

Modeling Desert Dust Exposures in Epidemiologic Short-term Health Effects Studies

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Background: Desert dust is assumed to have substantial adverse effects on human health. However, the epidemiologic evidence is still inconsistent, mainly because previous studies used different metrics for dust exposure and its corresponding epidemiologic analysis. We aim to provide a standardized approach to the methodology for evaluating the short-term health effects of desert dust.

Methods: We reviewed the methods commonly used for dust exposure assessment, from use of a binary metric for the occurrence of desert dust advections to a continuous one for quantifying particulate matter attributable to desert dust. We presented alternative time-series Poisson regression models to evaluate the dust exposure–mortality association, from the underlying epidemiological and policy-relevant questions. A set of practical examples, using a real dataset from Rome, Italy, illustrate the different modeling approaches.

Results: We estimate substantial effects of desert dust episodes and particulate matter with diameter $<10\ \mu\text{m}$ (PM_{10}) on daily mortality. The estimated effect of non-desert PM_{10} was 1.8% (95% confidence interval [CI] = 0.4, 3.2) for a $10\ \mu\text{g}/\text{m}^3$ rise of PM_{10} at lag 0 for dust days, 0.4% (95% CI = -0.1, 0.8) for non-dust days, and 0.6% (95% CI = -0.5, 2.1) for desert PM_{10} .

Conclusion: The standardized modeling approach we propose could be applicable elsewhere, in and near hot spots, which could lead to more consistent evidence on the health effects of desert dust from future studies.

Keywords: Air pollution; Desert dust; Modeling; Mortality; Particulate matter; Time-series

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Desert dust plays an important role in different aspects of weather, climate, and atmospheric chemistry and represents a severe hazard to environment and health.^{1,2} Dust storms last 1–24 hours at source points, and depending on meteorologic conditions the dust can be transported at surface level or lofted to high altitudes (up to 10 km).^{2,3} The influence of dust on air quality is a complex issue. Dust is typically made up of crustal components, clay minerals, and salt,³ and it can increase particulate-matter concentrations.^{2,3} Dust can also carry anthropogenic pollutants, previously deposited in the source areas or trapped by the high dust air mass during its atmospheric transport,^{4,5} and microorganisms and toxic biogenic allergens.^{6,7}

During the last decade, special attention has been given to mineral dust particles from desert dust. However, evidence on the health effects of desert dust remains unclear. Previous reviews, systematic or not, have reported inconsistent results on the health effects of desert dust across studies and geographical regions.^{8–12} The main sources of heterogeneity are the epidemiologic study design, the exposure assessment methods to identify dust events, and, most importantly, the exposure metric used to investigate the health effects of desert dust. Dust exposure can be defined using a binary metric, for example in a study design comparing the number of health events between days with and without dust events. Dust exposure can be defined further as a continuous metric, quantifying the amount of mineral dust during days with dust events and then estimating its association with the health outcome.

Thus, the apparently simple question “does desert dust impact human health?” requires a careful definition of what is the relevant dust exposure of interest and how such effects can be quantified, to identify and understand which health effects are plausible. We aim to review, clarify, and extend the statistical modeling approaches for investigating the short-term effects of desert dust on human health. We will propose a general modeling approach to make future studies comparable, with an illustrative example of the city of Rome, Italy, frequently affected by Saharan dust events.

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EXAMPLE DATASET

We collected daily counts of all-natural-cause mortality (International Classification of Diseases, 9th or 10th Revision–ICD-9/ICD-10 codes: 1–799/A00–R99), 24-hour average of particulate matter with aerodynamic diameter $<10\ \mu\text{m}$ (PM_{10}) and mean temperature in Rome, for the study period between 2005 and 2015. The city of Rome offers a useful environmental scenario in which to study the health effects of desert dust and air pollution.¹³ Rome is a highly urbanized area with frequent traffic congestion, many densely inhabited neighborhoods with multiple sources of air pollution from domestic and commercial activities, and elevated sea traffic due to tourism and shipping activities over the Mediterranean Sea, all of which enhance the formation and accumulation of atmospheric pollutants.¹⁴ It is also frequently affected by outflows from North African deserts with different seasonal incidences western to eastern across the region.¹⁵ The frequency of dust events has been 14.3% (575 days) during the study period (eTable 1; <http://links.lww.com/EDE/B723>), ranging between 7.7% in 2011 and 21.8% in 2007, and with a peak in the May to June period. Daily mortality is similarly distributed during dust (58.2 deaths) and non-dust days (59.0 deaths). However, the PM_{10} concentrations are higher during dust days (36.7 vs. 31.0 $\mu\text{g}/\text{m}^3$ for days without dust).

Statistical Analysis

We illustrate and discuss the modeling approaches commonly applied in the literature to estimate the short-term effects of desert dust,^{8–12} by using a time-series study design.¹⁶ In our example, we analyzed the data using an over-dispersed Poisson regression model adjusted for conventional time-varying confounders. These include time trends and air temperature. We adjusted long-term and seasonal time trends using a natural cubic spline with 4 degrees of freedom (df) per year; we chose the number to minimize the Akaike information criterion. We modeled weekdays and public holidays as indicator variables. We controlled for the confounding effect of air temperature by modeling cold and warm temperatures separately, following the MED-PARTICLES study protocol.^{13,17} Specifically, for high temperatures, we calculated the average temperature on the current and previous day (lag 0–1) and fit a natural cubic spline with 3 df on the lagged variable only for days when the lag 0–1 temperature was higher than the median value. Similarly, we adjusted for low temperatures by fitting a natural cubic spline with 2 df for the average temperature on the previous 6 days (lag 1–6) only for days when the lag 1–6 temperature was below the median. The statistical adjustment model follows:

$$\begin{aligned} \log(y_t) = & \beta_0 + ns \text{ (trend, df} = 4 \times \text{number of years)} \\ & + ns \left(\text{temp}_{\text{avg}(0,1)} \times I[\text{temp}_{\text{avg}(0,1)} > \text{median}], \text{ df} = 3 \right) \\ & + ns \left(\text{temp}_{\text{avg}(1,6)} \times I[\text{temp}_{\text{avg}(1,6)} < \text{median}], \text{ df} = 2 \right) \\ & + \beta_1 \text{holiday}_t + \sum \beta_k \text{weekday}_t^k + \varepsilon_t \end{aligned}$$

where: y_t is the variable with daily counts of all natural mortality on day t ; trend is the term for time trend, defined as a progressive number from 1 to 4017 (total number of days); $\text{temp}_{\text{avg}(0,1)}$ is the average of current and previous day air temperature; and $I(x)$ represents the indicator function assuming value 1 when the argument x is true; $\text{temp}_{\text{avg}(1,6)}$ represents the average of previous 6 days' air temperature; holiday_t is an indicator variable for public holidays (1) or regular days (0); weekday_t^k is a set of indicator variables for weekdays ($k = 1$ for Sunday, $k = 2$ for Monday, etc.); and ε_t is the residual error term.

Finally, we undertook the usual approach in time-series regression studies to assess the goodness of fit of the model residuals, plotting the deviance residuals versus time and the partial autocorrelation function plot of the deviance residuals.¹⁶ All the statistical analyses were conducted using R, version 3.6.3, and the R code is available at the GitHub repository <https://github.com/aureliotobias/dust>.

DUST AS BINARY METRIC

Methods to Identify Dust Events

There are a wide variety of methods to identify the occurrence of dust events. However, the methods vary considerably between geographical regions.⁹ In our example, we did follow the methodology by the MED-PARTICLES project to identify Saharan dust events in the Mediterranean region¹⁵ by using a combination of tools, including meteorologic products (National Centers for Environmental Predictions, and National Center for Atmospheric Research, NCEP/NCAR Reanalysis Project), aerosol maps (Barcelona Supercomputing Center-Dust Regional Atmospheric Model, BSC-DREAM; Navy Aerosol Analysis and Prediction System-Naval Research Laboratory, NAAPS-NRL; SKIRON dust operational model), air masses back-trajectories (Hybrid Single Particle Lagrangian Integrated Trajectory), and satellite images (Sea-viewing Wide Field-of-view Sensor). Moreover, in the studies conducted in the Middle East, the main criterion to define dust events has been exceedance of pre-specified thresholds for daily particulate matter concentrations. For example, in Israel^{18,19} investigators defined as dust days those with a PM_{10} concentration that was 2 SDs above the background value for that area, while in Iraq, Kuwait, and Saudi Arabia dust storm days were considered as those days with PM_{10} levels exceeding 200 $\mu\text{g}/\text{m}^3$.^{20–22} In Eastern Asia, the identification of Asian dust storms was commonly based on visibility measures.^{23–26} Finally, a study in the United States²⁷ used dust storm events as reported in the U.S. National Weather Service storm database, which comes from a variety of sources, including emergency management, law enforcement, sky warn spotters, damage surveys, media reports, and the general public. However, the dust events were not detected or reported using a consistent and standardized protocol, leading to substantial false negatives.²⁷

Dust as Health Risk

Regardless of the way desert dust episodes are identified, the analysis of the association between dust exposure as a binary metric and mortality addresses the following research (and policy) question: “Is mortality higher on dust days compared to non-dust days?”. Previous systematic reviews have shown that the mortality rate can increase during days affected by dust events in comparison with non-affected days.^{8,9} Thus, the underlying causal model is depicted in the directed acyclic graph (DAG) shown in Figure 1 (panel A). An example of the data for the year 2007 is displayed in eFigure 1; <http://links.lww.com/EDE/B723> (top panel) showing the daily mortality counts during dust and non-dust days.

In this model, the dust binary exposure variable is added to the adjustment model, at some short-term lag l , usually not longer than 1 week, as follows:

$$\log(y_t) = \text{adj.model} + \beta_{\text{dust}} \text{dust}_{t-l} + \varepsilon_t$$

where dust_{t-l} is the binary exposure variable for desert dust on day $t-l$, with l assuming lagged values, in turn, from 0

to 5; β_{dust} is the corresponding regression coefficient, usually converted into percent increased risk (IR) in mortality (calculated as $\text{IR} = [\exp(\beta_{\text{dust}}) - 1] \times 100\%$).

The results for lags 0–5 are reported in Figure 2 (left panel), which shows a positive association only for lag 0, with an IR of 2.8% (95% confidence interval [CI] = 1.0, 4.7). The dust–mortality association does not seem to be confounded by PM_{10} . When PM_{10} is added to the regression model, at the same lag as the dust exposure, the estimated effect of dust exposure did not change substantially (IR = 2.5% [95% CI = 0.6, 4.4]). Thus, dust events increase mortality through causal pathways not entirely explained by increased daily PM_{10} concentrations induced by the dust episode. This is depicted by the DAG in Figure 1 (panel B), with a focus on the arrow from dust to health even upon adjustment for PM_{10} .

Dust as Confounder

During a dust event, the urban concentrations of PM_{10} increase substantially,³ and it is well known that PM_{10} has a short-term positive association with daily mortality.²⁸ Therefore, the DAG in Figure 1 (panel B) can be read differently

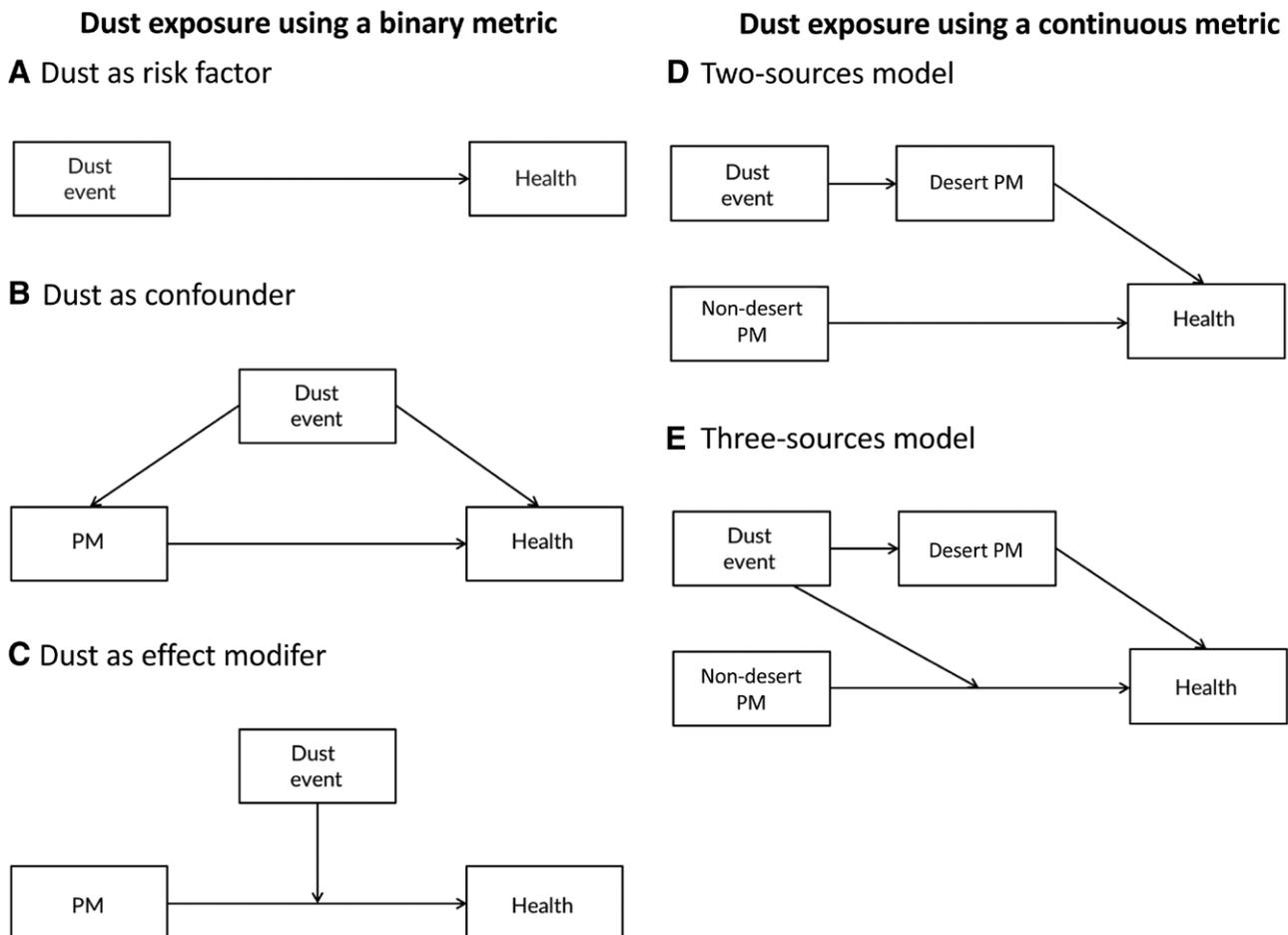


FIGURE 1. DAGs for the dust–health association considering dust exposure as binary metric (left panel) and as continuous metric (right panel). PM indicates particulate matter.

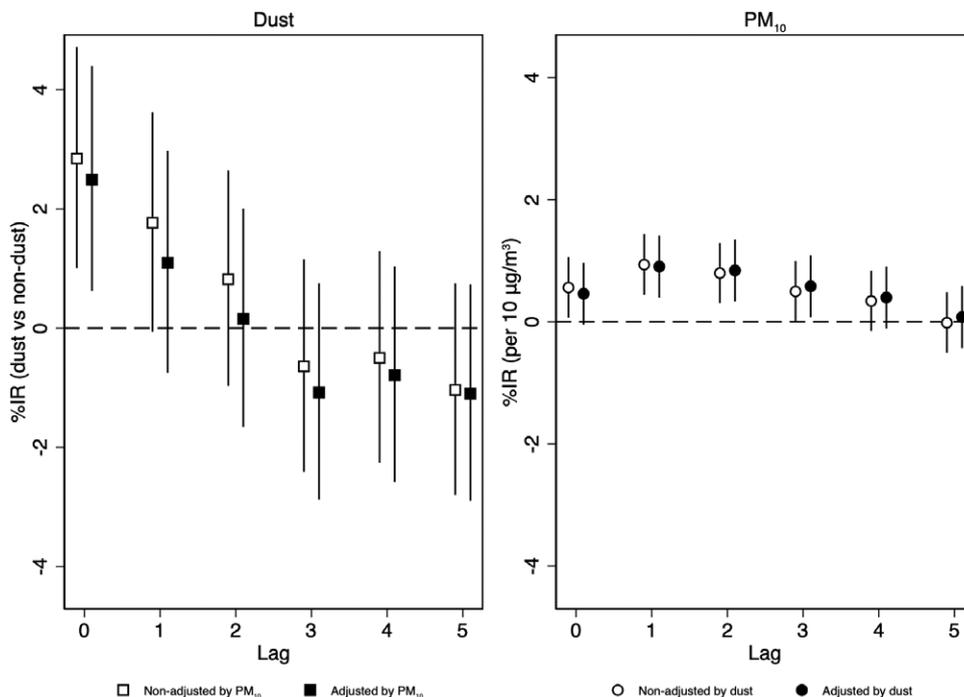


FIGURE 2. Percent increase of risk (%IR) of mortality using dust as binary metric exposure (left) for a PM₁₀ increase of 10 µg/m³ (right).

if the attention is shifted to PM₁₀ as the main exposure and the dust event is considered a potential confounder as dust is related to both the PM₁₀ exposure and the mortality outcome. In this case, the research question is the following: “Is there an association between daily PM₁₀ concentrations and mortality, independent of dust advections?”. This can be achieved, as in the previous case, by fitting both dust as binary exposure and PM₁₀ simultaneously in the regression model, and basing inferences on the coefficient for PM₁₀:

$$\log(y_t) = \text{adj.model} + \beta_{\text{dust}} \text{dust}_{t-1} + \beta_{\text{pm}_{10}} \text{PM}_{10,t-1} + \epsilon_t$$

where $\beta_{\text{pm}_{10}}$ represents the relative increase in mortality per unit increment of PM₁₀ at lag l , and usually expressed as percent IR per a fixed increment of PM₁₀ equal to 10 µg/m³.

We found an association between PM₁₀ concentrations and daily mortality up to several days after exposure (IR = 0.6% [95% CI = 0.1, 1.1] for 10 µg/m³ rise of PM₁₀ at lag 0, 0.9% [95% CI = 0.4, 1.4] at lag 1, 0.8% [95% CI = 0.3, 1.3] at lag 2, and 0.5%, [95% CI = 0.0, 1.0] at lag 3). When adjusting for dust as binary metric, the estimated effect of PM₁₀, again, did not change substantially (0.5% [95% CI = 0.0, 1.0] at lag 0, 0.9% [95% CI = 0.4, 1.4] at lag 1, 0.8% [95% CI = 0.3, 1.3] at lag 2, and 0.6% [95% CI = 0.1, 1.1] at lag 3) (Figure 2, right panel).

Dust as Effect Modifier

Exposure studies have suggested that the composition of PM₁₀ may be different on days with dust intrusion.³ This could

cause different health effects of PM₁₀ depending on whether it is a day with or without dust.^{29,30} In this situation, the binary dust exposure variable can be considered as an effect modifier of the PM₁₀–mortality association (DAG in Figure 1, panel C). Doing so addresses the research question: “Is the association between daily PM₁₀ and mortality different on dust versus non-dust days?”. eFigure 1; <http://links.lww.com/EDE/B723> (bottom panel) shows an example data for the year 2007 on how the PM₁₀ concentrations seem to be larger during dust days. In this case, the most relevant inference is done on the coefficient for the interaction term between the two exposure variables:

$$\log(y_t) = \text{adj.model} + \beta_{\text{dust}} \text{dust}_{t-1} + \beta_{\text{pm}_{10}} \text{PM}_{10,t-1} + \beta_{\text{interaction}} \text{dust}_{t-1} \times \text{PM}_{10,t-1} + \epsilon_t$$

where $\beta_{\text{interaction}}$ estimates the increment in the association between PM₁₀ and daily mortality on dust days compared to non-dust days at lag l . From the above model, it can easily be derived the relative increase in mortality on non-dust days ($\beta_{\text{pm}_{10}}$) and dust days ($\beta_{\text{pm}_{10}} + \beta_{\text{interaction}}$).

The association between PM₁₀ and daily mortality was higher on dust days for most lags. For lag 0, the association was 1.1% (95% CI = -0.1, 2.3) for dust days compared to 0.3% (95% CI = -0.2, 0.9) for non-dust days, for a 10 µg/m³ rise of PM₁₀. At lag 1, the association was 1.5%, (95% CI = 0.3, 2.7) for dust days and 0.8% (95% CI = 0.2, 1.3) for non-dust days. At lag 2, the association was 1.4% (95% CI = 0.2, 2.6) for dust days and 0.7% (95% CI = 0.2, 1.3)

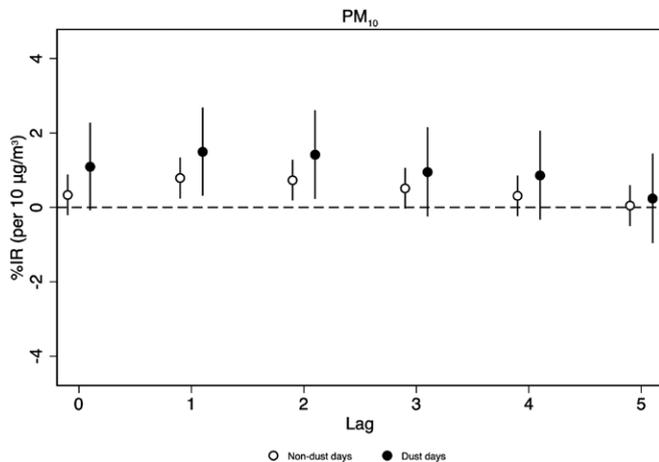


FIGURE 3. Percent increase of risk (%IR) of mortality for a 10 $\mu\text{g}/\text{m}^3$ rise of PM_{10} during dust and non-dust days.

for non-dust days. Finally, for lag 3, the association was 0.9% (95% CI = $-0.2, 2.2$) for dust days and 0.5% (95% CI = $0.0, 1.0$) for non-dust days. The estimates on dust days are more imprecise, showing large confidence intervals (Figure 3).

DUST AS CONTINUOUS METRIC

Methods to Quantify Dust

Dust quantification (i.e., calculation of PM_{10} concentrations from desert dust events at ground level) is especially complex because its most substantial and active sources are located in remote areas where there is little or no human activity. We used the EU Reference Method,^{31,32} which has been applied previously to quantify the Saharan dust and anthropogenic PM_{10} loads in the Mediterranean region.^{13,15} The method first identifies dust events, as described in the previous section. Next, for the dust days, we evaluate the PM_{10} levels only at the regional air quality monitoring sites following a multi-stage approach. First, we exclude the dust days from the time series, and compute a 30-day moving 40th percentile of the daily PM_{10} concentrations for each day of the series, representing the expected PM_{10} concentrations in the absence of desert dust advectations. Second, we quantify the dust contribution (desert PM_{10}) as the difference between the observed and the expected PM_{10} concentrations for dust days (it is set to zero for non-dust days). Finally, we assume the same amount of dust load in the regional and suburban background sites and compute the non-desert PM_{10} as the difference between the PM_{10} concentrations and the dust contributions.^{31,32}

Alternative methods are available in other regions. For example, studies conducted in Eastern Asia mainly used light detection and ranging (LIDAR) to calculate dust exposure.^{26,33} LIDAR utilizes polarized laser light to recognize shape differences and can distinguish Asian dust particles from other air pollutants, which are generally spherical. If the lower atmosphere is well mixed, the concentration of

Asian dust on the ground is similar to that between 120 and 270 m above ground.^{26,33} LIDAR can also estimate the dust extinction coefficients of non-spherical and spherical components. Here, the extinction coefficient for non-spherical particles of $0.1/\text{km}$ approximately corresponds to $100 \mu\text{g}/\text{m}^3$ of dust particles in South Korea and Japan.²³ An alternative to in situ observation is remote sensing. The World Meteorological Organization's Sand and Dust Storm Warning Advisory and Assessment System Regional Centre for Northern Africa, Middle East and Europe generates an ensemble multi-model product within its geographic domain, which is publicly available.³⁴ To cover other territories, we can use global reanalysis of dust at surface level by MERRA-2 produced and continuously updated by NASA.³⁵ However, none of these remote sensing and reanalysis products have been used yet in epidemiologic studies to estimate the short-term health effects of desert dust.

Two-sources Model

The distribution of desert and non-desert PM_{10} in the example dataset is presented in the eTable 1; <http://links.lww.com/EDE/B723>, and data for 2007 are shown in eFigure 2; <http://links.lww.com/EDE/B723>. The average of the dust load to PM_{10} was $1.5 \mu\text{g}/\text{m}^3$ (ranging from 0 to 130), while the PM_{10} load from non-desert sources was $30.3 \mu\text{g}/\text{m}^3$ (0–98.9). The difference between the two sources is driven by the non-dust days (when desert PM_{10} is zero by definition), whereas on dust days the two sources display a similar variability, as highlighted by the 10th–90th percentile range of $\sim 22 \mu\text{g}/\text{m}^3$, despite desert PM_{10} concentrations being, on average, smaller than non-desert PM_{10} sources.

The quantification of source-specific contributions (desert and non-desert) to total PM_{10} allows the disentangling of their independent effects through two-pollutant models.³ Here, the DAG in Figure 1 (panel D) shows a situation where dust occurrence influences desert PM_{10} concentrations, and these are causally linked to mortality independently from non-desert sources. The model addresses the following research question “are desert and non-desert sources of PM_{10} independently associated with mortality?”. The corresponding regression model is the following:

$$\log(y_t) = \text{adj.model} + \beta_{\text{non-desert}} \text{non-desert PM}_{10,t-1} + \beta_{\text{desert}} \text{desert PM}_{10,t-1} + \epsilon_t$$

where $\beta_{\text{non-desert}}$ and β_{desert} estimate the relative increase in mortality per unit increment of non-desert and desert PM_{10} , respectively. These estimates are usually converted into percent IR per fixed increments in the source-specific PM_{10} terms equal to $10 \mu\text{g}/\text{m}^3$. However, it is important to note that the distributions of the two sources are extremely different, therefore the same fixed amount (e.g., $10 \mu\text{g}/\text{m}^3$) might correspond to different proportions of populations exposed to desert and non-desert PM_{10} .

Figure 4 (left panel) shows the results of the two-source model, at different lags. The two sources of PM₁₀ are independently associated with mortality; desert PM₁₀ shows an association with mortality at lag 0 (1.2% [95% CI = 0.0, 2.3]) for a 10 µg/m³ rise of PM₁₀, which is almost twice as large as non-desert PM₁₀ (0.5% [95% CI = 0.0, 1.0]). In contrast, non-desert PM₁₀ shows estimated effects at longer lags, up to day 4 after exposure, and point estimates closer to those obtained for total PM₁₀.

Three-sources Model

Previous studies observed that a lowering of the mixing layer height during dust episodes allowed enhancement of local pollution (i.e., non-desert source) in addition to the desert source.³⁶ This could cause different health effects of the non-desert contribution to total PM₁₀ depending on whether it is a dust day or not.³⁷ In this scenario, we can estimate independent effects through a three-pollutant model. The corresponding DAG is shown in Figure 1 (panel E), where the dust exposure event has a double role of influencing desert PM₁₀ concentrations and modifying the association between non-desert PM₁₀ and mortality. This model allows the following two research questions to be addressed: “Is the association between non-desert PM₁₀ with mortality different on dust versus non-dust days? and are these associations independent from desert PM₁₀?” The corresponding regression model would be stated as follows:

$$\log(y_t) = \text{adj.model} + \beta_{\text{non-desert}} \text{non-desert PM}_{10,t-1} + \beta_{\text{desert}} \text{desert PM}_{10,t-1} + \beta_{\text{dus}} \text{dust}_{t-1} + \beta_{\text{interaction}} \text{dust}_{t-1} \times \text{non-desert PM}_{10,t-1} + \varepsilon_t$$

where $\beta_{\text{interaction}}$ estimates the relative increase of daily mortality per unit increment of non-desert PM₁₀ on dust days compared with non-dust days, upon adjustment for desert PM₁₀.

Figure 4 (right panel) shows higher estimated effects of non-desert PM₁₀ on dust days (2.2% [95% CI = 0.6, 3.8]) than non-dust days (0.3% [95% CI = -0.2, 1.9]), for a 10 µg/m³ rise of PM₁₀ at lag 0 and similarly for other lags. Estimates were smaller for desert PM₁₀ at any lag (e.g., 1.0% [95% CI = -1.4, 3.8] at lag 0).

DISCUSSION

In this study, we have reviewed all the different approaches in the literature that we are aware of to estimate the short-term effects of desert dust on human health. We propose a unified framework where different approaches can be compared in terms of underlying research and policy-relevant questions, to bring more consistent evidence to the question of the health effects of desert dust for future studies.

Most of the studies conducted in Asia used a binary metric of dust and consider it as a risk factor, comparing the

occurrence of health events (daily cause-specific mortality and hospital admissions) between dust and non-dust days.^{8,11} In general, these studies consistently found excess risks on dust days, especially for cardiovascular mortality and respiratory morbidity.^{8,11} Despite their intuitive designs, these studies might suffer from two major drawbacks. First, they are prone to residual confounding due to the poor adjustment for seasonality or meteorologic covariates, because dust days tend to occur in specific seasons and under particular atmospheric conditions, which might themselves be associated with excess mortality. Some of the published studies documented how such confounding factors were controlled for in the statistical models, but others failed to do so.⁸ Second, and most importantly, these studies cannot provide any information on the dose-response relationship between desert dust exposure and human health, as all dust intrusions are treated in the same way, with no attempt to quantify the dust load at the ground level and the consequent population exposure.

Studies mainly conducted in Southern Europe also used a binary metric but considered dust an effect modifier of the association between PM and health, under the assumption that PM composition might change between dust and non-dust days.^{9,11} Most of these found consistent evidence of higher effects of PM during dust days on cardiovascular mortality and respiratory morbidity, especially asthma.⁹ The limitation of this approach, however, is that total PM is a mixture of natural and anthropogenic sources, even within the dust days. Therefore, it is impossible to attribute the health effects to one or the other source simply by classifying days according to the presence of a dust advection episode. Some of the studies circumvented this problem by estimating separate effects for the fine and the coarse fractions of PM, providing consistent evidence of larger effects of the coarse PM on dust days, and larger effects of fine PM on non-dust days.⁹

The use of dust as a continuous exposure enables estimation of independent effects of the two sources of PM, desert and non-desert, because both exposures are fitted simultaneously in the regression model to the health outcome. In addition, since the two exposures are quantitative measures of PM concentrations, they can be modeled with flexible non-linear functions in order to estimate concentration-response relationships with health outcomes. For example, the EU Reference method for dust quantification easily allows description of the differential contribution of desert and non-desert sources on the fine and coarse fractions of PM, and their effects on human health.^{13,15} Similar effects of Saharan dust and non-desert PM₁₀ on mortality and morbidity outcomes have been reported in Southern Europe using this approach.¹³ However, when also accounting for the occurrence of dust events, a study conducted in Barcelona reported larger effect of non-desert PM₁₀ during dust days on cardiovascular mortality.³⁷ Alternative methods, such as LIDAR measurements or model estimates based on remote sensing retrievals, can also be used as valuable tools for dust exposures. Here, few studies

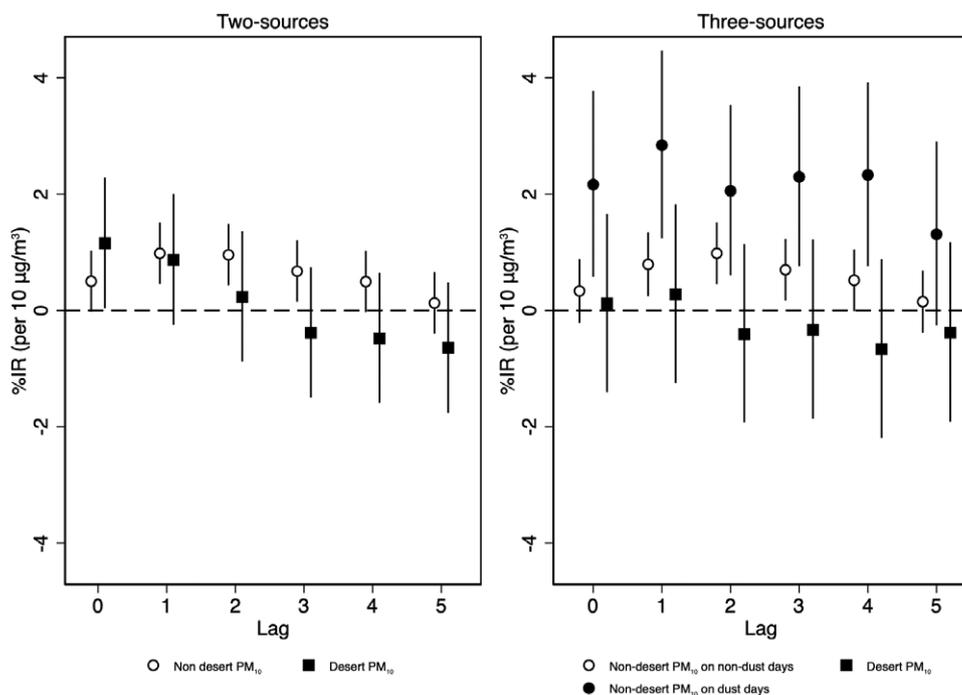


FIGURE 4. Percent increase of risk (%IR) of mortality for a 10 $\mu\text{g}/\text{m}^3$ rise of PM_{10} of desert and non-desert loads using two sources model (left) and three sources model (right).

conducted in Japan have reported larger effects of Asian dust than suspended particulate matter on daily mortality due to specific cardiovascular causes²³ and ambulance calls for specific respiratory causes.³⁸ However, some limitations should also be acknowledged. The current methods for quantifying dust events are not free of measurement error. While the EU Reference method relies on the availability of valid reference measurements from a regional or suburban background station, the use of LIDAR measurements is highly dependent on parameters like the height of the dust layer to reflect dust on the ground level or the cutoff level of the dust extinction coefficient, which may have a substantial impact on the health effect estimates. Remote-sensing data on dust concentrations at surface level from global reanalysis of such data could be a feasible alternative to in-situ PM observations. However, the use of remote reanalysis products has not yet been validated in epidemiologic studies to estimate the short-term effects of desert dust. Second, disentangling the health effects of desert and non-desert sources might be extremely challenging in regions characterized by extremely high concentrations of particles from local sources, because most of the adverse health outcomes might occur on non-dust days, and the additional contribution from dust would be negligible.³⁹

However, the main limitation in epidemiologic studies to assess the health effects of desert dust is still the lack of a unified definition or identification method for dust events.^{8,9} This is a gap in dust exposure research that needs further research. The InDust network aims to develop a standardized methodology to identify and quantify dust exposures for epidemiologic studies to make health effects comparable across regions.⁴⁰ An alternative is to use remote sensing and

reanalysis data, but these are not yet used routinely in environmental epidemiology studies.

Another relevant issue is the adjustment for temperature because of the strong seasonality of health outcomes, PM exposures, and dust events. We controlled for the effect of temperature by modeling high and low temperatures separately for consistency with our previous studies in Rome.^{13,17} This approach accounts for differences in the lag structures and effects of cold and warm temperatures on daily mortality while reducing the correlation between the two spline terms.¹⁷ We performed a sensitivity analysis using two terms, lag 0–1 and lag 1–6 of temperature, defined from the full range of temperature values. The estimates were slightly reduced (e.g., for the three-sources model, the estimated effect of non-desert PM_{10} was 1.8% (95% CI = 0.4, 3.2) for dust days and 0.4% (95% CI = -0.1, 0.8) for non-dust days, and 0.6% (95% CI = -0.5, 2.1) for desert PM_{10} at lag 0). Overall, estimates for dust exposures kept the same lag structure.

Finally, with regard to potential confounding by other co-pollutants in the desert dust exposure analyses, previous studies conducted in Barcelona²⁹ and Rome³⁰ show a similar distribution of other pollutants between dust and non-dust days, and a multicenter study conducted in 13 Southern European cities¹³ did not show confounding effects by NO_2 and gases. We conducted a sensitivity analysis adjusting each of the modeling approaches by NO_2 , and the results did not change substantially. However, we should acknowledge the importance of careful checks for confounding by other co-pollutants in different geographical areas affected by dust in or near hot-spots, as they might behave differently according to the source region.

In conclusion, a proper understanding of population exposure to desert dust in epidemiologic studies would help to develop appropriate mitigation measures to reduce impact on human health. Although the methods described in this paper have been applied in one city as an illustrative example, these can be easily replicated in other locations near hot-spots. This would allow standardization of epidemiologic studies with same methodologic characteristics in order to make short-term estimates of health effects of desert dust comparable between different regions affected by dust exposure.

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