

HEALTH IMPACT OF TEMPERATURE AND AIR POLLUTION IN ITALY

Massimo Stafoggia (a), Francesca de' Donato (a), Carla Ancona (a), Andrea Ranzi (b), Paola Michelozzi (a)

(a) *Dipartimento di Epidemiologia, Servizio Sanitario Regione Lazio, ASL Roma 1, Rome (Italy)*

(b) *Centro tematico regionale Ambiente prevenzione e salute, Agenzia regionale per la prevenzione, l'ambiente e l'energia dell'Emilia-Romagna, Modena (Italy)*

Mortality impact of heat in Italy

The short-term effects of temperatures and extreme events have been extensively studied in environmental epidemiology (1, 2).

Heat has been related to an increase in total and cause-specific mortality as well as non-fatal outcomes such as hospital admissions, emergency room visits and ambulance calls (1-3). In particular, a non-linear association between temperature and mortality has been identified, specific to each geographic location with increases in the risk of mortality as temperatures rise above or go below a specific value (4).

The purpose of this study is to quantify the short-term impact of heat on mortality in Italy in the summer of 2015.

Estimate of mean temperature exposure

Daily mean air temperature with a spatial resolution of 1 km² (years 2001-2015) was derived using satellite Land Surface Temperature (LST); for observed temperature data and spatio-temporal land use and land cover predictors (5) see Appendix A for details.

Figure 1 shows the geographical distribution of average summer (June-August) daily mean air temperature in the study period (2003-2015).

Short-term effects of air temperature on all-cause mortality

Health data

Mortality data for 8,092 municipalities in Italy for the period 2003-2015 was collected. Individual all-cause mortality records with information on the municipality and the 110 provinces were retrieved from the National Institute of Statistics (Istituto Nazionale di Statistica, ISTAT).

Statistical analysis

A time series study was carried out to estimate the association between daily mean air temperature and all-cause mortality.

Firstly, we modelled municipality specific daily time-series within each province by applying the Distributed Lag Nonlinear model (DLNM) approach, a flexible technique that simultaneously considers the non-linear and lag structure of the association (4,6). Details of the model are described in Appendix B.

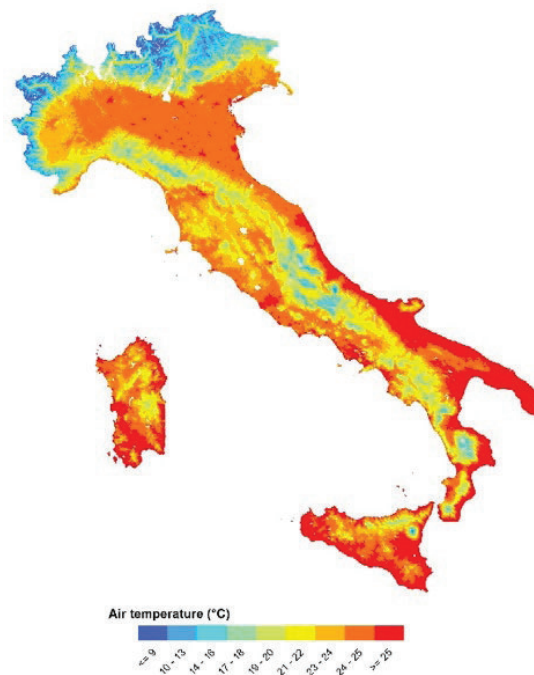


Figure 1. Average mean air temperature in Italy, Summer 2003-2015

Secondly, we pooled the reduced coefficients in a multivariate meta-regression to derive an overall national dose-response curve and the Best Linear Unbiased Prediction (BLUP) of the dose-response association in each province. Figure 2 shows the mean temperature-mortality curve for Italy with grey lines representing province specific curves and the bold coloured line the overall estimated curve (red heat effects, blue cold effects). The effect of heat was defined as the Relative Risk (RR), with 95% Confidence Intervals (95%CI) for temperature increases between the 75th and the 99th percentile.

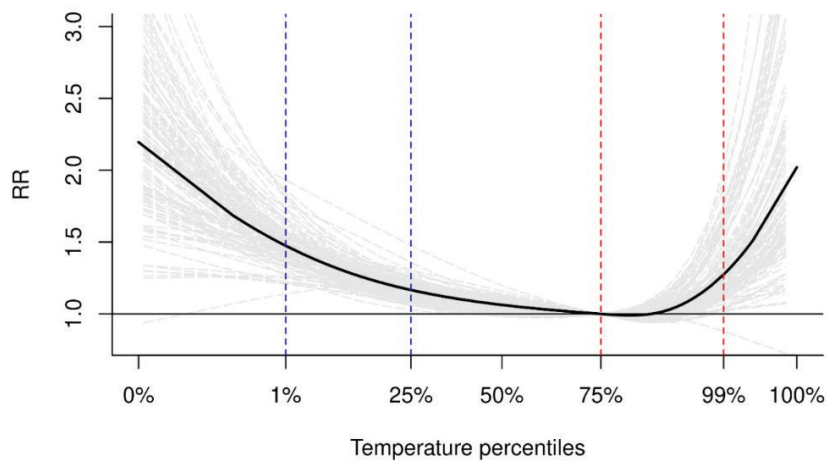


Figure 2. Mean temperature-mortality association for Italian provinces (grey curves) and overall curve for Italy (black line)

Heat attributable deaths in Italy

We used pooled associations to quantify the numbers of all-cause deaths attributable to heat during 2015. Specifically, on the same range of temperatures (75th to 95th percentile) we estimated the deaths attributable to heat, together with the attributable fraction (attributable deaths divided by the total number of observed deaths) and we calculated empirical 95%CI using Monte Carlo simulations. For 2015, a total of 14,521 deaths attributable to heat (temperatures between the 75th to 95th percentile) were estimated in Italy, corresponding to an attributable fraction of 2.3% of the total number of annual deaths (Table 1).

Table 1. Heat attributable deaths and fraction of total deaths in Italy in 2015

2015	Estimate	95%CI		
Attributable deaths (number)	14,521	9,870	-	18,975
Attributable fraction of total deaths (%)	2.3	1.5	-	2.9

This work is ongoing and aims to provide exposure and impact estimates for more recent years. Attributable deaths will also be reports by month, geographical area, age group and gender for each year to assess temporal variations in response to exposure and adaptation measures put in place from published literature showing a reduction in heat attributable deaths in Italy (7-9).

Health impact of particulate matter (PM) air pollution in Italy

The health risks associated long-term exposure to PM₁₀ and PM_{2.5} are of particular public health relevance. Both PM_{2.5} and PM₁₀ are capable of penetrating deep into the lungs but PM_{2.5} can even enter the bloodstream, primarily resulting in cardiovascular and respiratory impacts, and also affecting other organs (10). The WHO has published several volumes of Air Quality Guidelines (AQGs) to provide guidance to the public, especially to policy and other decision makers, on the health risks of air pollution. The new version was released on September 22, 2021 (11). In the guideline update, recommendations on AQG levels are formulated, together with interim targets. The WHO halved the recommended limits for average annual PM_{2.5} levels from 10 micrograms per cubic meter to 5. It also lowered the recommended limit for PM₁₀ from 20 to 15 micrograms. In Table 2, 2021 WHO AQG recommended level for PM are reported.

Table 2. 2021 WHO AQG recommended level and interim targets for PM_{2.5} and PM₁₀

Pollutant (µg/m ³)	Averaging time	Interim target				AQG level
		1	2	3	4	
PM _{2.5}	Annual	35	25	15	10	5
PM ₁₀	Annual	70	50	30	20	15

We aimed to quantify the short- and long-term impact of PM₁₀ and PM_{2.5} on the health of the Italian population. The short-term impact on mortality is already largely accounted for in the long-term impact on mortality and the two impact should not be added together. However, the

information remains interesting in order to present what could be a quick benefit of the decrease in AP concentration. A 2013 assessment by WHO's International Agency for Research on Cancer (IARC) concluded that outdoor air pollution is carcinogenic to humans, with the PM component of air pollution most closely associated with increased cancer incidence, especially lung cancer and secondarily with cancer of the urinary tract/bladder (12).

Estimate of particulate matter (PM) air pollution exposure

Estimates of daily mean concentrations of PM₁₀ (2006-2015) and PM_{2.5} (2013-2015) for each squared kilometre of Italy were obtained using a machine learning approach, the Random Forest, which leverages information from space-time predictors, satellite data, and air quality monitoring data. Details can be found in Stafoggia *et al.* 2019 (13). Figure 3 displays the annual average concentrations of PM₁₀ and PM_{2.5} for the year 2015.

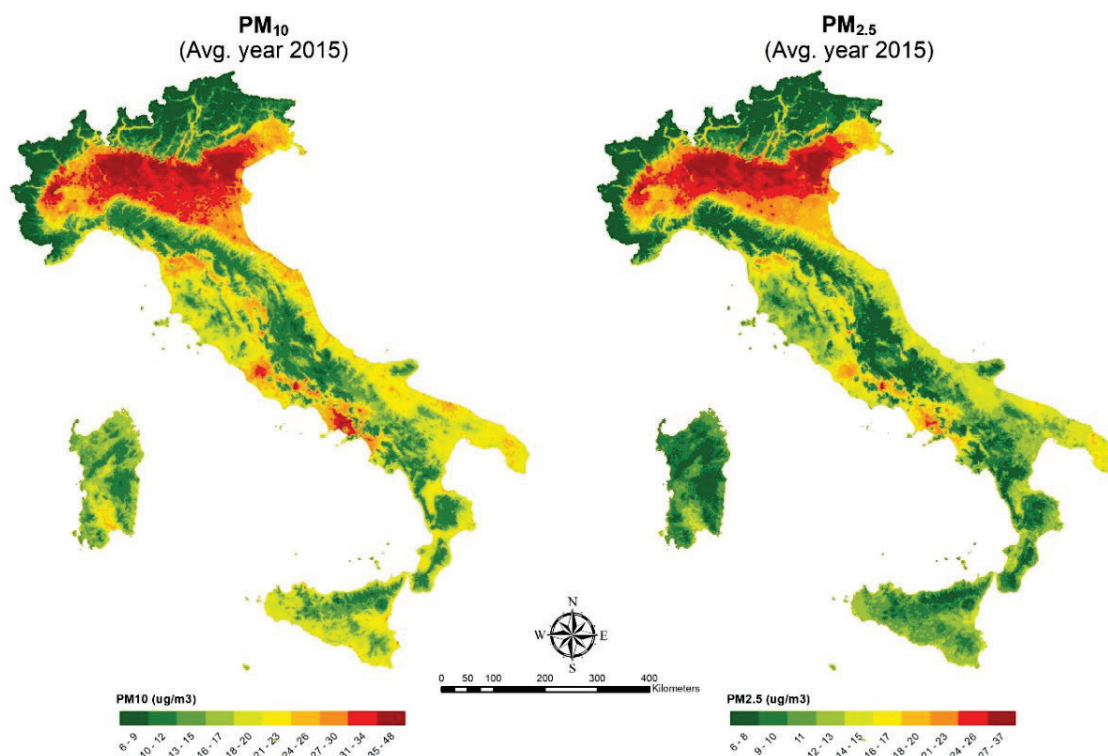


Figure 3. Annual average concentrations of PM₁₀ (left) and PM_{2.5} (right), Italy 2015

Short-term effects and impacts of particulate matter air pollution in Italy

Estimate of short-term effects of PM₁₀ and PM_{2.5} on all-cause mortality

In order to evaluate the association between short-term (e.g., daily) exposure to either PM₁₀ or PM_{2.5}, and all-cause mortality we adopted a multi-stage approach, consisting of mortality data collection, production of municipality-specific time series, fitting of Poisson regression multivariable model in each Italian province, and meta-analysis of the province-specific

regression coefficients. We obtained from ISTAT daily counts of mortality (all causes, both sexes, all ages) for each one of the 8,092 municipalities of Italy, for the period 2006-2015.

Daily mean concentrations of PM₁₀ (2006-2015) and PM_{2.5} (2013-2015) at the municipality level were derived by averaging, for each municipality, values of all the squared kilometre grid cells intersecting the municipality. Municipality-specific daily time series of potential confounders such as daily mean air temperature, weekly regional flu epidemics, bank holidays and summer population decrements were also collected. We fitted province-specific Poisson regression models, so obtaining, for each of the 110 Italian provinces, estimates of RR and 95% CI of all-cause mortality per unit increment of PM₁₀ (for the period 2006-2015) or PM_{2.5} (for the period 2013-2015), in turn. Finally, we ran random-effects meta-analytical techniques on the province-specific estimates and derived a national estimate of the association between short-term exposure to PM₁₀ and PM_{2.5} with all-cause mortality.

Table 3 reports the association between daily concentrations of PM₁₀ and PM_{2.5} (at different lags) and all-cause mortality, in Italy.

Table 3. Association* between daily mean PM concentrations (at different lags) and all-cause daily mortality in Italy: percent increases of risk (%IR), and 95% confidence intervals (95%CI) for 10 mg/m³ increment in the pollutant

Pollutant	Study period	Lag	IR%	95%CI	
PM ₁₀	2006-2015	0	0.71	0.53	0.88
		0-1	0.76	0.61	0.91
		2-5	0.45	0.26	0.64
		0-5	0.80	0.58	1.01
PM _{2.5}	2013-2015	0	1.17	0.77	1.56
		0-1	0.86	0.60	1.12
		2-5	0.29	0.02	0.55
		0-5	0.72	0.34	1.09

* Boxes around lag 0 estimates, i.e., those used for short-term impact assessment estimation

Short-term impacts of PM₁₀ and PM_{2.5} on all-cause mortality

The estimated pooled associations were used to quantify the numbers of all-cause deaths attributable to daily exceedances in PM₁₀ and PM_{2.5} above predefined thresholds during 2015. Methodological details are reported in Appendix C.

Table 4 reports the numbers of all-cause deaths attributable to PM levels exceeding predefined 24-hour thresholds in Italy during 2015: the thresholds internationally recognized as standards for PM₁₀ and PM_{2.5} are reported in grey (WHO AQG 2005) and in blue (WHO AQG 2021).

Exceedances of the threshold of 15 µg/m³ for PM_{2.5} occurred on 35.6% of the days and were responsible for an extremely high impact: an intervention able to contain daily PM_{2.5} levels below 15 µg/m³ would have prevented 4.773 deaths – 95%CI 3.183-6.345. Similarly, had daily PM₁₀ concentrations always been below 45 µg/m³, 1.021 (769-1.272) deaths would have been prevented.

Table 4. All-cause deaths attributable to PM levels exceeding predefined thresholds, Italy 2015

Pollutant	Threshold ($\mu\text{g}/\text{m}^3$)	% days \geq threshold	n. deaths	AD	95%CI		AF (%)
PM ₁₀	50	5.7	63,655	772	581	961	1.2
	45	7.4	80,183	1,021	769	1,272	1.3
	40	9.6	102,405	1,336	1,007	1,664	1.3
	35	12.8	134,344	1,743	1,313	2,170	1.3
	30	18.1	190,699	2,298	1,732	2,862	1.2
	25	27.8	286,130	3,117	2,348	3,881	1.1
	20	44.3	414,707	4,333	3,265	5,396	1.0
PM _{2.5}	25	14.1	132,299	2,460	1,641	3,270	1.9
	20	21.1	192,413	3,367	2,246	4,476	1.8
	15	35.6	316,583	4,773	3,183	6,345	1.5
	10	67.6	521,715	7,146	4,764	9,503	1.4

In grey WHO AQG 2005; in blue WHO AQG 2021

95%CI 95% Confidence Interval; **AD** Attributable Deaths; **AF** Attributable Fraction

Long-term health effects of PM₁₀ and PM_{2.5} from the epidemiological literature

A systematic review of evidence of associations between long-term exposure to PM_{2.5} in relation to all-cause and cause-specific mortality found a combined Risk Ratio for PM_{2.5} and natural-cause mortality equal to 1.08 (95%CI 1.06-1.09) per 10 $\mu\text{g}/\text{m}^3$ (14).

The combined effect estimate was larger for cardiovascular (particularly ischemic heart disease) than for natural-cause mortality associated with exposure to PM_{2.5}.

The European multicentre study ESCAPE (European Study of Cohorts for Air Pollution Effects, www.escapeproject.eu) studied the chronic effects of air pollution in cohorts of adult subjects. ESCAPE results highlighted the existence of an association between chronic exposure to air pollutants and natural mortality and cardiovascular events (15-18) and cancer of the lung, brain, breast and digestive system (19-21).

Table 5 reports the estimates of association between long-term exposure to PM and cause-specific mortality from the literature.

Table 5. Association between exposure to PM_{2.5} and PM₁₀ and cause specific mortality from literature: relative risk (RR) and 95%CI for increments of 10 $\mu\text{g}/\text{m}^3$

Cause specific mortality	ICD9	ICD10	Age in years	PM _{2.5} RR	95% CI			PM ₁₀ RR	95%CI	
Natural mortality	001-629; 677-799			1.08	1.06	1.09		1.04	1.03	1.06
Lung cancer	162	C33 C34	30+	1.12	1.07	1.16		1.08	1.04	1.13
Cardiovascular diseases	390-459	I		1.11	1.09	1.14		1.04	0.99	1.10
Respiratory diseases	460-519	J		1.10	1.03	1.18		1.12	1.06	1.19

Long-term impacts of PM₁₀ and PM_{2.5} on all-cause mortality

The impact of long-term exposure to PM_{2.5} was estimated according to the Integrated Environmental Health Impact Assessment (IEHIA, www.integrated-assessment.eu) methodology which involves the definition of target population, the estimation of the Population Weighted Exposure, the choice of adequate Concentration-Response Functions (FCR) and a basic understanding of the disease and mortality rates of the population.

The population data (people aged 30 and over) used for the IEHIA of PM_{2.5} and PM₁₀ were referred to 2020 and provided by ISTAT at census block level. Population exposure was obtained using the 4-stage Random Forest (13).

The cause specific mortality rates were provided by the Statistics Service of the Istituto Superiore di Sanità based on official data of ISTAT, in compliance with the Regulation (EU) 2016/679 for General Data Protection (GDPR).

The model was updated to the most recent years (2016-2019), in collaboration with the Italian Institute for Environmental Protection and Research (ISPRA, Istituto Superiore per la Protezione e la Ricerca Ambientale) with a spatial resolution of 1x1 km.

The concentration-response functions for mortality (natural, respiratory and cardiovascular) and lung cancer were taken from the last publication from the WHO working group (14). Thresholds of 10 µg/m³ for PM_{2.5}, 20 for PM₁₀, were applied in the assessment, following WHO recommendations on the HIA procedure. Further evaluation was provided for the just published updated thresholds for pollutants (11).

The estimates of the long-term impacts of PM_{2.5} and PM₁₀ on cause-specific mortality in Italy (2016-2019) are reported in Tables 6 and 7, respectively.

Table 6. PM_{2.5} long-term exposure attributable deaths, Italy (2016-2019)

Area	Population	PWE	Threshold: 10 mg/m³				Threshold: 5 mg/m³			
	30+	(mg/m³)	AD	95% CI		AF (%)	AD	95% CI		AF (%)
Natural causes										
Italy	42 952 673	16.5	28906	22083	32225	4.69	50856	38974	56608	8.26
North	19 354 371	20.5	20841	15952	23213	7.45	30589	23507	34003	10.93
Central	8 664 082	14.5	3916	2979	4375	3.10	8511	6501	9489	6.75
South	14 934 220	12.6	4149	3152	4637	1.98	11755	8966	13115	5.60
CVD										
Italy	42 952 673	16.5	13536	11273	16785	2.20	24125	20152	29788	3.92
North	19 354 371	20.5	9484	7914	11727	3.38	13884	11630	17073	4.95
Central	8 664 082	14.5	1911	1586	2384	1.52	4145	3452	5140	3.30
South	14 934 220	12.6	2141	1774	2674	1.02	6096	5070	7575	2.91
RESP										
Italy	42 952 673	16.5	2662	852	4471	0.43	4638	1502	7701	0.75
North	19 354 371	20.5	1945	627	3244	0.69	2853	932	4692	1.01
Central	8 664 082	14.5	371	117	634	0.30	799	256	1344	0.64
South	14 934 220	12.6	346	109	593	0.17	986	314	1665	0.47

PWE Population Weighted Exposure

CVD CardioVascular Diseases

RESP Respiratory diseases

AD Attributable Deaths

AF Attributable Fraction

Table 7. PM₁₀ long-term exposure attributable deaths, Italy (2016-2019)

Area	Population	PWE	Threshold: 10 mg/m³				Threshold: 5 mg/m³			
	30+	(mg/m³)	AD	95% CI		AF (%)	AD	95% CI		AF (%)
Natural causes										
Italy	42 952 673	24.9	12291	9307	18091	2.00	22745	17248	33385	3.70
North	19 354 371	28.2	9010	6828	13242	3.22	13954	10594	20430	4.98
Central	8 664 082	22.4	1337	1010	1977	1.09	3503	2651	5162	2.85
South	14 934 220	21.7	1943	1468	2872	0.93	5288	4002	7792	2.53
CVD										
Italy	42 952 673	24.9	4270	0	10102	0.69	8034	0	18855	1.31
North	19 354 371	28.2	3056	0	7197	1.08	4754	0	11073	1.67
Central	8 664 082	22.4	479	0	1148	0.39	1268	0	3008	1.04
South	14 934 220	21.7	735	0	1757	0.35	2012	0	4774	0.96
RESP										
Italy	42 952 673	24.9	2561	1353	3818	0.42	4658	2480	6887	0.76
North	19 354 371	28.2	1898	1007	2817	0.67	2905	1557	4264	1.02
Central	8 664 082	22.4	295	154	445	0.24	754	397	1127	0.62
South	14 934 220	21.7	368	192	556	0.18	999	526	1495	0.48

PWE Population Weighted Exposure**CVD** CardioVascular Diseases**RESP** Respiratory diseases**AD** Attributable Deaths**AF** Attributable Fraction

PM_{2.5} Population Weighted Exposure in Italy in the period 2016-2019 is equal to 16.5 mg/m³ (20.5 in North Italy and 12.6 in South Italy). This value is under the EU law limit (25 mg/m³ as annual mean) but it exceeds the 2021 WHO AQG recommended value by more than three times (more than 4 in the North of Italy).

According to the 2021 WHO limits every year PM_{2.5} is responsible of 50,856 deaths in Italy (8.3% of national mortality for all natural causes, with higher values (11%) in the Northern part of Italy).

Every year 22,745 deaths are attributable to PM₁₀, 3.7% of mortality for all natural causes, with higher values (5%) in the Northern part of Italy. These deaths would not occur if the levels of concentrations of these pollutants did not exceed the values set by 2021 WHO AQG to protect health.

Most of the deaths attributable to air pollution in Italy are due to cardiovascular diseases.

Data on lung cancer mortality are underestimated, due to limited availability of municipality data by age classes only for privacy rules. Available data indicate 13% as a fraction attributable to PM_{2.5} exposure for lung cancer mortality when the 2021 WHO AQG threshold is considered.

Results confirm that ambient air pollution is the environmental risk factor causing the largest measurable health impact. As such, the leverage of preventive action is substantial: most, if not all, climate change mitigation policies in transport, energy, industry, agriculture etc would entail reductions in concentrations of air pollutants, in turn resulting in preventing large numbers of premature deaths and disease.

References

1. Benmarhnia T, Deguen S, Kaufman JS, Smargiassi A. Review Article. *Epidemiology*. 2015 Nov;26(6).
2. Cheng J, Xu Z, Bambrick H, Prescott V, Wang N, Zhang Y, *et al.* Cardiorespiratory effects of heatwaves: A systematic review and meta-analysis of global epidemiological evidence. *Environmental Research*. 2019 Oct;177.
3. Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S. Ambient temperature and morbidity: a review of epidemiological evidence. *Environmental Health Perspectives*. 2012 Jan;120(1).
4. Gasparrini A, Leone M. Attributable risk from distributed lag models. *BMC Medical Research Methodology*. 2014 Dec 23;14(1).
5. de'Donato F. The use of satellite data, meteorology and land use data to define high resolution temperature exposure for the estimation of health effects in Italy. [London]; 2019. Available from: <https://spiral.imperial.ac.uk/bitstream/10044/1/77795/1/dedonato-FK-2019-PhD-Thesis.pdf>
6. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Statistics in Medicine*. 2010 Sep 20;29(21).
7. Schifano P, Leone M, de Sario M, de' Donato F, Bargagli AM, D'Ippoliti D, *et al.* Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environmental Health*. 2012 Dec 3;11(1).
8. de'Donato F, Scortichini M, de Sario M, de Martino A, Michelozzi P. Temporal variation in the effect of heat and the role of the Italian heat prevention plan. *Public Health*. 2018 Aug;161.
9. Scortichini M, de'Donato F, de Sario M, Leone M, Åström C, Ballester F, *et al.* The inter-annual variability of heat-related mortality in nine European cities (1990-2010). *Environmental Health*. 2018 Dec 8;17(1).
10. Thurston GD, Kipen H, Annesi-Maesano I, Balmes J, Brook RD, Cromar K, *et al.* A joint ERS/ATS policy statement: what constitutes an adverse health effect of air pollution? An analytical framework. *European Respiratory Journal*. 2017 Jan;49(1).
11. WHO. *WHO global air quality guidelines: particulate matter (PM_{2.5} and PM₁₀), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide*. Geneva: World Health Organization; 2021. Available from: <https://apps.who.int/iris/handle/10665/345329>
12. Hamra GB, Guha N, Cohen A, Laden F, Raaschou-Nielsen O, Samet JM, *et al.* Outdoor particulate matter exposure and lung cancer: a systematic review and meta-Analysis. *Environmental Health Perspectives*. 2014 Sep;122(9).
13. Stafoggia M, Bellander T, Bucci S, Davoli M, de Hoogh K, de' Donato F, *et al.* Estimation of daily PM₁₀ and PM_{2.5} concentrations in Italy, 2013–2015, using a spatiotemporal land-use random-forest model. *Environment International*. 2019 Mar;124.
14. Chen J, Hoek G. Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis. *Environment International*. 2020 Oct;143.
15. Cesaroni G, Forastiere F, Stafoggia M, Andersen ZJ, Badaloni C, Beelen R, *et al.* Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. *BMJ*. 2014 Jan 21;348(jan21 3).
16. Beelen R, Stafoggia M, Raaschou-Nielsen O, Andersen ZJ, Xun WW, Katsouyanni K, *et al.* Long-term exposure to air pollution and cardiovascular mortality. *Epidemiology*. 2014 May;25(3).
17. Stafoggia M, Cesaroni G, Peters A, Andersen ZJ, Badaloni C, Beelen R, *et al.* Long-term exposure to ambient air pollution and incidence of cerebrovascular events: results from 11 european cohorts within the ESCAPE Project. *Environmental Health Perspectives*. 2014 Sep;122(9).

18. Fuks KB, Weinmayr G, Basagaña X, Gruzieva O, Hampel R, Oftedal B, *et al.* Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the European study of cohorts for air pollution effects (ESCAPE). *European Heart Journal*. 2016 Oct 24;
19. Raaschou-Nielsen O, Andersen ZJ, Beelen R, Samoli E, Stafoggia M, Weinmayr G, *et al.* Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE). *The Lancet Oncology*. 2013 Aug;14(9).
20. Nagel G, Stafoggia M, Pedersen M, Andersen ZJ, Galassi C, Munkenast J, *et al.* Air pollution and incidence of cancers of the stomach and the upper aerodigestive tract in the European Study of Cohorts for Air Pollution Effects (ESCAPE). *International Journal of Cancer*. 2018 Oct 3;143(7).
21. Andersen ZJ, Stafoggia M, Weinmayr G, Pedersen M, Galassi C, Jørgensen JT, *et al.* Long-term exposure to ambient air pollution and incidence of postmenopausal breast cancer in 15 European cohorts within the ESCAPE Project. *Environmental Health Perspectives*. 2017 Oct 3;125(10).