 10.7 μg/m$^3$ of

**Table 5**
Adjusted HRs (95% CI) for increments corresponding to interquartile ranges (IQRs) for natural, cardiovascular, and respiratory mortality according to different exposure models, Rome 2001–2015.

| Pollutant | Model | n. data | IQR | Natural (n = 98,480) HR[a] (95% CI) | Cardiovascular (n = 39,393) HR[a] (95% CI) | Respiratory (n = 6,558) HR[a] (95% CI) |
|---|---|---|---|---|---|---|
| $NO_2$ | PMSS_4m | 416,766 | 16.7 | 1.013 (1.004,1.022) | 1.028 (1.014,1.042) | 1.014 (0.980,1.050) |
| | PMSS_12m | 480,197 | 16.4 | 1.012 (1.004,1.021) | 1.029 (1.016,1.043) | 1.006 (0.973,1.039) |
| | PMSS_24m | 482,259 | 16.5 | 1.013 (1.004,1.022) | 1.030 (1.016,1.044) | 1.004 (0.970,1.039) |
| | PMSS_52m | 482,259 | 16.0 | 1.015 (1.005,1.024) | 1.033 (1.018,1.048) | 1.004 (0.969,1.041) |
| | PMSS_100m | 482,259 | 15.8 | 1.017 (1.007,1.027) | 1.037 (1.021,1.053) | 1.016 (0.977,1.056) |
| | PMSS_200m | 482,259 | 14.9 | 1.018 (1.007,1.028) | 1.037 (1.020,1.055) | 1.016 (0.975,1.059) |
| | RF_200m | 482,259 | 14.4 | 1.016 (1.005,1.027) | 1.022 (1.005,1.039) | 1.002 (0.962,1.044) |
| | FARM_1km | 482,259 | 5.1 | 1.018 (1.008,1.028) | 1.042 (1.025,1.058) | 1.014 (0.975,1.054) |
| $PM_{10}$ | PMSS_4m | 416,766 | 13.1 | 1.013 (1.004,1.022) | 1.027 (1.013,1.041) | 1.007 (0.973,1.041) |
| | PMSS_12m | 480,197 | 13.2 | 1.012 (1.004,1.021) | 1.029 (1.015,1.042) | 0.999 (0.966,1.032) |
| | PMSS_24m | 482,259 | 13.5 | 1.013 (1.004,1.022) | 1.029 (1.015,1.043) | 0.996 (0.963,1.032) |
| | PMSS_52m | 482,259 | 13.6 | 1.015 (1.005,1.025) | 1.034 (1.018,1.049) | 0.996 (0.959,1.034) |
| | PMSS_100m | 482,259 | 13.6 | 1.018 (1.007,1.029) | 1.039 (1.022,1.057) | 1.007 (0.966,1.050) |
| | PMSS_200m | 482,259 | 13.1 | 1.020 (1.008,1.031) | 1.042 (1.024,1.061) | 1.009 (0.965,1.055) |
| | RF_200m | 482,259 | 2.5 | 1.010 (1.000,1.020) | 1.028 (1.012,1.044) | 1.011 (0.973,1.052) |
| | FARM_1km | 482,259 | 6.8 | 1.017 (1.007,1.026) | 1.041 (1.025,1.057) | 1.007 (0.970,1.046) |

[a] Adjusted for sex, marital status, place of birth, education, occupation, and area-based socioeconomic position.

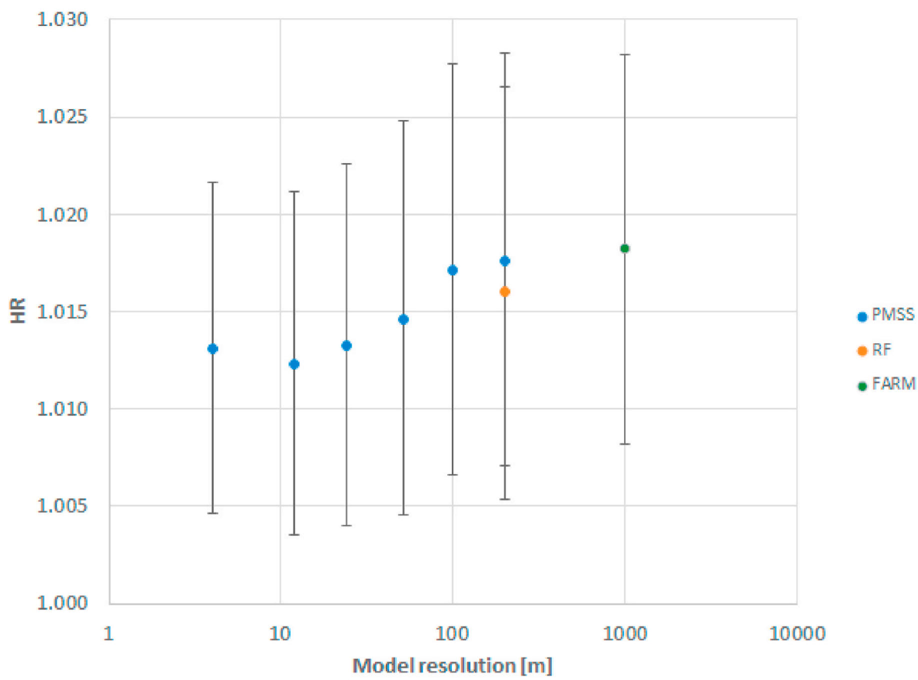


**Fig. 3.** Adjusted HRs for increments corresponding to IQR by model resolution for $NO_2$ natural mortality.

$NO_2$ using a LUR exposure model (Cesaroni et al., 2012). The same study found HRs of 1.02 (CI 1.02–1.03) and 1.04 (CI 1.03–1.05) for non-accidental and cardiovascular mortalities for increments of IQR of 5.8 $\mu g/m^3$ of $PM_{2.5}$ estimated by using the same CTM model (FARM) used in this study, but run for a different year. Similarly Cesaroni et al. (2013) also obtained no statistically significant positive association with respiratory mortality.

Our results are within the ranges of these local studies and of other systematic reviews (Hoek et al., 2013; Atkinson et al., 2018; Chen and Hoek, 2020). Small differences can be ascribed to different models used to assess exposure, size and age ranges of the populations under study and the different characteristics of the study areas.

While there are many studies comparing modelling approaches and their performance in assessing exposure (Yu et al., 2018; Chen et al., 2019; Buteau et al., 2017; de Hoogh et al., 2014; Beverland et al., 2012), there are few studies about the influence of exposure models and related errors on the assessment of health effects.

Sellier et al. (2014) compared four exposure models, including two LUR models and a dispersion model to evaluate the effect on the estimation of birth weight in two French metropolitan areas. They found effect estimates of $NO_2$ on birth weight varying in accordance with the exposure model, while $PM_{10}$ effects were more consistent across exposure models, indicating a possible effect induced by spatially heterogeneous pollutants like $NO_2$.

Yap et al. (2012) carried out a study about black smoke effects on long-term mortality in a Scottish population, using three different spatial-temporal models. They found that long-term mortality was critically sensitive to the exposure assignment model used, highlighting the critical importance of reliable estimation of exposures on intra-urban spatial scales to avoid potential misclassification bias.

Butland et al. (2020) compared LUR models, dispersion models and two hybrid combinations of LUR and dispersion models, for nitrogen dioxide and ozone exposures in the context of a multilevel epidemiological analysis. They found that combining outputs from different air pollution modeling approaches may reduce bias in health effect estimation.

Vodonos et al. (2018) in a systematic review of cohort studies examining the association between long-term exposure to $PM_{2.5}$ and mortality, found that differences of exposure assessment methodology may influence the effect size estimation.

Conversely, other studies found consistent results among different exposure methods (McGuinn et al., 2017; Wang et al., 2015).

Our study found consistent HR results among exposure models and resolution, although IQRs ranges showed some marked differences (5.1–16.7 and 2.5–13.6 $\mu g/m^3$ for $NO_2$ and $PM_{10}$, respectively). We found slightly higher estimates for coarser resolution estimates of exposure. Common data used to feed each model (emissions for FARM and PMSS models, FARM results as predictor for RF model) might have affected such results. Furthermore, we found differences among HRs results when they are calculated for increments of 10 $\mu g/m^3$ (see SM, Figure S5), particularly for models with the lower spatial resolution such as RF and FARM. We used increments of IQRs to compare consistently HRs among the different models and we provided HRs results for increment of 10 $\mu g/m^3$ for comparison with the correspondent literature values. However, the latter results might produce artefacts when comparing them among model, as the exposure ranges are very different among different models classes and resolutions (eg: PMSS, RF and FARM), including different levels of population exposure. In this study an increment of $NO_2$ concentration of 10 $\mu g/m^3$ is about twice the IQR of FARM model (5 $\mu g/m^3$), but only 62% of the corresponding value for PMSS model (about 16 $\mu g/m^3$). This produces differences in the corresponding estimations of HRs and their confidence intervals.

Our study has some strengths. First, this is the first long-term epidemiological study that uses an air dispersion model which includes the effect of flow around the buildings to assess the exposure with higher accuracy. This is particularly important considering the low dispersion conditions determined by the city's structure (e.g. street canyons and larger surface roughness caused by the presence of buildings, etc.), which might cause accumulation of pollutants. The spatial smoothing at different buffer sizes allowed evaluating not only the effects of the exposure at the residential address (4m data), but also the surroundings level. Hot spots produced by the urban structures can consequently be considered in the assessment of health effects.

Second, this study gave the opportunity to compare exposure results using this micro-scale approach with those provided by state of art methods like machine learning and CTM ones.

Third, an important aspect of this study is the comparison of health effects estimated from different types of exposure models. All these models have different approaches in estimating exposure, with different spatial resolutions and computational resources. Comparing HRs among such exposure data provides an added value to this study.

This work has some limitations. It included a portion of the whole city of Rome and, consequently, the full RoLS cohort population was not involved. This could limit its representativeness over the whole city, although both the study area and the resident population were chosen to keep differences as low as possible. In addition, the RoLS is a cohort built on administrative data and information on individual risk factors such as smoking habit, diet, alcohol consumption, BMI and obesity were not available. We adjusted for small-area socioeconomic position, which might be a predictor of smoking habits. In addition, the incomplete availability of occupational risk factors should be considered as respiratory and cardiovascular mortality are correlated with traditional and recently recognized work related risk factors (Wang et al., 2018; Kivimäki et al., 2006, 2015); respiratory mortality is significantly correlated with different occupations and jobs (GBD, 2016).

## 5. Conclusions

Our study provided pollutants exposure estimations using different methods from very fine (4m) to coarse (1 km) spatial resolutions for a portion ($12 \times 12$ km$^2$) of the city of Rome. Despite the differences in both the spatial details of the estimated pollutants maps provided by the models used, and the distribution of the cohort population exposure, the effect estimates for $NO_2$ and $PM_{10}$ exposure at the RoLS residential addresses for non-accidental and cardiovascular mortality were consistent among the exposure models when they are calculated for increment of IQR. In particular, the effect of buildings in the assessment of exposure did not seem to impact on estimation of long-term health effects. However, the variation of effect estimates when using fixed increments are noteworthy and should be considered for external comparisons and impact assessment.

## Funding

This work has been partially funded by the National Institute for Insurance against Accidents at Work, within the project “BEEP” (project code B72F17000180005).

The Rome Longitudinal Study is part of the National Statistical Program and was approved by the Italian Data Protection Authority.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.110351.

## Author contribution

Claudio Gariazzo: Conceptualization, Resources, Methodology, Writing - original draft; Giuseppe Carlino: Software, Formal analysis, Validation, Writing - original draft; Camillo Silibello: Software, Formal analysis, Validation, Writing - original draft; Gianni Tinarelli: Software, Formal analysis, Validation, Writing - original draft; Matteo Renzi: Resources, Software; Sandro Finardi: Resources, Software, Formal analysis; Nicola Pepe: Resources, Software, Formal analysis; Daniela Barbero: Software, Formal analysis, Validation; Paola Radice: Resources, Software, Formal analysis; Alessandro Marinaccio: Writing - review & editing; Francesco Forastiere: Writing - review & editing; Paola Michelozzi: Writing - review & editing; Giovanni Viegi: Project administration, Writing - review & editing; Massimo Stafoggia: Conceptualization, Methodology, Supervision, Writing - review & editing.

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