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Short-term effects of $PM_{2.5}$, PM_{10} and $PM_{2.5–10}$ on daily mortality in the Netherlands

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HIGHLIGHTS

- European studies on the effects of $PM_{2.5}$ on daily mortality are still relatively limited.
- For the entire Netherlands (population 16 million) significant associations with $PM_{2.5}$ are found.
- Effects of $PM_{2.5}$ could not be disentangled from effects of PM_{10} due to their high correlation.
- Daily variability in levels in the coarse fraction was found to be low in the Netherlands.

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ABSTRACT

Introduction: Information on the relationship between levels of particulate matter (PM) smaller than 2.5 μm and mortality rates in Europe is relatively sparse because of limited availability of $PM_{2.5}$ measurement data. Even less information is available on the health effects attributable to $PM_{2.5–10}$, especially for North-West Europe.

Objectives: To investigate the relationship between various PM size fractions and daily mortality rates.

Methods: Daily concentrations of PM from the Dutch National Ambient Air Quality Monitoring Network as well as all cause and cause-specific mortality rates in the Netherlands were obtained for the period 2008–2009. Poisson regression analysis using generalized additive models was used, with adjustment for potential confounding including long-term and seasonal trends, influenza incidence, meteorological variables, day of the week, and holidays.

Different measures of PM ($PM_{2.5}$, PM_{10} and $PM_{2.5–10}$) were analysed.

Results: PM_{10} and $PM_{2.5}$ levels were statistically significantly ($p < 0.05$) associated with all cause and cause-specific deaths. For example, a 10 μg/m^3 increase in previous day PM was associated with 0.8% (95% CI 0.3–1.2) excess risk in all cause mortality for $PM_{2.5}$ and a 0.6% (CI 0.2–1.0) excess risk for PM_{10}. No appreciable associations were observed for $PM_{2.5–10}$. Effects of PM_{10}, and $PM_{2.5}$ were insensitive to adjustment for $PM_{2.5–10}$, and vice-versa. PM_{10} and $PM_{2.5}$ were too highly correlated to disentangle their independent effects.

Conclusions: PM_{10} and $PM_{2.5}$ both were significantly associated with all cause and cause-specific mortality. We were unable to demonstrate significant effects for $PM_{2.5–10}$, possibly due to the lower temporal variability and the higher exposure misclassification in $PM_{2.5–10}$ compared to PM_{10} or $PM_{2.5}$. The lack of effects of $PM_{2.5–10}$ in our study should therefore not be interpreted as an indication that $PM_{2.5–10}$ can be considered harmless.

1. Introduction

A large number of epidemiological studies have shown that short-term exposure to ambient particulate matter (PM) in outdoor air is associated with total and cause-specific mortality. This led to outdoor air pollution standards for PM_{10} in the European Union for daily and yearly averaging times. PM_{10} was seen as the most health relevant PM size fraction and is therefore measured on a regular basis in specified locations in all EU countries. Evidence is increasing, mainly based on studies from the US, that the smaller $PM_{2.5}$ fraction is more consistently associated with health outcomes, and that this

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fraction is more specific for anthropogenic combustion-related emissions. EU registration therefore decided to put, following regulation in the US, a $PM_{2.5}$ standard in force starting 2015 with an anticipated limit value of 25 μg/m^3 (yearly average). Contrary to the large amount of US studies on health effects of $PM_{2.5}$, European studies on $PM_{2.5}$ are sparse and studies in the literature on mortality effects of $PM_{2.5}$ could only be identified for 10 European cities (Anderson et al., 2001; Atkinson et al., 2010; Branis et al., 2010; Garrett and Casimiro, 2011; Halonen et al., 2009; Mate et al., 2010; Mallone et al, 2011; Meister et al., 2012; Ostro et al., 2011; Stolzel et al, 2007). Our study, which is based on mortality data from the whole Netherlands (population 16 million) could add valuable evidence to the advice on health effects of $PM_{2.5}$ to the European Commission.

In addition to effects of $PM_{2.5}$, there is increasing evidence that coarse particles ($PM_{2.5-10}$) may play a role in generating adverse health effects (Brunekreef and Forsberg, 2005; Sandstrom et al., 2005). In a national, multi-city time-series study of the acute effects of $PM_{2.5}$ and $PM_{2.5-10}$ in the US, Zanobetti and Schwartz (2009) found that both $PM_{2.5}$ and $PM_{2.5-10}$ were significantly associated with increased mortality for all and specific causes. Less evidence of effects of $PM_{2.5}$ and $PM_{2.5-10}$ is available from European studies. Several European studies failed to demonstrate significant effects of $PM_{2.5}$ on all cause or cause specific mortality (Branis et al., 2010; Garrett and Casimiro, 2011; Halonen et al., 2009; Mallone et al., 2011; Stolzel et al., 2007). However, these studies generally comprised relatively small populations (≤1 million) (Garrett and Casimiro, 2011; Halonen et al., 2009; Stolzel et al., 2007) or short study periods (1 year) (Branis et al., 2010). In a recent study that included 6 years of data on particulate matter air pollution and mortality in London, UK, $PM_{2.5}$ was not statistically significantly associated with all cause or cardiovascular mortality, and the effect on respiratory mortality was only statistically significant for one of the seven lags studied (lag2) (Atkinson et al., 2010). Even less information is available for $PM_{2.5-10}$, especially for North-West Europe.

Validated Dutch ambient measurement results of PM_{10} started in 1992 while measurement of $PM_{2.5}$ first became available in 2008. We therefore evaluated the association between different size fractions of PM ($PM_{2.5}$, PM_{10} and $PM_{2.5-10}$) and daily mortality in the Netherlands.

2. Methods

2.1. Data collection

2.1.1. Mortality, influenza and meteorology data

Data on daily mortality, influenza and meteorology were obtained as described by Fischer et al. (2011). Briefly, data for the entire Dutch population over the years 2008 and 2009 were obtained from Statistics Netherlands (CBS). Weekly incidence of influenza-type illnesses (as a well-known confounder) were provided by the Continuous Morbidity Registration of the Netherlands Institute for Health Services Research (NIVEL) (Dijkstra et al., 2009; Donker, 2010), and one hour mean temperature, T (°C), relative humidity, RH (%), and atmospheric pressure, P (hPa), were obtained from the Royal Dutch Meteorological Institute (KNMI).

The Dutch population approximated 16.5 million in 2008. Selection of total and cause-specific mortality was the same as described by Fischer et al. (2011).

2.1.2. Air quality

Air quality data were obtained from our institute, which operates the National Air Quality Monitoring Network (NAQMN) in the Netherlands (Van Elzakker, 2001). This network currently comprises approximately 50 monitoring sites in both regional and urban areas. Their mutual distance increases with decrease in population density. Measuring stations for $PM_{2.5}$ and PM_{10} in the Netherlands are shown in Fig. 1. In the years 2008 and 2009 PM_{10} was measured at 16 regional and 7 urban background stations (total 23 stations). For $PM_{2.5}$ these numbers were 6 and 9 respectively (total 15 stations). Both PM_{10} and $PM_{2.5}$ were measured at 6 regional and 4 urban background stations (total 10 stations). PM_{10} measurements were conducted using a continuous particulate monitor, type FH62-I-R (ESM Andersen Instruments, Erlangen, Germany). The relative uncertainty of the configuration used in the NAQMN compared to a reference method (equivalence) was found to be 17%, which is in compliance with the European quality objective of 25% (Beijk et al, 2008). $PM_{2.5}$ was measured gravimetrically, using a Derenda PNS 16T3.1/6.1 (Derenda, Stahnsdorf, Germany).

We used 24-hour average concentrations (midnight to midnight). Missing values were imputed as described by Fischer et al. (2011). Briefly, it amounts to estimating a missing value at stations s on day d as the mean of all available concentration data of the other stations on day d multiplied by the ratio of the yearly mean at station s and the overall yearly mean of all stations. Daily nationwide average concentrations of $PM_{2.5}$ and PM_{10} were calculated as the average of the 10 stations where both PM_{10} and $PM_{2.5}$ were measured. Concentrations of $PM_{2.5-10}$ were calculated as the difference between PM_{10} and $PM_{2.5}$. For comparison, daily nationwide average PM concentrations were also calculated using all 23 stations for PM_{10} and all 15 stations for $PM_{2.5}$.

2.2. Data analysis

We analysed the data using Poisson regression in generalized additive models (GAM) with R version 2.10.0 (R Development Core Team, 2009). Functions in the mgcv-package of R were used to build GAMs with penalised splines. For all pollutants five lags were evaluated (lags 0, 1, 2, and 3 days and the average of lags 0–6 days). Daily nationwide average PM concentrations, calculated as the average of the 10 stations where both PM_{10} and $PM_{2.5}$ were measured, were entered as continuous variables. All pollution–mortality associations were adjusted for long term and seasonal trend (cubic regression spline), influenza incidence (average over previous week, thin plate regression spline), mean temperature, relative humidity, and barometric pressure using thin plate regression splines on lag1 values. The number of knots for each spline was set at 16, based on the procedure described by Wood (2001). For the different models, the degrees of freedom used ranged from 11 to 14 for the seasonal trend, from 1 to 5 for the different meteorological parameters (i.e. temperature, relative humidity and barometric pressure) and from 1 to 12 for influenza. The models were adjusted for day of the week and holidays using dummy variables. Regression coefficients (and standard errors) were transformed into percentage excess risk estimates ($ER = 100(RR - 1)$) and 95% confidence intervals associated with an increase in pollutant concentration of 10 μg/m^3. As a sensitivity analyses, ERs were also calculated using nationwide $PM_{2.5}$ and PM_{10} concentrations based on all 23 stations for PM_{10} and all 15 stations for $PM_{2.5}$. Effect estimates were considered statistically significant if $p < 0.05$, and borderline significant if $p < 0.10$.

3. Results

3.1. Air pollution data

3.1.1. Descriptive statistics

Descriptive statistics of the data used in the statistical analysis (daily mortality, influenza counts, air pollution concentrations, and weather variables) are presented in Table 1. Yearly average PM_{10} levels are well below the EU standard of 40 μg/m^3, which is also the case for the anticipated EU yearly standard of 25 μg/m^3. As shown in the table, approximately 60% of PM_{10} mass can be attributed to $PM_{2.5}$ mass. On one day, the nationwide average $PM_{2.5}$ concentration (10.84 μg/m^3) was higher than the nationwide average PM_{10} concentration (10.35 μg/m^3), resulting in a negative $PM_{2.5-10}$ concentration of −0.49μg/m^3. This value was retained as such in the data analysis. Interquartile ranges (IQR) were the same for both $PM_{2.5}$ and PM_{10}: 12 μg/m^3 for the 24-h averaged concentrations and

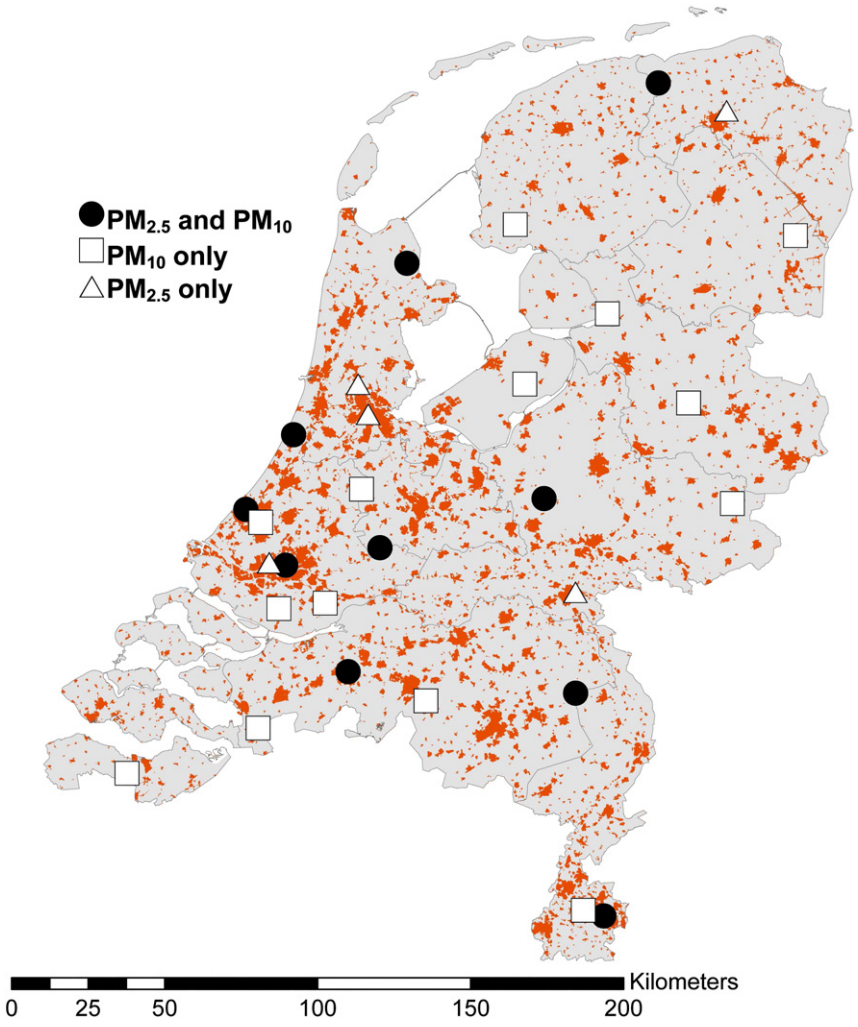

Fig. 1. Location of monitoring sites.

Table 1
Overall summary statistics of daily mortality, pollutants and meteorological data for the study period (2008–2009).

Variable	Mean	Std	Min	25%	Median	75%	Max
All cause mortality (# per day)	353.4	38.3	262.0	326.0	348.0	375.0	507.0
Cardiovascular mortality (# per day)	107.7	15.7	69.0	96.0	107.0	118.0	161.0
Respiratory mortality (# per day)	38.0	12.7	14.0	30.0	35.0	44.0	90.0
Pneumonia mortality (# per day)	15.1	6.5	2.0	11.0	14.0	18.0	47.0
COPD mortality (# per day)	17.2	6.1	4.0	13.0	16.0	20.0	44.0
Influenza incidence (per 10,000)	5.5	4.3	0.5	2.4	4.7	7.3	22.1
$PM_{2.5}$ ($\mu g/m^3$)	16.3	11.1	3.1	8.7	13.1	20.9	106.1
PM_{10} ($\mu g/m^3$)	23.9	12.9	7.9	16.1	20.6	27.9	154.0
$PM_{2.5-10}$ ($\mu g/m^3$)	7.7	4.0	−0.5	5.3	7.2	9.5	53.9
Average temperature (°C)	10.4	6.3	−8.4	5.7	10.8	15.6	24.2
Minimum temperature (°C)	6.0	5.7	−12.2	2.0	6.2	10.7	18.8
Maximum temperature (°C)	14.5	7.3	−5.3	8.9	14.8	20.4	34.6
Atmospheric pressure (hPa)	1014	10	973	1008	1015	1021	1045
Relative humidity (%)	81.2	9.5	46.6	75.0	82.4	88.4	99.2

9 $\mu g/m^3$ for weekly averaged concentrations. This suggests that the daily variation in PM_{10} concentrations in the Netherlands is mainly driven by the variation in $PM_{2.5}$ concentrations, as is demonstrated in Fig. 2. The highest PM concentrations (>100 $\mu g/m^3$ for $PM_{2.5}$ and PM_{10}; >40 $\mu g/m^3$ for $PM_{2.5-10}$) were measured on 1-1-2008 and 1-1-2009 and can be attributed to the Dutch custom of mass firework festivities during New Year's Eve.

3.1.2. Comparison with concentrations averaged over all available stations

As described in Section 2.1.2, daily nationwide $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ concentrations were calculated as the average of 10 monitoring stations where both PM_{10} and $PM_{2.5}$ were measured. Daily nationwide average concentrations based on all available monitoring sites (23 stations for PM_{10} and 15 stations for $PM_{2.5}$) were similar to and highly correlated with daily nationwide averages based on the 10 sites where both $PM_{2.5}$ and PM_{10} were measured (Spearman $R = 0.99$ for PM_{10} and $PM_{2.5}$, and 0.92 for $PM_{2.5-10}$).

3.1.3. Correlation between individual stations

Concentrations measured at the 10 individual monitoring sites were highly correlated for both PM_{10} and $PM_{2.5}$, with Spearman R between two individual stations ranging from 0.63 to 0.96 for $PM_{2.5}$ and from 0.41 to 0.88 for PM_{10} (Supplemental material, Table S.1). The lowest correlations were calculated for the most Southern station, which showed the lowest correlation with the three most Northern

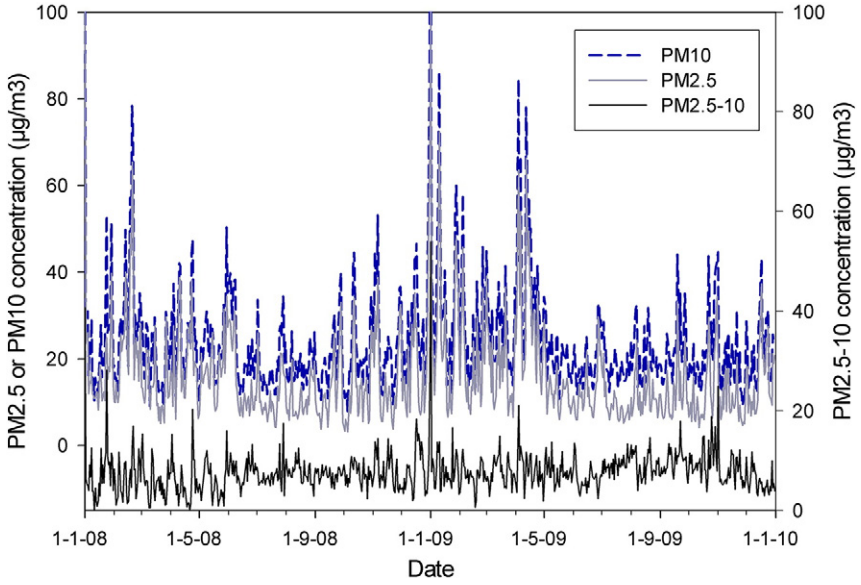

Fig. 2. Daily variation in PM_{10}, $PM_{2.5}$ and $PM_{2.5-10}$ concentrations throughout the measurement period (PM_{10} and $PM_{2.5}$ concentrations at 1-1-2008 and 1-1-2009 truncated to 100 µg/m^3).

stations (Spearman R 0.63 for $PM_{2.5}$ and 0.41–0.45 for PM_{10}). Daily variations in $PM_{2.5-10}$ concentrations were less spatially homogeneous, with Spearman R between two individual stations ranging from 0.11 to 0.62. The lower correlations were generally observed for the monitoring sites that were furthest apart (>200 km); the highest correlations (Spearman R > 0.6) were observed between sites that were situated closest (<30 km) to each other (i.e. the three sites in the West of the Netherlands).

3.1.4. Correlation among PM fractions

Fig. 3 presents the correlation between $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ concentrations. A full correlation table, including the correlation with meteorological variables is presented in the Supplemental Material (Table S.2). PM_{10} and $PM_{2.5}$ concentrations were highly correlated (R = 0.95) because emission sources are mainly the same for the different measures (i.e. mobile sources and agricultural activities). This high correlation between PM_{10} and $PM_{2.5}$ will complicate interpretation of the role of the specific fractions in further statistical analyses. However, for completeness and comparability with previous results on PM_{10}, we decided to analyse both components separately. $PM_{2.5-10}$ was not highly correlated with either PM_{10} (R = 0.57) or $PM_{2.5}$ (R = 0.29).

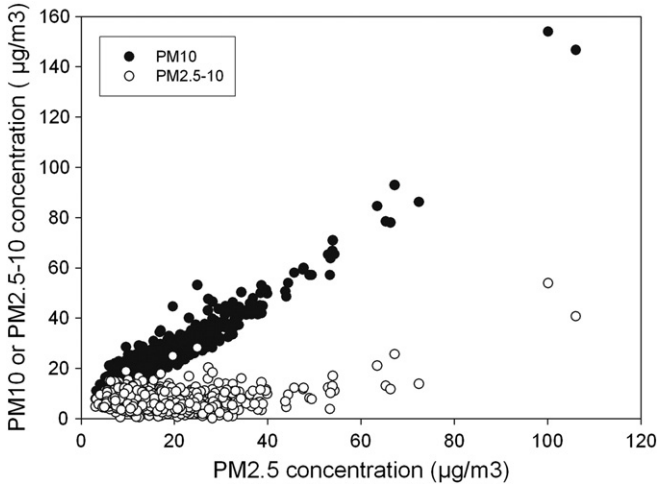

Fig. 3. Relation between PM_{10}, $PM_{2.5}$ and $PM_{2.5-10}$ concentrations. (Regression equations: $PM_{10} = 6.0 + 1.1 \times PM_{2.5}$; $PM_{2.5-10} = 6.0 + 0.1 \times PM_{2.5}$.)

3.2. Association between PM and daily mortality

Table 2 shows the excess risk estimates (ER) and 95% confidence intervals (CI) for daily mortality by cause of death for various lags, associated with a change in air pollutant concentration of 10 µg/m^3. PM_{10} and $PM_{2.5}$ are both statistically significantly associated with all cause as well as cause-specific mortality, whereas no statistically significant associations were found for $PM_{2.5-10}$. For all cause mortality, significant effects of PM_{10} and $PM_{2.5}$ were observed for all lags studied, whereas for respiratory mortality, statistically significant effects were found for the later lags (i.e. lag2, lag3 and the weekly average). PM_{10}, $PM_{2.5}$ and cardiovascular mortality are less strongly associated. ERs calculated using all available monitoring stations for PM_{10} (23 stations) and $PM_{2.5}$ (15 stations) were similar (Supplemental Material, Table S.3.).

ERs per 10 µg/m^3 for $PM_{2.5}$ are generally higher compared to the ERs for PM_{10}, especially for the shortest lags (i.e. lag0 and lag1). As the IQR is 12 µg/m^3 for both $PM_{2.5}$ and PM_{10}, ERs expressed per IQR are equally higher for $PM_{2.5}$ compared to PM_{10}. Confidence intervals overlap, however.

Table 3 shows the results of two-pollutant models, where $PM_{2.5}$ and $PM_{2.5-10}$ were both included in the model. Effect estimates for $PM_{2.5}$ were not affected after adjustment for $PM_{2.5-10}$, and vice versa.

4. Discussion

PM_{10} and $PM_{2.5}$ are statistically significantly associated with all cause and cause-specific mortality. No such associations were observed for $PM_{2.5-10}$. Effects of PM_{10} and $PM_{2.5}$ were insensitive to adjustment for $PM_{2.5-10}$, and vice-versa. PM_{10} and $PM_{2.5}$ are too highly correlated to disentangle their independent effects.

Table 2
Excess risk estimates (ER)[a] and 95% confidence intervals (CI) for daily mortality by cause of death for various lags, associated with a change in air pollutant concentration of 10 μg/m^3.

Pollutant (μg/m^3)	Lag	All cause		Cardiovascular		Total respiratory		Pneumonia		COPD	
		ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)
$PM_{2.5}$	0	0.8	(0.3–1.2)**	1.1	(0.2–1.9)*	0.9	(−0.5–2.3)	−0.1	(−2.2–2.1)	2.5	(0.5–4.6)*
	1	0.8	(0.3–1.2)**	0.8	(0.0–1.6)#	1.0	(−0.3–2.4)	0.2	(−1.8–2.4)	3.5	(1.6–5.4)**
	2	0.9	(0.5–1.3)**	0.6	(−0.2–1.4)	1.6	(0.4–2.9)*	3.1	(1.2–5.1)**	2.1	(0.3–4.0)*
	3	1.0	(0.6–1.4)**	0.5	(−0.2–1.3)	2.3	(1.1–3.5)**	3.1	(1.2–4.9)**	2.7	(0.9–4.5)**
	0–6	2.1	(1.4–2.8)**	1.7	(0.5–2.9)**	4.2	(2.2–6.3)**	5.3	(2.2–8.6)**	6.1	(3.2–9.1)**
PM_{10}	0	0.4	(0.0–0.8)*	0.5	(−0.2–1.2)	0.6	(−0.6–1.7)	0.0	(−1.8–1.8)	1.5	(−0.3–3.3)
	1	0.6	(0.2–1.0)**	0.4	(−0.3–1.1)	0.7	(−0.5–1.8)	0.1	(−1.7–1.9)	2.5	(0.9–4.1)**
	2	0.8	(0.4–1.2)**	0.5	(−0.1–1.2)	1.6	(0.5–2.6)**	2.6	(1.0–4.2)**	2.0	(0.4–3.5)*
	3	0.8	(0.4–1.2)**	0.6	(−0.1–1.2)#	1.9	(0.9–2.9)**	2.3	(0.8–3.9)**	2.3	(0.9–3.8)**
	0–6	1.8	(1.2–2.4)**	1.4	(0.3–2.5)*	3.5	(1.7–5.3)**	4.4	(1.6–7.2)**	4.9	(2.3–7.5)**
$PM_{2.5-10}$	0	−1.3	(−2.4 to −0.1)*	−1.9	(−3.9–0.1)#	−0.2	(−3.4–3.1)	0.2	(−4.8–5.4)	1.0	(−3.7–6.0)
	1	−0.2	(−1.3–1.0)	−1.4	(−3.3–0.7)	−0.4	(−3.6–2.9)	−0.6	(−5.6–4.6)	−0.1	(−4.8–4.8)
	2	0.9	(−0.2–2.1)	1.0	(−1.0–3.0)	3.8	(0.6–7.2)*	3.4	(−1.6–8.7)	4.3	(−0.5–9.3)#
	3	0.6	(−0.5–1.8)	1.8	(−0.2–3.7)#	2.5	(−0.6–5.8)	1.6	(−3.3–6.7)	5.3	(0.6–10.3)*
	0–6	1.2	(−1.2–3.6)	0.6	(−3.4–4.8)	3.4	(−3.6–10.8)	4.2	(−6.3–15.8)	3.5	(−6.5–14.7)

[a] Generalized Additive Models (GAM) adjusted for long-term and seasonal trends (cubic regression spline), influenza incidence (average over previous week, thin plate regression spline), mean temperature, relative humidity, and barometric pressure (thin plate regression splines, lag1), day of the week and holidays.
# $p < 0.10$.
* $p < 0.05$.
** $p < 0.01$.

Table 3
Excess risk estimates (ER)[a] and 95% confidence intervals (CI) for daily mortality associated with a change in $PM_{2.5}$ and PM_{25-10} in single and in two-pollutant models.

	Single pollutant model				2-Pollutant model			
	PM_{25}		PM_{25-10}		PM_{25}		PM_{25-10}	
	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)
All cause mortality								
Lag0	0.8	(0.3–1.2)**	−1.3	(−2.4–0.1)*	1.0	(0.5–1.5)**	−1.7	(−2.9 to −0.6)*
Lag1	0.8	(0.3–1.2)**	−0.2	(−1.3–1.0)	0.9	(0.4–1.4)**	−1.0	(−2.1–0.2)
Lag2	0.9	(0.5–1.3)**	0.9	(−0.2–2.1)	0.9	(0.4–1.3)**	0.4	(−0.7–1.6)
Lag3	1.0	(0.6–1.4)**	0.6	(−0.5–1.8)	1.0	(0.6–1.5)**	−0.3	(−1.4–0.9)
Lag0–6	2.1	(1.4–2.8)**	1.2	(−1.2–3.6)	2.2	(1.5–3.0)**	−1.1	(−3.5–1.4)
Cardiovascular mortality								
Lag0	1.1	(0.2–1.9)*	−1.9	(−3.9–0.1)#	1.4	(0.5–2.3)**	−2.8	(−4.9 to −0.8)*
Lag1	0.8	(0.0–1.6)#	−1.4	(−3.3–0.7)	0.9	(0.1–1.8)*	−1.6	(−3.6–0.5)
Lag2	0.6	(−0.2–1.4)	1.0	(−1.0–3.0)	0.6	(−0.3–1.4)	0.4	(−1.6–2.5)
Lag3	0.5	(−0.2–1.3)	1.8	(−0.2–3.7)#	0.3	(−0.5–1.1)	1.7	(−0.3–3.8)#
Lag0–6	1.7	(0.5–2.9)**	0.6	(−3.4–4.8)	1.8	(0.5–3.1)**	−0.9	(−5.1–3.4)
Respiratory mortality								
Lag0	0.9	(−0.5–2.3)	−0.2	(−3.4–3.1)	0.9	(−0.6–2.4)	−0.3	(−3.6–3.2)
Lag1	1.0	(−0.3–2.4)	−0.4	(−3.6–2.9)	1.2	(−0.3–2.6)	−1.3	(−4.7–2.1)
Lag2	1.6	(0.4–2.9)*	3.8	(0.6–7.2)*	1.3	(−0.1–2.6)#	2.7	(−0.7–6.2)
Lag3	2.3	(1.1–3.5)**	2.5	(−0.6–5.8)	2.3	(1.0–3.6)**	0.3	(−3.0–3.7)
Lag0–6	4.2	(2.2–6.3)**	3.4	(−3.6–10.8)	4.3	(2.0–6.6)**	−0.6	(−7.7–7.0)
Pneumonia mortality								
Lag0	−0.1	(−2.2–2.1)	0.2	(−4.8–5.4)	−0.2	(−2.5–2.2)	0.6	(−4.6–6.2)
Lag1	0.2	(−1.8–2.4)	−0.6	(−5.6–4.6)	0.4	(−1.8–2.7)	−1.4	(−6.7–4.1)
Lag2	3.1	(1.2–5.1)**	3.4	(−1.6–8.7)	3.1	(1.0–5.2)**	0.4	(−4.8–5.8)
Lag3	3.1	(1.2–4.9)**	1.6	(−3.3–6.7)	3.2	(1.2–5.3)**	−1.3	(−6.3–4.0)
Lag0–6	5.3	(2.2–8.6)**	4.2	(−6.3−15.8)	5.5	(2.1−9.2)**	−1.3	(−12.1−10.7)
COPD mortality								
Lag0	2.5	(0.5−4.6)*	1.0	(−3.7−6.0)	2.5	(0.3−4.8)*	−0.1	(−4.9−5.1)
Lag1	3.5	(1.6−5.4)**	−0.1	(−4.8−4.8)	3.8	(1.7−6.0)*	−3.3	(−8.1−1.8)
Lag2	2.1	(0.3−4.0)*	4.3	(−0.5−9.3)#	1.7	(−0.2−3.7)#	2.8	(−2.1−8.0)
Lag3	2.7	(0.9−4.5)**	5.3	(0.6−10.3)*	2.4	(0.5−4.4)*	1.5	(−3.3−6.5)
Lag0−6	6.1	(3.2−9.1)**	3.5	(−6.5−14.7)	6.9	(3.6−10.2)**	−5.2	(−14.7−5.3)

[a] Generalized Additive Models (GAM) adjusted for long-term and seasonal trends (cubic regression spline), influenza incidence (average over previous week, thin plate regression spline), mean temperature, relative humidity, and barometric pressure (thin plate regression splines, lag1), day of the week and holidays.
# $p < 0.10$.
* $p < 0.05$.
** $p < 0.01$.

4.1. PM_{10} and $PM_{2.5}$

Effect estimates for PM_{10} are generally similar to those reported previously for the Netherlands (Fischer et al., 2011) and to results of a meta-analysis that included all effect estimates for PM_{10} from European studies published up to February 2003 (Anderson et al., 2004). Effect estimates are also generally similar to results of a recent meta-analysis that included seven European studies that had measured both PM_{10} and BS (Janssen et al., 2011).

Less information from European studies is available for $PM_{2.5}$. Studies conducted in Helsinki (Finland), Erfurt (Germany), Prague (Czech Republic), Lisbon (Portugal), Rome (Italy), West-Midlands (UK) and London (UK) failed to demonstrate significant effects of $PM_{2.5}$ with all cause and cardiovascular mortality (Anderson et al., 2001; Atkinson et al., 2010; Branis et al., 2010; Breitner et al., 2009; Garrett and Casimiro, 2011; Halonen et al., 2009; Mallone et al., 2011; Stolzel et al, 2007). Respiratory mortality was only significantly associated with $PM_{2.5}$ in London at lag2 (Atkinson et al., 2010). However, with the exception of the two studies conducted in the UK and the study in Rome, these studies included relatively small populations ($\leq$1 million) and/or short study periods (1 year), and effect estimates were generally similar to what we observed in the Netherlands. Of the four studies that also included associations for PM_{10}, no significant associations with all cause or cause specific mortality were observed in West-Midlands and Erfurt (Anderson et al., 2001; Stolzel et al., 2007). In London, PM_{10} was significantly associated with all cause (lag1) and respiratory mortality (lag1 and lag2), but not with cardiovascular mortality (Atkinson et al., 2010). In Rome, PM_{10} was significantly associated with all cause, cardiac and circulatory mortality, but not with respiratory mortality (Mallone et al., 2011). In London, the magnitude of the significant effects was similar to what we observed in the Netherlands. For example, a 10 $\mu g/m^3$ increase in PM_{10} at lag1 (measured by TEOM) in London was associated with a 0.5% (95% CI 0.0–0.9) in all cause mortality, compared to 0.5% (95% CI 0.1–0.9) in our study. A 10 $\mu g/m^3$ increase in $PM_{2.5}$ at lag2 (measured by TEOM) in London was associated with a 2.1% (95% CI 0.6–3.7%) increase in respiratory mortality, compared to 1.6% (95% CI 0.4–2.9%) in our study. In Rome, PM_{10} effects were larger compared to the Netherlands ($\pm$1.5% per 10 μg/m3 in Rome compared to $\pm$0.5% in the Netherlands).

Significant associations between $PM_{2.5}$ and daily mortality were observed in Stockholm (Sweden), Barcelona (Spain) and Madrid (Spain). Effect estimates were generally larger than what we observed in the Netherlands. For example, the increase in all cause mortality associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ ranged from 1.4% (95% CI 0.6–2.3) in Barcelona and 1.5% (95% CI 0.1–2.8) in Stockholm to 2.7% (95% CI 1.4–4.1) in Madrid, compared to 0.8% (95% CI 0.3–1.2%) in the Netherlands (Guaita et al., 2011; Mate et al., 2010; Meister et al., 2012; Ostro et al., 2011; Tobias et al., 2011).

In a previous analysis on the effects of ambient air pollution on daily mortality (Fischer et al., 2011) our results suggested that effects of ambient air pollution on the cardiovascular system act immediately, while effects of air pollution on the respiratory system act somewhat delayed. In our current study again we found effects on respiratory mortality at longer lags than effects on total or cardiovascular mortality, however this was only the case for $PM_{2.5}$; for PM_{10} also effects on cardiovascular mortality were statistical significant only at the longer lags. Therefore our results are inconclusive to add to the evidence that, in general, (particulate) air pollution affects cardiovascular mortality at a different time lag than respiratory mortality.

Effect estimates were calculated for the entire Dutch population, without age stratification. However, this does not imply that mortality from air pollution is evenly distributed across the whole population, as effect estimates are driven by the age categories with the highest number of death (i.e. the elderly). From previous work on Dutch data (Fischer et al., 2003) we know that between age categories effect estimates can be slightly different, with moderately increased estimates in the oldest age groups. We do not expect however that excluding specific age groups from the statistical analyses will change the overall effects markedly.

PM_{10} and $PM_{2.5}$ were too highly correlated to disentangle their independent effects. In single pollutant models, ERs for $PM_{2.5}$ were generally higher compared to ERs for PM_{10}, especially for the shortest lags (i.e. lag0 and lag1). These differences cannot be attributed to differences in the underlying concentration distribution, as IQRs were the same for both PM metrics, suggesting that $PM_{2.5}$ is on mass basis more relevant for public health than PM_{10}. However, since confidence intervals largely overlap, our findings do not provide a strong argument for preferring $PM_{2.5}$ over PM_{10} in future EU policies or health impact assessment.

4.2. $PM_{2.5-10}$

Effects of coarse particles in North-Western Europe on mortality were studied in West-Midlands, London, Helsinki and Stockholm (Anderson et al, 2001; Atkinson et al, 2010; Halonen et al., 2009; Meister et al., 2012). These studies generally do not provide strong evidence for effects of $PM_{2.5-10}$ on mortality. In London, $PM_{2.5-10}$ was significantly associated with all cause mortality at lag1 (1.9% increase per 10 $\mu g/m^3$), whereas effect estimates for lag0 and lag2 were non-significantly negative (Atkinson et al., 2010). No effect of $PM_{2.5-10}$ on all cause mortality was observed in the West-Midlands (Anderson et al., 2001). For respiratory mortality, a significant increase in association with $PM_{2.5-10}$ was observed in Helsinki and London, whereas the effect estimate was significantly negative in the West-Midlands. $PM_{2.5-10}$ was not significantly associated with cardiovascular mortality in any of the three studies (Anderson et al., 2001; Atkinson et al., 2010; Halonen et al., 2009). The most pronounced effect is observed in Stockholm (Sweden), where a 10 $\mu g/m^3$ increase in $PM_{2.5-10}$ was associated with a 1.7% (95% CI 0.2–3.2%) increase in all cause mortality (cause-specific mortality not studied) (Meister et al., 2012).

Stronger, more significant effects of $PM_{2.5-10}$ were observed in Rome (Italy), Madrid (Spain) and Barcelona (Spain). For all cause mortality, effect estimates associated with a 10 $\mu g/m^3$ increase in $PM_{2.5-10}$ ranged from 2.1% (95% CI 0.7–3.5) in Madrid to 2.7% in both Rome and Barcelona (95% CI 1.1–4.4 and 0.8–4.6 respectively) (Mallone et al., 2011; Perez et al., 2008; Tobias et al., 2011). Studies in Rome and Barcelona also showed significant effects on cardiovascular and respiratory mortality (Mallone et al., 2011; Perez et al., 2009). In all three cities, the influence of Saharan dust was evaluated, which suggested stronger adverse health effects of $PM_{2.5-10}$ during Saharan dust outbreaks. In Stockholm, a Northern-European city where significant effects of $PM_{2.5-10}$ were observed, the association with $PM_{2.5-10}$ was stronger for November through May, when road dust is more important compared to the rest of the year (Meister et al., 2012).

4.3. $PM_{2.5}$ and PM_{10} compared to $PM_{2.5-10}$

In our study, PM_{10} and $PM_{2.5}$ were both statistically significantly associated with all cause and cause-specific mortality, whereas no such associations were observed for $PM_{2.5-10}$. In a national analysis that included 112 cities in the United States, Zanobetti and Schwartz (2009) found significant effects of both $PM_{2.5}$ and $PM_{2.5-10}$ on all cause and cause-specific mortality. Effect estimates for $PM_{2.5}$ were similar to what we observed in the Netherlands, especially for all cause mortality (1.0% 95% CI 0.8–1.2) and cardiovascular mortality (0.9% 95% CI 0.5–1.2). Effects for $PM_{2.5-10}$ were 0.5% (95% CI 0.2–0.7), 0.3% (95% CI 0.0–0.6) and 1.2% (95% CI 0.4–1.9) for all cause, cardiovascular and respiratory mortality respectively.

4.3.1. Temporal variability

The absence of significant of $PM_{2.5-10}$ in our study can partly be due to the low concentrations and low day-to-day variability in $PM_{2.5-10}$

concentrations, and therefore low statistical power to detect effects. Similarly low $PM_{2.5-10}$ concentrations (average $<10\ \mu g/m^3$) were observed in Helsinki, London en the West-Midlands, where also little significant effects of $PM_{2.5-10}$ were found. With the exception of Stockholm, where $PM_{2.5-10}$ levels were also low, cities in which significant effects of $PM_{2.5-10}$ were observed all had higher levels ($\geq 15\ \mu g/m^3$). In addition, $PM_{2.5-10}$ was not directly monitored but calculated as the difference between PM_{10} and $PM_{2.5}$. Therefore precision is lower for $PM_{2.5-10}$ compared to $PM_{2.5}$ or PM_{10}.

4.3.2. Exposure misclassification

Nationwide average ambient PM concentrations were used to estimate exposure for the entire population of the Netherlands. For $PM_{2.5}$ and PM_{10}, concentrations measured at each of the individual monitoring sites were highly correlated with concentrations measured at the other 9 sites, indicating that the day-to-day variability in $PM_{2.5}$ and PM_{10} concentrations across the country is well represented by the temporal variability in the nationwide average. However, these correlations were lower for $PM_{2.5-10}$, indicating higher exposure misclassification of $PM_{2.5-10}$ compared to $PM_{2.5}$ or PM_{10}. This adds to a lower power to detect significant effects of $PM_{2.5-10}$ in our study. Puustinen et al (2007) evaluated the spatial variation in PNC, soot, $PM_{2.5}$, PM_{10} and $PM_{2.5-10}$ in four European cities (Amsterdam, Athens, Birmingham and Helsinki). Median temporal correlations between central site and residential outdoor concentrations were also generally lower for $PM_{2.5-10}$ compared to $PM_{2.5}$ or PM_{10}. In addition, with the exception of Athens, correlations between indoor and outdoor concentrations in the same study were also much lower for $PM_{2.5-10}$ than for $PM_{2.5}$ (Hoek et al., 2008).

5. Conclusion

PM_{10} and $PM_{2.5}$ were both significantly associated with all cause and cause-specific mortality. We were unable to demonstrate significant effects for $PM_{2.5-10}$, possibly due to the lower temporal variability and higher exposure misclassification in $PM_{2.5-10}$ compared to PM_{10} or $PM_{2.5}$. The lack of effects of $PM_{2.5-10}$ in our study should therefore not be interpreted as an indication that $PM_{2.5-10}$ can be considered harmless.

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Appendix A. Supplementary data

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