

BMJ Open Do exposure to outdoor temperatures, NO₂ and PM₁₀ affect the work-related injuries risk? A case-crossover study in three Italian cities, 2001–2010

Patrizia Schifano,¹ Federica Asta,¹ Alessandro Marinaccio,² Michela Bonafede,² Marina Davoli,¹ Paola Michelozzi¹

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¹Department of Epidemiology, Lazio Regional Health Service, Rome, Italy

²Occupational and Environmental Medicine, Epidemiology and Hygiene Department, Italian Workers' Compensation Authority (INAIL), Rome, Italy

Correspondence to

Dr Federica Asta;
f.asta@deplazio.it

ABSTRACT

Objectives Studies on the effect of temperature on rates of work-related injuries (WRIs) are very recent, and are evolving in depth and scope. However, less is known about potential effects of air pollutants. Our objective was to analyse the association between WRI and NO₂, PM₁₀ and air temperature in three major Italian cities, and to identify groups of workers more at risk in Italy.

Design Time-stratified case-crossover study.

Settings Milan, Turin, Rome, years 2001–2010.

Participants A total of 468 816 WRI occurred between 2001 and 2010 in Milan, Turin and Rome were extracted from the Italian national workers' compensation authority database.

Main outcomes Associations between WRI and temperature, PM₁₀, NO₂, separately in the warm and in the cold season (WS, May–September; CS, November–February). Effect modification was studied by economic sector, occupational activity and indoor/outdoor job activity.

Results Exposure to NO₂ (lag 0–8) showed the highest effect on the risk of WRI, with ORs ranging from 1.20 (95% CI 1.16 to 1.24) in Milan to 1.30 (95% CI 1.24 to 1.37) in Turin in the WS. The effect of exposure to PM₁₀ was milder but consistent across all cities: ORs from 1.09 (95% CI 1.05 to 1.12) in Turin to 1.15 (95% CI 1.11 to 1.18) in Rome. Temperature was associated with risk of WRI only among those working in construction (highest association in Rome 1.06; 95% CI 1.01 to 1.12), transportation (highest association in Milan 1.05; 95% CI 0.96 to 1.14) and the energy industry (highest association in Milan 1.57; 95% CI 1.03 to 2.38) in the WS in all cities. A weak effect of low temperatures was observed in the CS only in Rome.

Conclusions Exposures to NO₂ resulted as strongest hazard for WRIs, mainly in warm months, while the independent effect of temperature was significant only in specific subgroups of workers. These results could be considered to better plan safety prevention programmes.

BACKGROUND

Extreme weather events are becoming more frequent and intense as a result of climate change¹ and the relationship between extreme temperature and population health has been well documented.² Furthermore, air quality is influenced by a changing climate,

Strengths and limitations of this study

- We used a very large dataset that was not derived from self-reported data.
- We analysed data from three major Italian cities with different meteorological and pollution condition.
- We estimated the independent effects of temperature and air pollution, controlling one for the other in the model.
- Daily injury claims may be underestimated because of under-reporting of workers' compensation claims and due to incomplete coverage of the public insurance system lead by Italian national workers' compensation authority.
- All exposure measures used were daily averages deriving from fixed points of measurement in the city.

which in turn impacts population health.³ The association between outdoor temperature and air pollutants with mortality and morbidity in the general population has stimulated a large body of research, identifying susceptible subgroups, such as the elderly, people with chronic respiratory and cardiovascular diseases, and children.^{4,5}

However, the consequences of climate and pollutants on work environments and their subsequent effects on job performance and safety are only recently coming to light.

Numerous factors such as worksite location and weather conditions may affect occupational exposure to air pollution; and likewise, indoor workplace environments may affect and exacerbate the adverse health effects of exposure to outdoor air pollutants. This is particularly a concern in workers with pre-existing health conditions and could theoretically lead to an increase in safety issues. The association between intense and prolonged occupational exposure to heat and health effects on workers is characterised

by dehydration and spasms, increased perceived fatigue, exacerbating hazards resulting from sweaty palms, fogged-up safety glasses, dizziness, and reduced brain function, reduced productivity and decreased reaction capacities.^{6–11} Young, male workers and those in occupations requiring physical labour, and outdoor workers, are at higher risk of adverse impact because of their exposure to heat and humid conditions, as well as prolonged exposure to solar radiation and/or other artificial heat sources.^{12–15} Furthermore, cultural social and ethnical characteristics of workers could play a significant role.¹⁶ As well, workers exposed to extreme cold may be at risk of cold stress, increased cardiovascular and respiratory diseases risks, musculoskeletal and dermatological disorders, loss of dexterity and injuries related to hypothermia.^{7,17}

There is good evidence of the negative effects of short-term exposure to PM₁₀ on respiratory health, such as aggravated asthma, respiratory symptoms and an increase in hospital admissions.¹⁸ Nitrogen dioxide (NO₂) is a strong respiratory irritant gas originating from high-temperature combustion; a large study has shown a positive association between daily increases of NO₂ and natural, cardiovascular and respiratory mortality.¹⁹ Also, air pollution has been shown to negatively affect other outcomes such as productivity of agricultural workers.²⁰ To the best of our knowledge, there is a lack of study on the association between air pollution and occupational injuries. Only recently, acute neuropsychological effects have been studied on humans by Sunyer *et al*²¹ showing an acute effect of air pollution on fluctuations in attention in children that probably arises through the same mechanism as the long-term association. A recent review²² on this topic stated there is consistent evidence from animal studies showing impairments for short term memory due to air pollution exposure these deteriorations could be involved also as potential explanation of work-related injuries (WRIs). Another potential mechanism of action that could be involved occurs through acute cardiovascular events triggered by air pollution²³ and leading to a decreased level of attention and lower capacity of reaction to unexpected dangerous situations at work as an acute secondary effect of this correlation.

In addition, levels of exposure to pollutants might also vary according to several factors, such as socio economic status (SES), educational level, air conditioning use, proximity to roadways, and work environment.²⁴

The warm season has been seen to be the strongest effect modifier of the effect of some pollutants on natural mortality^{25,26}; this might be due to the fact that in summer, measured concentrations of air pollutants are more representative of true exposure because people spend more time outside and open windows more often.

A recently published review²⁷ summarised what is known about the heat and cold effects on WRIs, and identified categories of workers at risk and evaluated heterogeneity and sources of bias of the included studies. Authors concluded that most studies had design limitations with

regards to establishing a causal relationship and underlined the need for good quality studies that provide accurate estimates of relative risk of heat effects on occupational injuries.

The objective of this study is to estimate the short-term effects of summer and winter outdoor temperatures and air pollution on the risk of WRIs, and to identify susceptible groups of workers.

METHODS

Study population

We examined all work injuries that occurred between May and September and between November and February in the years 2001–2010 in three major Italian cities: Milan, Turin and Rome.

Data were extracted from the Italian national workers' compensation authority (INAIL) database, which covers about 85% of Italian workers. For each injury episode that caused absences of three or more days, we gathered sociodemographic characteristics, occupation, and job title, and modalities and causes of the injury. Injuries in subjects younger than 17 years of age were excluded.

Meteorological and air pollution data

Rome, Milan and Turin are large metropolitan areas with different climatic conditions. Milan and Turin are located in Northern Italy and have a cold humid subtropical or mild continental climate, characterised by hot, humid summers with frequent thunderstorms and cold, damp winters often featuring fog in low-lying areas. Rome is located in central Italy 20 km from the Tyrrhenian Sea and has a typical Mediterranean climate with hot, dry summers and mild, wet winters.

Based on previous heat studies conducted in the same cities we chose maximum daily apparent temperature (MAT)^{28–30} for the warm season (May–September),³¹ and maximum daily temperature (TMAX) for the cold season (November–February) as indicators of temperature.³² The choice of using two different indicators in the two seasons was driven by statistical reasons; we choose, among the more common indicators used, the one with the best akaike information criterion (AIC) values. These were measured at the airport station closest to each city.

With regards to air pollutants, we used the 24 hours mean daily value of nitrogen dioxide (NO₂) and of particulate matter with an aerodynamic diameter of 10 µm (PM₁₀). Data were extracted from the Regional Environmental Protection Agency; values were obtained by averaging monitor-specific daily measurements available from different monitoring stations; we used city-specific daily mean values for all subjects.³³

Statistical analysis

The analysis was organised in three steps. Because not much is already known about the relationship between WRIs and temperature and air pollution variations, we first explored the city and season-specific lag structures

of each exposure. We used a non-linear distributed lag model,³⁴ allowing a maximum lag structure of 30 days, with the aim of selecting the lags showing the strongest association, using crossbasis centred on the median values of each exposure distribution using a natural cubic spline with df equals 4. As a second step we checked the linearity of the environmental exposure-injury risk relationship, at the lag defined by the previous step, through a Poisson generalised additive model, in each city and season. In both steps models were adjusted for long and seasonal trends using a triple interaction between year, month and day of the week, for holiday days and for influenza epidemics (only in cold season models).

As a third step the effect of environmental exposures on work-injury risk was evaluated using a time stratified case-crossover design separately for each city.³⁵ For each 'case' (the day a work injury occurred) three more days were chosen as controls, matched by day of the week, month and year with the case day, to control for long-term trends, seasonality and day of the week. We estimated ORs and 95% CIs through a conditional logistic regression model, further adjusted for holidays and influenza epidemics (only in the cold season). Models were exposure, season and city specific. Lags and shapes of the relationship were those defined in the previous two steps. Lagged exposure was computed as the average exposure in the days identified by the lag.

We adjusted one exposure with the others in the model only when their correlation was lower than 0.4.

We tested potential effect modification of the environmental exposure-injury risk relationship by economic sectors (using the Statistical Classification of Economic Activities in the European Community, 'Rev. 2–2008'), time spent outdoors or indoors (indoor/outdoor job activity) and occupational activity, including an interaction term between each variable and the exposure in the model.

Patient and public involvement

Patients and or public were not involved in this study.

RESULTS

Study population

We analysed a total of 468 807 WRIs, that is about 52 000 per month independently by the season (table 1).

Meteorological and air pollutants data

Warm season

Rome and Milan showed a common median value of MAT of about 28°C, while Turin showed a median MAT of 26°C. Rome had the higher minimum value for MAT (online supplementary eTable 1). As for pollution, values were quite similar in the three cities; we observed a moderate correlation between PM₁₀ and NO₂ ($\rho \geq 0.5$) in all cities and between MAT and PM₁₀ ($\rho = 0.4$) in Rome (online supplementary eTable 2).

Table 1 Injury distribution by workers' demographic and job characteristics, 2001–2010

	Warm season	Cold season
Total: 468 807	262 804	206 003
Age group, n (%)		
<30	60 599 (23.0)	48 408 (23.5)
30–50	158 086 (60.2)	121 997 (59.2)
>50	44 119 (16.8)	35 598 (17.3)
Gender, n (%)		
Male	165 054 (62.8)	124 671 (60.5)
Female	97 750 (37.2)	81 332 (39.5)
Economic sector, n (%)		
Transport	31 914 (12.1)	24 257 (11.8)
Agro-industry	1242 (0.5)	969 (0.5)
Fishery	2 (0.0)	2 (0.0)
Mineral extraction	179 (0.1)	140 (0.1)
Electricity gas and water	1725 (0.7)	1418 (0.7)
Construction	23 373 (8.9)	16 208 (7.9)
Food, textile and wood industry	6588 (2.5)	5264 (2.5)
Electrical, chemical, petrochemical and rubber processing industry	8445 (3.2)	6511 (3.2)
Mechanical and metallic industry	10 860 (4.1)	7413 (3.6)
Business and food service	44 810 (17.0)	34 690 (16.8)
Healthcare system	14 719 (5.6)	11 980 (5.8)
Public services, financial activities	118 947 (45.3)	97 151 (47.2)
Indoor/outdoor job activity, n (%)		
Indoor	105 215 (40.0)	87 578 (42.5)
Indoor high temperature exposure	7099 (2.7)	5669 (2.8)
Indoor/outdoor	88 231 (33.6)	65 299 (31.7)
Outdoor	23 585 (9.0)	16 442 (8.0)
Missing	38 674 (14.7)	31 015 (15.0)

Cold season

Rome was the warmest city with a median TMAX of 13°C, while Turin and Milan were cooler and had similar median TMAX values of about 8°C. We observed a minimum of –8°C for TMAX in Turin and of –3°C in Milan, while Rome never went below 5°C of TMAX (online supplementary eTable 1). As for air pollution we observed similar values of NO₂ in the three cities, and higher values of PM₁₀ in Turin and Milan (online supplementary eTable 1). We observed positive correlations between PM₁₀ and NO₂ in Turin ($\rho = 0.5$) and Milan ($\rho = 0.6$) (online supplementary eTable 2).

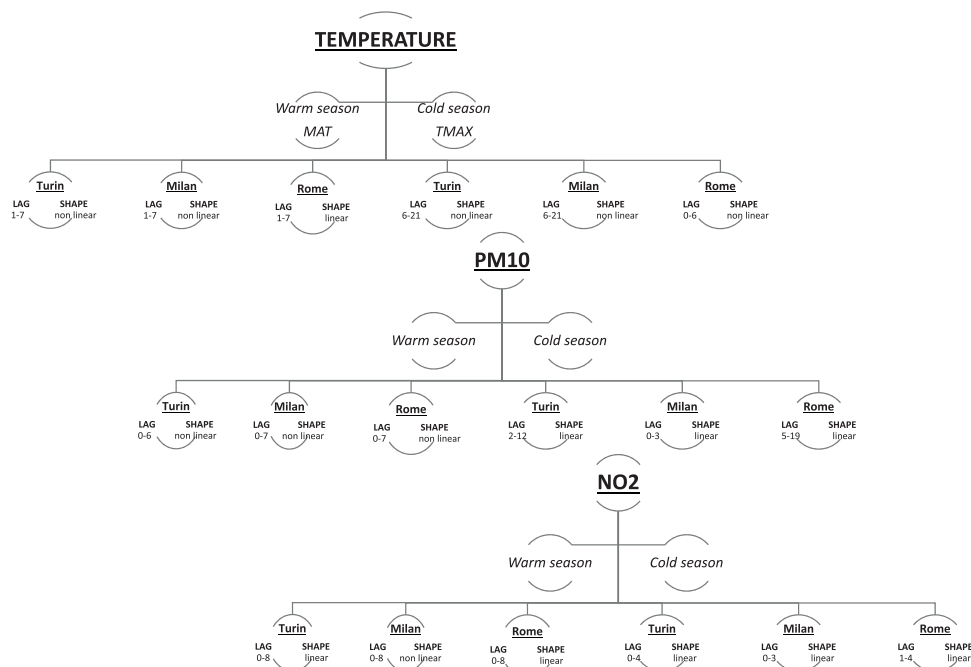


Figure 1 Graphical summary of lags and shapes of exposures/WRI relationship (linear/non-linear) by season and city. MAT, maximum daily apparent temperature; TMAX, maximum daily temperature; WRI, work-related injury.

Lag structure and shape of the exposure-work injury relationship (step 1 and step 2)

Analysis of the lag structure indicated a delayed effect on injury risk for all analysed exposures; during the warm period the greatest effects were observed within the first week after exposure, while in the cold period effects could persist up to 20 days (online supplementary eFigures 1–3). A summary, for all exposures, of chosen lags and of the shape of relationship (linear/non-linear) with WRI risk were reported in [figure 1](#).

In the warm period the WRI/temperature relationship was linear in Rome (online supplementary eFigure 4) and non-linear in Turin and Milan. In these two cities we estimated ORs comparing city-specific MAT levels chosen in order to maximise the contrast. These points were identified by observing the injury-temperature relationship in online supplementary file 1. In particular, we compared the 90th percentile (33°C) versus the 50th (26°C) in Turin and 90th percentile (34°C) versus the 10th (21°C) in Milan; results for Rome were reported for the interquartile range (32°C vs 24°C). As for air pollutants, the PM₁₀/WRI relationship was linear in Rome and non-linear in Turin and Milan (online supplementary eFigure 5), while the NO₂/WRI relationship was linear in Rome and Turin and non-linear in Milan (online supplementary eFigure 6).

In the cold months, the WRI/temperature relationship was non-linear in the three cities (online supplementary eFigure 4). As for the warm period we estimated ORs comparing city-specific TMAX's levels in order to maximise the effect in each city; in particular we compared the 10th percentile (4°C) versus the first percentile (2°C) in Turin, the 25th percentile (6°C) versus the fifth (4°C)

in Milan and the 25th percentile (10°C) versus the fifth (8°C) in Rome. Air pollutants–WRI relationship was linear in all the three cities for both PM₁₀ and NO₂. In both climatic periods we estimated effects comparing the 95th percentile versus the 25th when the relationship was non-linear and for one unit increase when it was linear. Results were always reported for the 95th percentile versus the 25th (online supplementary eFigure 5 and 6).

Conditional logistic regression models (step 3)

In the warm season, the univariate analysis showed a positive association between WRI and MAT, PM₁₀ and NO₂ in all cities. In the cold season, we observed an inverse association between WRI and TMAX and a positive one between WRI and NO₂ in all cities, and between WRI and PM₁₀ only in Rome.

When adjusting temperature for one pollutant at a time in the warm months, the association with WRI resulted to be non-significant, while there was a positive significant effect when adjusting for temperature of both PM₁₀ and NO₂ in all cities; in the cold months we observed a significant association of NO₂ with WRI in all cities, and of TMAX and PM₁₀ in Rome. We reported only adjusted estimates ([table 2](#)).

Effect of NO₂

Exposure to NO₂ showed the highest positive association with the risk of being injured at work in both seasons and in all cities. In the warm season, an increase of NO₂ from the 25th to the 95th percentile was associated with an increase in work injuries ranging between 1.20 (95% CI 1.16 to 1.24) in Milan and 1.30 (95% CI 1.24 to 1.37) in Turin; in the cold season the effect of NO₂ was lower,

Table 2 Adjusted ORs of work-related injury for temperature and air pollutants levels variations in Turin, Milan and Rome. Period 2001–2010

Environmental exposures	OR (95% CI)	Comparison (percentile)
Warm season (May–September)*		
Turin		
Daily maximum apparent temperature (°C) (Lag† 1–7)‡	1.02 (0.99 to 1.06)	90th versus 50th
PM ₁₀ (µg/m ³) (Lag† 0–6)§	1.09 (1.05 to 1.12)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 0–8)§	1.30 (1.24 to 1.37)	95th versus 25th
Milan		
Daily maximum apparent temperature (°C) (Lag† 1–7)‡	1.01 (0.98 to 1.04)	90th versus 10th
PM ₁₀ (µg/m ³) (Lag† 0–7)§	1.13 (1.10 to 1.16)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 0–8)§	1.20 (1.16 to 1.24)	95th versus 25th
Rome		
Daily maximum apparent temperature (°C) (Lag† 1–7)‡	1.00 (0.99 to 1.02)	75th versus 25th
PM ₁₀ (µg/m ³) (Lag† 0–7)§	1.15 (1.11 to 1.18)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 0–8)§	1.22 (1.16 to 1.28)	95th versus 25th
Cold season (November–February)¶		
Turin		
Daily maximum temperature (°C) (Lag† 6–21)‡	1.05 (0.93 to 1.18)	1st versus 10th
PM ₁₀ (µg/m ³) (Lag† 2–12)**	0.98 (0.94 to 1.02)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 0–4)**	1.11 (1.06 to 1.17)	95th versus 25th
Milan		
Daily maximum temperature (°C) (Lag† 6–21)‡	0.94 (0.92 to 0.96)	5th versus 25th
PM ₁₀ (µg/m ³) (Lag† 0–3)**	1.00 (0.98 to 1.03)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 0–3)**	1.09 (1.06 to 1.11)	95th versus 25th
Rome		
Daily maximum temperature (°C) (Lag† 0–6)‡	1.02 (1.00 to 1.04)	5th versus 25th
PM ₁₀ (µg/m ³) (Lag† 5–19)**	1.05 (1.03 to 1.08)	95th versus 25th
NO ₂ (µg/m ³) (Lag† 1–4)**	1.04 (1.02 to 1.06)	95th versus 25th

*Final conditional regression model adjusted by holidays.

†Lags expressed in days.

‡Adjusted for NO₂.

§Adjusted for maximum daily apparent temperature.

¶Final conditional regression model adjusted by influenza epidemics and holidays.

**Adjusted for maximum daily temperature.

ranging between 1.04 (95% CI 1.02 to 1.06) in Rome and 1.11 (95% CI 1.06 to 1.17) in Turin (table 2). No effect modifiers of the NO₂/WRI relationship in either season were found.

Effect of PM₁₀

An increase of PM₁₀ from the 25th to the 95th percentile in the warm season was associated with an increase in WRI ranging between 1.09 (95% CI 1.05 to 1.12), in Turin, and 1.15 (95% CI 1.11 to 1.18), in Rome. During the cold season, we found a significant effect of PM₁₀ only in Rome with a 1.05 (95% CI 1.03 to 1.08) increase in WRI (table 2). No effect modifiers of the PM₁₀/WRI relationship in either season were found.

Effect of temperature

No significant association between temperature and injury risk was observed in the warm season overall, but for workers in the following economic sectors: transportation (Turin 1.00%—95% CI 0.89 to 1.13; Milan 1.05; 95% CI 0.96 to 1.14; Rome 1.04; 95% CI 1.00 to 1.09), construction (Turin 1.07%—95% CI 0.95 to 1.21; Milan 1.07; 95% CI 0.97 to 1.17; Rome 1.06; 95% CI 1.01 to 1.12) and energy industries (Turin 1.56%—95% CI 0.95 to 2.58; Milan 1.57; 95% CI 1.03 to 2.38; Rome 1.00; 95% CI 0.85 to 1.18) (figure 2). However, the effect was modest.

The association between WRI and temperature or air pollutants by occupational activity was estimated only for those injuries occurred in one of the three economic

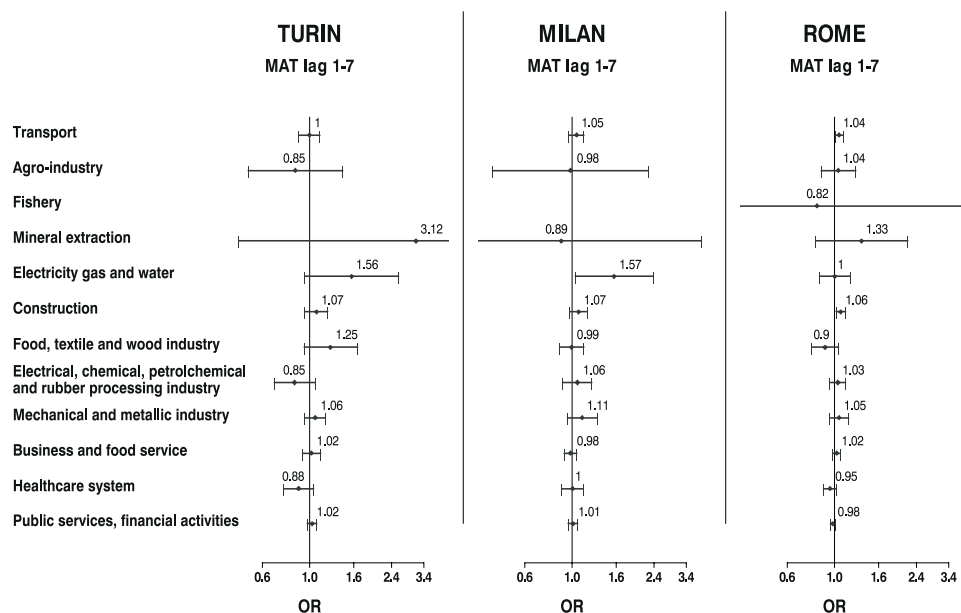


Figure 2 ORs of WRI, adjusted for NO_2 , for MAT (lag 1–7) increase*, by economic sectors, during warm season (May–September) in Turin, Milan and Rome. *Turin: 90° versus 50° percentile of MAT; Milan: 90° versus 10° percentile of MAT; Rome: 75° versus 25° percentile of MAT. MAT, maximum daily apparent temperature; WRI, work-related injury.

sectors with a significant association between temperature and WRI, and only in the warm season (transportation, construction, electricity gas and water—figure 2). In order to have enough statistical power we aggregated into a single category all those occupational activities for which less than 20 injuries were reported in at least one city. Blacksmith, mechanic, installer, motor worker, road worker, warehouse worker, attendant and asphalter were the only activities for which we observed a significant effect of temperature on WRI. The highest effects were observed for road workers (OR: 4.05%—95% CI 1.20 to 13.66), warehouse workers (OR 4.45%—95% CI 1.10 to 18.02) and attendants (OR: 6.91%—95% CI 1.42 to 33.57) (figure 3).

We also observed a significant effect of MAT among those working outdoors in Milan (OR: 1.12%—95% CI 1.02 to 1.23) and Rome (OR: 1.07%—95% CI 1.01 to 1.12), and among those working both outdoors and indoors only in Rome (OR: 1.03%—95% CI 1.00 to 1.06). No effect was observed among those working only indoors (figure 4).

In the cold season, a decrease of TMAX from 4°C to 2°C was associated with a weak and not significant increase in WRI (OR: 1.02; 95% CI 1.00 to 1.04) in Rome (table 2) while in Turin and Milan no effect was observed. No effect modifiers of TMAX-WRI in the cold season were found.

DISCUSSION

This is the first study conducted in Italy to analyse the independent effects of temperature (hot and cold) and air pollutants on the risk of WRIs. The strongest effects on WRI risk was due to exposure to NO_2 in the warm season, with a WRI risk up to 1.3 times higher when NO_2

levels increased from the 25th to 95th percentile of its city-specific distribution.

In general, we observed a significant association between exposure to NO_2 and WRI in both seasons and in all cities; and between PM_{10} and WRI only in Rome during the cold season and in all the three cities during summer. Temperature showed a significant effect only in specific occupational activities during the warm season (May to September).

The relationship between NO_2 and the occurrence of WRIs had a similar shape in the three cities in both periods (online supplementary eFigure 6). As expected, NO_2 values were lower in the warm than in the cold season, with median values in the three cities of about $50 \mu\text{g}/\text{m}^3$ and $73 \mu\text{g}/\text{m}^3$, respectively (online supplementary eTable 1). Despite this, there was a stronger association between NO_2 and WRI in the warm than in the cold season, although levels of NO_2 in the cold season are always higher. It is also noticeable that the effect of NO_2 remained constant regardless of economic sector or occupational activity.

The relationship between PM_{10} and the occurrence of WRIs had a non-linear shape in Turin and Milan, while was linear in Rome in the warm season; during winter, instead, the shape was similar in the three cities (online supplementary eFigure 5). PM_{10} levels showed a similar trend as NO_2 , with lower levels in the warmer months and higher levels and a low day by day variability in the cold period. Only in Rome, the southern of the three cities, PM_{10} showed lower and more variable levels in the cold period (online supplementary eTable 1); and it is interesting to observe that an increase of PM_{10} is associated to an increase in WRI in this season only in Rome. In the

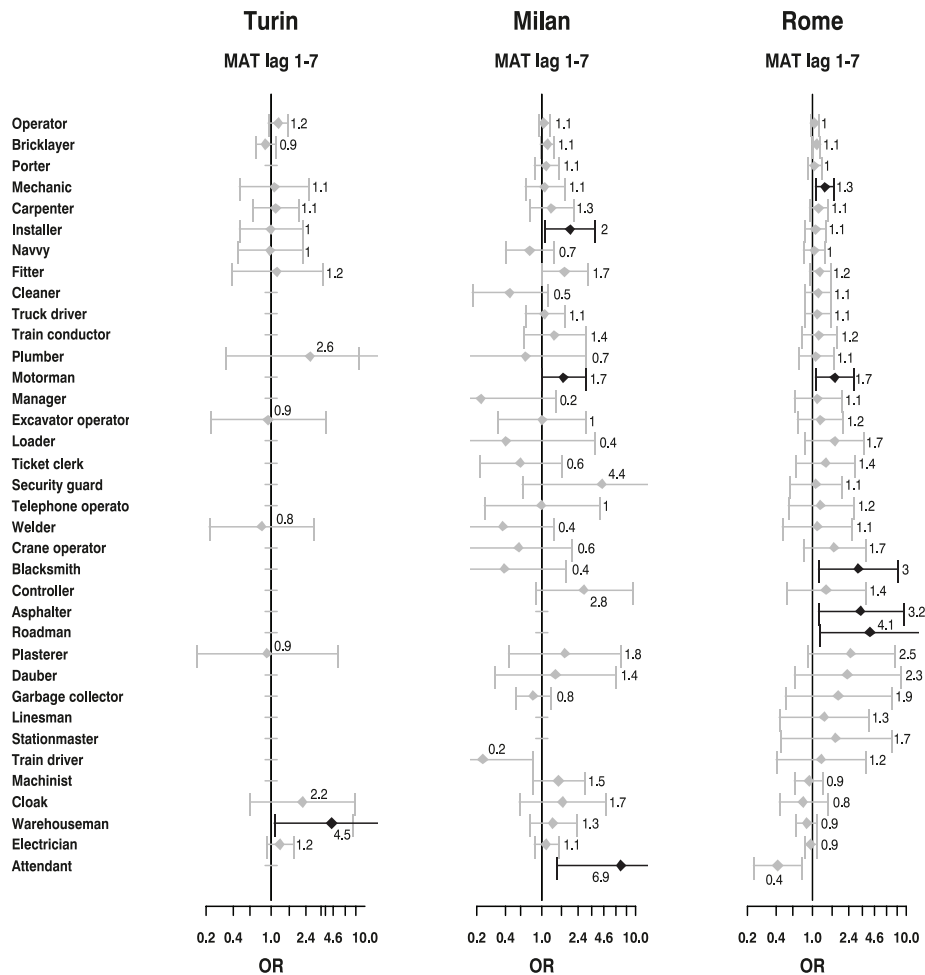


Figure 3 ORs of WRI, adjusted for NO_2 , for MAT (lag 1–7) increase* by occupational activities, in transportation, construction, electricity gas and water industries, during warm season (May–September) in Turin, Milan and Rome. *Turin: 90° versus 50° percentile of MAT; Milan: 90° versus 10° percentile of MAT; Rome: 75° versus 25° percentile of MAT. MAT, maximum daily apparent temperature; WRI, work-related injury.

warm months the effect of PM_{10} is consistent in the three cities, but lower than that of NO_2 . On days in which PM_{10} levels reach the 95th percentile of the city specific distribution the risk of WRI is circa 10% higher than on days when PM_{10} levels are around their 25th percentile.

The differences observed in the shape of the pollutant-WRI risk among cities could be explained by the different geographical and climatic characteristics and also by sources of air pollution; for example, in Rome there are additional sources on particulate matters levels, above all Saharan dust storms.³⁶

Mounting experimental evidence suggests in addition to the well-known short-term effects on various health outcomes,^{23 37 38} such as cardiopulmonary system, the brain may be a target of air pollution. Specific mental and neurological disorders, such as depression and headache, as well as suicide have all been linked to ambient air pollution.^{39 40} Moreover, evidence on acute neuropsychological effect has been studied only very recently on humans by Sunyer *et al.*²¹ showing a short-term association between air pollutants and fluctuations in attention

in children. These effects could probably arise through the same mechanism as the long-term association, since a recent review²² showed as potential mechanisms oxidative stress/inflammation, altered levels of dopamine and/or glutamate and changes in synaptic plasticity/structure based on consistent evidence from animal studies. Inhaled concentrated ambient particulate matter is deposited in pulmonary alveolar regions of lung from which it can pass to the blood circulation and thus impact other organs and produce neuroendocrine and neuropathological alterations.⁴¹ Another gateway to the brain involve translocation of pollution across the olfactory epithelium in the nasal cavity.²² In our study the lag of PM_{10} and NO_2 effects was short, 2 or 3 days⁴²; so it is reasonable to think that these exposures might explain the association between pollution and WRIs. Some previous studies have analysed health-related outcomes in specific categories of workers, particularly those exposed to urban stressors, such as street vendors and policemen, and they showed some effects on cardiovascular diseases, pregnancy outcomes and respiratory diseases.^{20 43–47} One study measured a

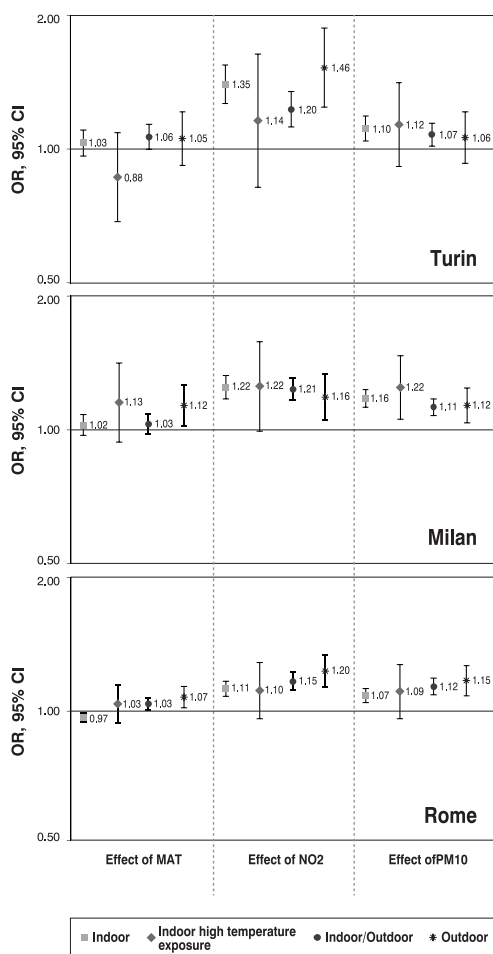


Figure 4 ORs of WRI for MAT*, NO₂[§] and PM₁₀[§] increases by 'indoor/outdoor job activity' during warm season (May–September) in Turin, Milan and Rome. *Turin: 90° versus 50° percentile of MAT; Milan: 90° versus 10° percentile of MAT; Rome: 75° versus 25° percentile of MAT. §95° versus 25° percentile of the distribution of the both air pollutants in the three cities. MAT, maximum daily apparent temperature; WRI, work-related injury.

negative economic impact of exposure to air pollutants in agriculture workers, finding lower productivity on more polluted days.²⁰ Finally, a recent study⁴³ tried to measure the association between occupational exposure to ozone and respiratory diseases, with no conclusive results. It could be considered that above mentioned mechanisms may differ between seasons; during the warm season, part of the observed effect of pollutants may be attributable to the synergistic effect between temperature and air quality as previously suggested in the general population studies.⁴⁸ One mechanism involve the higher frequency of air pollution peaks occurring during stagnation events common in summer season. Moreover, during the hottest months the activation of thermoregulatory mechanisms such as the increase in ventilation rate could increase the intake of air pollutants into the airways.

As for heat, our study showed an increase of injuries only among bricklayers, blacksmiths, mechanics, installers and asphalters working in transportation, construction

and energy economic sectors, and in the more generic group of those working outdoor or performing both outdoor and indoor tasks, but not among those who work only indoors. These results are consistent with previous studies.^{31 49 50}

It is interesting that the unadjusted OR of MAT on WRI during the warm season ranged from 1.03 in Rome (75° vs 25° percentile, range=8°C) to 1.06 in Turin (90° vs 50° percentile, range=7°C), but these effects lowered to 1.01 and became not significant when adjusting for air pollution. The observed confounding of temperature by pollution should be considered when comparing our results to unadjusted estimates of temperature-WRI associations from other published studies.

Two previous studies conducted in Italy⁵¹ and in Australia⁴⁹ found an inverse U-shaped relationship between high temperatures and WRI in summer, with maximum risk on warm days but not on extremely hot days. The relationship observed in Turin and Milan (online supplementary eFigure4) also suggest a similar trend, even if quite weak. Also, the values of MAT in correspondence of which the highest rates of injuries were observed were 33°C–34°C, while they remained stable or decreased afterwards. In Rome, which experiences warmer summer conditions than Milan and Turin, we found a linear relationship consistent with what was observed in two recent studies conducted in Melbourne and in Quebec.^{12 50} Different population characteristics as well as temperature distributions might influence these differences between cities. Furthermore, it has to be considered that the trend in the effects observed in Milan and Turin might be biased by the lower statistical power in the highest extremes of the temperature distribution, due to the fewer days observed with those temperature levels. This is not the case in Rome where temperatures even above 34°C are adequately represented.

Ambient heat might increase metabolic heat that is normally produced in activities requiring physical exertion; accordingly, we have observed an effect of heat in more physically demanding economic sectors and occupational activities. We categorised workers according to three different criteria as suggested in a previous study¹²: economic sector, occupational activity and outdoor or indoor location. This classification allowed us to measure both the risk associated with physical demands (economic sector and occupational activity) and the gradient of exposure to outdoor heat. Our results showed higher susceptibility among those working outdoors and no effects on those working only indoors, confirming that those working outdoors are more susceptible to pollution and temperatures exposure. However, when analysing single occupational activity, we found that among the most susceptible to heat there were some (mechanics, warehouse workers and attendants) who spend more time indoor than outdoor but still require high physical exertion. Strenuous activity, and use of heavy impermeable personal protective clothing might increase metabolic heat and increase the risk of injuries. This might

suggest that the level of physical strength required by the occupation might be an important effect modifier to be taken into account for heat-related risk, independent of work location.¹²

Our study also examines the effect of temperature and air pollutants in the cold season. As for pollution, the effect is lower than in summer; for temperature, we did not observe an effect of cold. A previous study conducted in Tuscany, in the centre of Italy, found significant cold effects on outdoor occupational injuries especially among agricultures and in drivers of vehicles other than cars.⁵²

An important strength of this study is that we estimated the independent effects of temperature and air pollution, controlling one for the other in the model. Also, we used a very large dataset that was not derived from self-reported data. However, our study presents some limits. The study population was drawn from the Italian public insurance system database that covers all WRIs due to violent causes that leads to death, permanent disability or temporary total disability lasting at least 3 days, and all occupational diseases. It is remarkable to consider that workers covered by the public insurance system for injuries and occupational diseases make up approximately 80%–85% of the whole workforce in Italy. However, daily injury claims may be underestimated because of under-reporting of workers' compensation claims and due to incomplete coverage of the public insurance system lead by INAIL. Some occupational activities, such as firefighters and the armed forces, benefit from a specific welfare system in Italy and are not included in the analysed dataset. The distribution of daily injury claims by economic sector varies greatly and the relatively small numbers in some sectors dictates a cautious interpretation of results for less represented subgroups.

All exposure measures used were daily averages deriving from fixed points of measurement in the city, implying each worker was attributed the same level of exposure independently of his location in the city at the moment of injury, thus having a potential bias in exposure due to different temperatures and pollutants within the city on a given day. However, the error associated with this generalisation in exposure is considered to be low.⁵³ Finally collinearity among NO₂ and PM₁₀ didn't allow to adjust one pollutant for the other, so that the estimate of pollutant effect might be confounded by concomitant exposure to the other one. This limit is proper of almost all air pollution studies.

CONCLUSIONS

Our results show that, after removing the confounding effect of co-exposure to air pollution, the exposure to high temperature represents a risk only among workers who have heavier workloads and among those who spend most of their time outdoors. Our results also suggest that exposure to air pollution, especially NO₂, seems also to increase the risk of WRIs with a stronger effect in the warm months. These results suggest the need to further look

into this association, to confirm our findings and to better understand the underlying mechanisms. In conclusion, our results confirm that in Italy, which is a Mediterranean country with a generally mild climate, ambient exposures represent a hazard for WRIs. These results contribute to the increasing knowledge about the association between temperature and WRIs, and add new evidence about the potential effects of pollutants that have not yet been studied in Italy except on very specific subgroups.

Identifying specific subgroups of workers as the most susceptible to these specific exposures is crucial information for public health organisations in order to properly target prevention plans.

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REFERENCES

1. IPCC. *Climate change 2014: mitigation of climate change*. Cambridge, United Kingdom and New York, NY, USA: Cambridge University Press, 2014.
2. Arbutnott K, Hajat S, Heaviside C, *et al*. Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change. *Environ Health* 2016;15.
3. Orru H, Ebi KL, Forsberg B. The interplay of climate change and air pollution on health. *Curr Environ Health Rep* 2017;4:504–13.
4. de' Donato FK, Leone M, Scortichini M, *et al*. Changes in the effect of heat on mortality in the last 20 years in nine European cities. results from the phase project. *Int J Environ Res Public Health* 2015;12:15567–83.
5. Iñiguez C, Schifano P, Asta F, *et al*. Temperature in summer and children's hospitalizations in two Mediterranean cities. *Environ Res* 2016;150:236–44.
6. Schulte PA, Bhattacharya A, Butler CR, *et al*. Advancing the framework for considering the effects of climate change on worker safety and health. *J Occup Environ Hyg* 2016;13:847–65.
7. Williams WJ, Musolin K, Jacklitsch B. *NIOSH criteria for a recommended standard: occupational exposure to heat and hot environments*. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2016-106, 2016.
8. Bonauto D, Anderson R, Rauser E, *et al*. Occupational heat illness in Washington state, 1995-2005. *Am J Ind Med* 2007;50:940–50.

9. CDC - Centers for Disease Control and Prevention. Heat-Related deaths among crop workers-United States, 1992-2006. *MMWR Morb Mortal Weekly Rep* 2008;57:649-53.
10. Mirabelli MC, Quandt SA, Crain R, et al. Symptoms of heat illness among Latino farm workers in North Carolina. *Am J Prev Med* 2010;39:468-71.
11. Fleischer NL, Tiesman HM, Sumitani J, et al. Public health impact of heat-related illness among migrant farmworkers. *Am J Prev Med* 2013;44:199-206.
12. McInnes JA, Akram M, MacFarlane EM, et al. Association between high ambient temperature and acute work-related injury: a case-crossover analysis using workers' compensation claims data. *Scand J Work Environ Health* 2017;43:86-94.
13. Balbus JM, Malina C. Identifying vulnerable subpopulations for climate change health effects in the United States. *J Occup Environ Med* 2009;51:33-7.
14. Lundgren K, Kuklane K, Gao C, et al. Effects of heat stress on working populations when facing climate change. *Ind Health* 2013;51:3-15.
15. Antoine M, Pierre-Edouard S, Jean-Luc B, et al. Effective exposure to solar UV in building workers: influence of local and individual factors. *J Expo Sci Environ Epidemiol* 2007;17:58-68.
16. Yardley J, Sigal RJ, Kenny GP. Heat health planning: the importance of social and community factors. *Global Environmental Change* 2011;21:670-9.
17. Mäkinen TM, Hassi J. Health problems in cold work. *Ind Health* 2009;47:207-20.
18. Faustini A, Stafoggia M, Colais P, et al. Air pollution and multiple acute respiratory outcomes. *Eur Respir J* 2013;42:304-13.
19. Chiusolo M, Cadum E, Stafoggia M, et al. Short-Term effects of nitrogen dioxide on mortality and susceptibility factors in 10 Italian cities: the EpiAir study. *Environ Health Perspect* 2011;119:1233-8.
20. Zivin JG, Neidell M. The impact of pollution on worker productivity. *Am Econ Rev* 2012;102:3652-73.
21. Sunyer J, Suades-González E, García-Esteban R, et al. Traffic-Related air pollution and attention in primary school children: short-term association. *Epidemiology* 2017;28:181-9.
22. Allen JL, Klocke C, Morris-Schaffer K, et al. Cognitive effects of air pollution exposures and potential mechanistic underpinnings. *Curr Environ Health Rep* 2017;4:180-91.
23. Mills IC, Atkinson RW, Kang S, et al. Quantitative systematic review of the associations between short-term exposure to nitrogen dioxide and mortality and hospital admissions. *BMJ Open* 2015;5:e006946.
24. Pinault L, van Donkelaar A, Martin RV. Exposure to fine particulate matter air pollution in Canada. *Health Reports* 2017;28.
25. Analitis A, Michelozzi P, D'Ippoliti D, et al. Effects of heat waves on mortality: effect modification and confounding by air pollutants. *Epidemiology* 2014;25:15-22.
26. Stafoggia M, Schwartz J, Forastiere F, et al. Does temperature modify the association between air pollution and mortality? A multicity case-crossover analysis in Italy. *Am J Epidemiol* 2008;167:1476-85.
27. Bonafede M, Marinaccio A, Asta F, et al. The association between extreme weather conditions and work-related injuries and diseases. A systematic review of epidemiological studies. *Ann Ist Super Sanit* 2016;52:357-67.
28. Michelozzi P, De Sario M, Accetta G, et al. Temperature and summer mortality: geographical and temporal variations in four Italian cities. *J Epidemiol Community Health* 2006;60:417-23.
29. Baccini M, Biggeri A, Accetta G, et al. Heat effects on mortality in 15 European cities. *Epidemiology* 2008;19:711-9.
30. Kalkstein LS, Valimont KM. An evaluation of summer discomfort in the United state using a relative Climatological index. *Bull Am Meteorol Soc* 1986;67:842-8.
31. Riccò M. Air temperature exposure and agricultural occupational injuries in the autonomous Province of Trento (2000-2013, north-eastern Italy). *Int J Occup Med Environ Health* 2018;31:317-31.
32. Barnett AG, Tong S, Clements ACA. What measure of temperature is the best predictor of mortality? *Environ Res* 2010;110:604-11.
33. Berti G, Chiusolo M, Grechi D, et al. [Environmental indicators in ten Italian cities (2001-2005): the air quality data for epidemiological surveillance]. *Epidemiol Prev* 2009;33(6 Suppl 1):13-26.
34. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med* 2010;29:2224-34.
35. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991;133:144-53.
36. Alessandrini ER, Stafoggia M, Faustini A, et al. Saharan dust and the association between particulate matter and daily hospitalisations in Rome, Italy: Table 1. *Occup Environ Med* 2013;70:432-4.
37. Atkinson RW, Mills IC, Walton HA, et al. Fine particle components and health--a systematic review and meta-analysis of epidemiological time series studies of daily mortality and hospital admissions. *J Expo Sci Environ Epidemiol* 2015;25:208-14.
38. Li M-H, Fan L-C, Mao B, et al. Short-Term exposure to ambient fine particulate matter increases hospitalizations and mortality in COPD: a systematic review and meta-analysis. *Chest* 2016;149:447-58.
39. Vodonos A, Novack V, Zlotnik Y, et al. Ambient air pollution, weather and daily emergency department visits for headache. *Cephalalgia* 2015;35:1085-91.
40. Szyszkowicz M, Rowe B, Colman I. Air pollution and daily emergency department visits for depression. *Int J Occup Med Environ Health* 2009;22:355-62.
41. Sirivelu MP, MohanKumar SMJ, Wagner JG, et al. Activation of the stress axis and neurochemical alterations in specific brain areas by concentrated ambient particle exposure with concomitant allergic airway disease. *Environ Health Perspect* 2006;114:870-4.
42. Bakian AV, Huber RS, Coon H, et al. Acute air pollution exposure and risk of suicide completion. *Am J Epidemiol* 2015;181:295-303.
43. Adam-Poupard A, Labrèche F, Busque MA, et al. Association between outdoor ozone and compensated acute respiratory diseases among workers in Quebec (Canada). *Ind Health* 2015;53:171-5.
44. Vimercati L, Gatti M, Baldassarre A, et al. Occupational exposure to urban air pollution and allergic diseases. *Int J Environ Res Public Health* 2015;12:12977-87.
45. Amegah AK, Jaakkola JJK. Work as a street vendor, associated traffic-related air pollution exposures and risk of adverse pregnancy outcomes in Accra, Ghana. *Int J Hyg Environ Health* 2014;217:354-62.
46. Torén K, Bergdahl IA, Nilsson T, et al. Occupational exposure to particulate air pollution and mortality due to ischaemic heart disease and cerebrovascular disease. *Occup Environ Med* 2007;64:515-9.
47. Palli D, Saieva C, Munnia A, et al. Dna adducts and PM10 exposure in traffic-exposed workers and urban residents from the EPIC-Florence City study. *Science of The Total Environment* 2008;403:105-12.
48. Scortichini M, De Sario M, de'Donato F, et al. Short-Term effects of heat on mortality and effect modification by air pollution in 25 Italian cities. *Int J Environ Res Public Health* 2018;15:pii: E1771.
49. Xiang J, Bi P, Pisaniello D, et al. Association between high temperature and work-related injuries in Adelaide, South Australia, 2001-2010. *Occup Environ Med* 2014;71:246-52.
50. Adam-Poupard A, Smargiassi A, Busque M-A, et al. Effect of summer outdoor temperatures on work-related injuries in Quebec (Canada). *Occup Environ Med* 2015;72:338-45.
52. Morabito M, Cecchi L, Crisci A, et al. Relationship between work-related accidents and hot weather conditions in Tuscany (central Italy). *Ind Health* 2006;44:458-64.
52. Morabito M, Iannuccilli M, Crisci A, et al. Air temperature exposure and outdoor occupational injuries: a significant cold effect in central Italy. *Occup Environ Med* 2014;71:713-6.
53. Sheppard L, Burnett RT, Szpiro AA, et al. Confounding and exposure measurement error in air pollution epidemiology. *Air Qual Atmos Health* 2012;5:203-16.