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Environmental Risk Factors

Cardiovascular morbidity and mortality associations with biomass- and fossil-fuel-combustion fine-particulate-matter exposures in Dhaka, Bangladesh

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Abstract

Background: Fine-particulate-matter (i.e. with an aerodynamic diameter of $\leq 2.5\,\mu m$, $PM_{2.5}$) air pollution is commonly treated as if it had 'equivalent toxicity', irrespective of the source and composition. We investigate the respective roles of fossil-fuel- and biomass-combustion particles in the $PM_{2.5}$ relationship with cardiovascular morbidity and mortality using tracers of sources in Dhaka, Bangladesh. Results provide insight into the often observed levelling of the $PM_{2.5}$ exposure–response curve at high-pollution levels.

Methods: A time-series regression model, adjusted for potentially confounding influences, was applied to 340 758 cardiovascular disease (CVD) emergency-department visits (EDVs) during January 2014 to December 2017, 253 407 hospital admissions during September 2013 to December 2017 and 16 858 CVD deaths during January 2014 to October 2017.

Results: Significant associations were confirmed between $PM_{2.5}$-mass exposures and increased risk of cardiovascular EDV [0.27%, (0.07% to 0.47%)] at lag-0, hospitalizations [0.32% (0.08% to 0.55%)] at lag-0 and deaths [0.87%, (0.27% to 1.47%)] at lag-1 per 10-$\mu g/m^3$ increase in $PM_{2.5}$. However, the relationship of $PM_{2.5}$ with morbidity and mortality effect slopes was less steep and non-significant at higher $PM_{2.5}$ concentrations (during crop-burning-dominated exposures) and varied with $PM_{2.5}$ source. Fossil-fuel-combustion $PM_{2.5}$ had roughly a four times greater effect on CVD mortality and double the effect on CVD hospital admissions on a per-$\mu g/m^3$ basis than did biomass-combustion $PM_{2.5}$.

Conclusion: Biomass burning was responsible for most $PM_{2.5}$ air pollution in Dhaka, but fossil-fuel-combustion $PM_{2.5}$ dominated the CVD adverse health impacts. Such by-source variations in the health impacts of $PM_{2.5}$ should be considered in conducting ambient particulate-matter risk assessments, as well as in prioritizing air-pollution-mitigation measures and clinical advice.

Keywords: $PM_{2.5}$, source apportionment, fossil-fuel combustion, biomass combustion, crop burning, cardiovascular disease

Key Messages

- This study found that, although biomass burning was associated with extreme fine-particulate-matter (i.e. with an aerodynamic diameter of $\leq$2.5 μm, $PM_{2.5}$) exposures in Dhaka, cardiovascular hospital admissions and mortality outcomes were more strongly associated with fossil-fuel-combustion-related $PM_{2.5}$, which is highly enriched in oxidative stress inducing transition metals and sulphur.
- This study is the first to evaluate variations in pollution source and $PM_{2.5}$ composition as a possible underlying cause of this sublinear health-effects relationship with particulate air pollution at high concentrations.
- Plateauing of the exposure–response curve at higher $PM_{2.5}$ exposures likely resulted from a lower cardiovascular toxicity from the biomass-burning $PM_{2.5}$ that dominates the highest $PM_{2.5}$-pollution days.
- Study findings indicate that focusing on $PM_{2.5}$ mass alone may not be the best particle-exposure metric to guide clinical or regulatory policies to achieve the greatest air-quality health benefits.
- Source-specific air-pollution-control policies are needed to maximize the health benefits of clean-air action in South Asia and elsewhere.

Introduction

South Asian countries, including Bangladesh, experience extremely high air-pollution events, especially during the crop-burning seasons.[1] Despite elevated exposures to fine particulate matter (i.e. with an aerodynamic diameter of $\leq$2.5 μm, $PM_{2.5}$), few epidemiological studies have been performed to investigate the acute effects of region-specific $PM_{2.5}$ air pollution on cardiovascular disease (CVD) health[2,3] due in large measure to a lack of centralized health-outcome records to perform such analyses. As a result, doubt remains regarding the extent of health effects induced by air pollution in South Asia, even given the high exposures.[4,5]

Recent evidence suggests that there is variability in the adverse health effects associated with $PM_{2.5}$ exposures around the world.[6] However, because there are limited studies in the developing world, estimates of the health effects attributable to air pollution have largely relied on studies conducted in the developed world. Thus, there is uncertainty in health-effects estimations,[7] since the dominant sources of air pollution differ by region, and available evidence suggests that particulate-matter (PM) toxicity can differ, depending on its source and chemical composition.[8,9]

Prior studies have found a plateauing, or 'flattening-out', of the exposure–health response curve at high $PM_{2.5}$-concentration levels,[10–14] but the reason for this is not yet well explained. This study is the first to evaluate varying pollution source and composition as a possible underlying cause of the non-linear health-effects behaviour of particulate air pollution in South Asia. In addition, this research investigates the appropriateness of the 'equivalent-toxicity' assumption commonly applied in $PM_{2.5}$ health-impact analyses: all $PM_{2.5}$ has the same health effect, irrespective of its local PM source or composition.[15]

We seek to determine the variability in the $PM_{2.5}$-mass relationship with adverse CVD health outcomes as a function of particle source and composition. This will investigate whether quantitative estimations of fine-particle toxicity as a function of composition and source type might provide more informative evaluations of $PM_{2.5}$ health effects than $PM_{2.5}$ mass alone. This information will potentially enable more accurate predictions of the effects of $PM_{2.5}$ mass on CVD around the world, as well as a more efficient CVD risk mitigation from $PM_{2.5}$ exposure, once regional differences in the pollution composition and their respective health impacts are incorporated.

Materials and methods

Study area

The focused area for this research was the Greater Dhaka, which spreads over an area of 1500 km^2 with a population of >18 million people in 2011.[16] Greater Dhaka incorporates the districts of Dhaka, Gazipur and Narayanganj (Supplementary Figure 1, Supplementary Appendix A, available as Supplementary data at *IJE* online).

Environmental data

As described by us in more detail in the Supplemental Material, available as Supplementary data at *IJE* online, and elsewhere,[17] daily weather and air-pollution records, including both fine-particulate-matter mass ($PM_{2.5}$) and composition records, were procured from a variety of governmental and research resources. Daily 24-hr average fine particulate matter ($PM_{2.5}$) was retrieved from the Department of the Environment (DoE, CASE project) in Dhaka, Bangladesh. Resource limitations restricted gravimetric $PM_{2.5}$ sampling (24-hr) for trace analyses to generally twice per week on nuclepore filters using a Gent stacked-filter sampler at the Atomic Energy Center in Dhaka. The air pollution in this region is well known to be greatly affected by the crop-burning emissions during non-monsoon periods.[17,18] As reported elsewhere, we developed an adjusted potassium index (K_{adj}) of biomass-burning $PM_{2.5}$ after subtracting sea-salt and soil potassium $PM_{2.5}$ from total potassium $PM_{2.5}$.[17] In addition, past studies have found sulphur (S) in $PM_{2.5}$, which is primarily derived from fossil-fuel combustion.[19–23] We therefore apportioned the $PM_{2.5}$ mass, using the single key tracer regression method, across all sampling days into fossil-fuel-$PM_{2.5}$ mass (predominantly from fossil-fuel combustion) and biomass-$PM_{2.5}$ mass (predominantly from crop burning).[17] The remaining unattributed $PM_{2.5}$ mass ('other $PM_{2.5}$'; predominately from dust) was then calculated by subtracting the fossil-fuel-associated $PM_{2.5}$ and biomass-associated $PM_{2.5}$ from total $PM_{2.5}$ mass. In Dhaka, fossil-fuel sources include brick kilns, traffic and diesel electric generators; biomass sources include household biomass cooking and agricultural crop burning; and other sources include soil dust, road dust, construction dust, industrial and incinerators.[17,24]

Health data

Unlike in the developing world, digitized records of daily deaths or visits/admissions to hospitals were not available for hospital records in Bangladesh. We therefore directly procured and then digitized daily written records from the National Institute of Cardiovascular Diseases (NICVD). The NICVD is the preeminent cardiovascular healthcare facility in Dhaka to which most CVD patients are sent.

The daily counts of CVD emergency-department visit (EDV) data for all ages and both sexes were from the NICVD for January 2014 to December 2017, and CVD hospitalizations data for all ages and both sexes for the period of September 2013 to December 2017. Although daily records were not available by cause, the annual counts of all patients from all ages and both sexes at NICVD in 2014 have been reported, including: acute myocardial infarction (30.3%); hypertensive heart disease (15.8%): congenital malfunctions of cardiac chambers and connections (9.4%); multiple-valve disease (8.7%); heart failure (8.6%); atherosclerosis (8.4%); acute and subacute infective endocarditis (6.8%); and other CVD diseases (12.0%).[25] The total daily cardiovascular mortality counts data for all ages and both sexes for NICVD were provided in electronic form by the Directorate General of Health Services under the Ministry of Health and Family Welfare, Bangladesh for January 2014 to October 2017. The annual mortality counts for all ages and both sexes at NICVD in 2014 have been reported; these included acute myocardial infarction (33.3%), unstable angina (8.8%), cardiac arrest (8.6%), acute myocardial infarction, unspecified (7.4%), left-ventricular failure (4.7%), old myocardial infarction (4.4%), ischaemic cardiomyopathy (4.1%) and other cardiovascular causes (28.7%).[25]

Statistical analysis and modelling

Time-series modelling was applied to investigate associations between daily air-pollution variations and daily CVD hospital-care counts. Consistently with past analyses, a quasi-Poisson model, adjusted for overdispersion, was applied.[26–28] We performed a single-day lag model (i.e. a linear parameterization for each of the individual lags) for total $PM_{2.5}$ mass, $PM_{2.5}$ constituents and sources. Further, an unconstrained distributed-lag model was also applied for the total $PM_{2.5}$ mass only, in order to assess whether the cumulative effects were greater than the effects for the single highest-day lag. This distributed-lag approach requires everyday exposure data and so could not be applied to the constituent or source-specific analyses, as elemental analyses samples were only collected twice per week.

To address long-term trends and seasonality influences in the model, we included a smooth function of time with 12 degrees of freedom per year, yielding the lowest Akaike Information Criterion value. Terms were also included in the base model for weather, temperature and relative humidity, with 3 df.[27,29–31] Day of week was included as a categorical variable and holidays as a dummy variable,

including government-shutdown days. An autoregressive term addressed any remaining autocorrelation.[32] An analysis was also conducted including a dummy variable for monsoon (June–September) vs non-monsoon (October–May) season, to test for the effect modification between seasons. We also addressed the potential influences of holidays. In each study year, the analyses included a dummy variable denoting that Ramadan period. In addition, there were several blockade days (locally called 'Hartal') in Dhaka during the study, so another dummy-variable 'shutdown' was added for these days, as identified from the national newspaper and records on the US Embassy website.

We conducted several sensitivity analyses to investigate the robustness of the association to model choice. One analysis was conducted by considering different degrees of freedom (6 to 13) per year (i.e. choice of smoothing function) and another was conducted by changing the degree of freedom for temperature and humidity. We also considered models that added a lag-1- to lag-3-day moving average of temperature and relative humidity with different degrees of freedom to control any delayed effects.

We determine the excess risks of CVD outcomes as percent excess per 10 $\mu g/m^3$, for lag-0 (same day) through lag-3 for all exposure variables, as well as for a cumulative effect of lag-0 to lag-3 from a distributed-lag model for $PM_{2.5}$ mass. Exposure–response (E–R) curves were also plotted with a natural spline, allowing a visual evaluation of potential non-linear relations. All analyses were done using R software, version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria), using the stats, splines and dlnm packages.

Results

Descriptive analyses

We analysed 340 758 EDVs, 253 407 hospital admissions and 16 858 CVD deaths during the study period to evaluate possible associations of particulate air pollution with cardiovascular outcomes in Dhaka, Bangladesh (Table 1). There were higher mean values of EDV, hospital admissions and mortality during the non-monsoon period vs the monsoon season (Table 1). The day-of-week analysis showed that Friday (a religious day in Bangladesh) had a lower number of patients (Supplementary Figure 1, Supplementary Appendix B, available as Supplementary data at *IJE* online), as adjusted for in our statistical analyses.

A strong seasonal pattern was identified in air-pollution levels, with higher concentrations during the non-monsoon period: the 24-hr average concentrations of $PM_{2.5}$ during the monsoon and non-monsoon were 36.2 ± 21.5 and $126.1 \pm 67.2\ \mu g/m^3$, respectively (Table 1). Based on our source apportionment, fossil-fuel-related sulphur $PM_{2.5}$ mass contributed an average of 21.6% (19.5 $\mu g/m^3$) of the total $PM_{2.5}$ mass on an annual basis, whereas biomass-burning-related adjusted potassium $PM_{2.5}$ mass was larger, contributing 40.2% (36.3 $\mu g/m^3$) (Table 1). Fossil-fuel-combustion-associated sulphur-related $PM_{2.5}$ mass was 44.3% (13.9 $\mu g/m^3$) of total fine particulate mass during the monsoon season, but fell to 18.9% (22.3 $\mu g/m^3$) of total mass during the non-monsoon season. Alternatively, the biomass-burning-associated $PM_{2.5}$ mass was 41.4% (48.6 $\mu g/m^3$) of the total $PM_{2.5}$ mass during the non-monsoon time (Table 1).

Table 1 Distribution of daily cardiovascular health outcomes, air pollution and weather variables

Variables	All year		Monsoon		Non-monsoon	
	Mean ± SD	IQR	Mean ± SD	IQR	Mean ± SD	IQR
Health outcomes (counts/day)						
ED visits ($N = 340\,758$)	233 ± 47	64	221 ± 51	74	242 ± 41	55
Hospital admissions ($N = 253\,407$)	160 ± 43	62	148 ± 43	59	169 ± 40	58
Mortality ($N = 16\,858$)	11 ± 12	5	9 ± 3	5	12 ± 16	6
Weather (24-hr average)						
Temperature (°C)	26. 3 ± 4.1	6.2	28.8 ± 1.6	2.1	24.4 ± 4.3	6.7
Relative humidity (%)	72.4 ± 10.7	14	79.1 ± 7.1	10	67.5 ± 10.3	12
Air pollution (24-hr average, $\mu g/m^3$)						
$PM_{2.5}$ ($\mu g/m^3$) (all 1582 days)	87.9 ± 69.0	107.1	30.2 ± 15.1	22.4	115.9 ± 67.5	119.2
$PM_{2.5}$ ($\mu g/m^3$) (sampling 388 days)	90.2 ± 68.0	111.0	31.4 ± 15.4	18.5	117.5 ± 66.2	99.0
BC ($\mu g/m^3$)	7.5 ± 4.6	5.6	5.2 ± 3.2	3.2	9.2 ± 4.7	5.7
S ($\mu g/m^3$)	1.2 ± 1.05	0.8	0.8 ± 0.5	0.6	1.6 ± 1.3	0.9
K_{adj} ($\mu g/m^3$)	0.2 ± 0.2	0.2	0.1 ± 0.1	0.1	0.3 ± 0.2	0.2
Fossil-fuel-combustion $PM_{2.5}$ ($\mu g/m^3$)	19.5 ± 11.8	12.4	13.9 ± 8.2	11.9	22.3 ± 12.6	13.3
Biomass-burning $PM_{2.5}$ ($\mu g/m^3$)	36.3 ± 29.9	36.2	11.8 ± 8.3	15.9	48.6 ± 32.3	40.2

BC, black carbon; ED, emergency department; IQR, interquartile range; K_{adj}, adjusted potassium (non-soil and non-sea-salt potassium); $PM_{2.5}$, fine particulate matter with an aerodynamic diameter of ≤ 2.5 μm; S, sulphur; SD, standard deviation.

Health-effects analyses

Associations with $PM_{2.5}$ mass

$PM_{2.5}$ yielded significant associations for cardiovascular EDV, hospitalizations and mortality: a 10-$\mu g/m^3$ increase in $PM_{2.5}$ mass was associated with an estimated 0.27% (0.07% to 0.47%) at lag-0, 0.32% (0.08% to 0.55%) at lag-0 and 0.67% (0.07% to 1.28%) at lag-0 increase, respectively (Figure 1). $PM_{2.5}$ mass was also significant for CVD mortality at lag-1 [0.87% (0.27% to 1.47%)] and lag-2 [0.74% (0.14% to 1.33%)]. The strongest $PM_{2.5}$-mass association with CVD mortality was found at lag-1 and with hospital admission and ED visits at lag-0, which are consistent with prior studies elsewhere.[19,31,33,34] The results from a distributed-lag model showed $PM_{2.5}$ effect sizes (per 10 $\mu g/m^3$) to be larger than for the single day for both EDV [0.38% (0.11% to 0.67%)] and hospitalizations [0.34% (0.01% to 0.68%)]. The larger effect sizes found from the distributed-lag model are consistent with cumulative effects from multi-day events. The associations with EDV, hospitalizations and mortality per interquartile increase in $PM_{2.5}$ constituents S, K_{adj} and black carbon (BC) are presented in Supplementary Figures 2, 3 and 4, Supplementary Appendix B, available as Supplementary data at *IJE* online, respectively.

$PM_{2.5}$-effect modification by season

During the monsoon season, $PM_{2.5}$ was significantly associated with EDV and hospital admissions, with an estimated 1.08% (0.57% to 1.59%) at lag-0 and 0.86% (0.24% to 1.48%) at lag-0 excess risk, respectively, and marginally significantly association with mortality, with an estimated 1.57% (–0.07% to 3.20%) at lag-1 per 10-$\mu g/m^3$ increase in $PM_{2.5}$ mass. During the non-monsoon period, these associations were reduced per unit mass, at 0.15% (–0.05% to 0.36%) at lag-1, 0.24% (–0.01% to 0.49%) at lag-0 and 0.77% (0.14% to 1.40%)

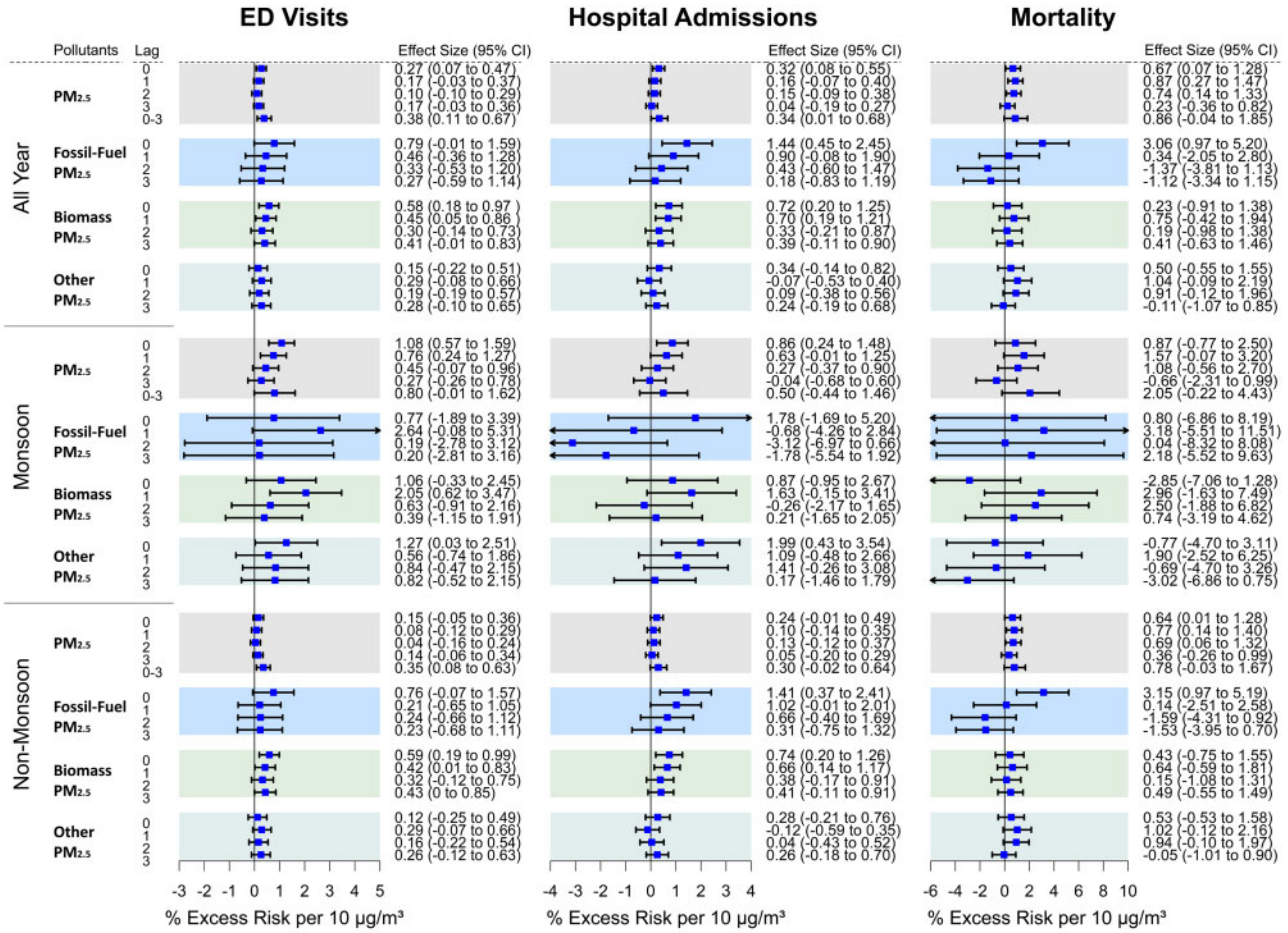

Figure 1 The % Excess Risk for cardiovascular emergency departments visits, hospital admissions and mortality at single lag-0 to lag-3 (and lag 0–3 from a distributed lag model for PM2.5 mass) per 10 $\mu g/m^3$ increase in PM2.5 mass, fossil-fuel PM2.5 mass, biomass PM2.5 mass and other-PM2.5 mass during study period, monsoon (June–September) and non-monsoon (October–May), adjusted for long-term trends and seasonality, day-of-week, holidays, Ramadan, blockade days and the temperature and relative humidity. For PM2.5 sources, single-day lag models were applied on 388 days during September 2013 to December 2017, 129 days during monsoon season and 259 days during non-monsoon season. ED, emergency department; PM2.5, fine particulate matter with an aerodynamic diameter of $\leq$2.5 μm.

at lag-1 excess risk for EDV, hospital admissions and mortality per 10 $\mu g/m^3$ $PM_{2.5}$, respectively. $PM_{2.5}$ mass during non-monsoon season was also associated with mortality at lag-1 and lag-3. Although the $PM_{2.5}$ association with increased EDV was not significant in the single-lag models, the result from the multi-day distributed-lag model showed the strongest association during the non-monsoon period [0.35% (0.08% to 0.63%)] excess risk per 10-$\mu g/m^3$ increase in $PM_{2.5}$ mass.

Effect modification as a function of the $PM_{2.5}$-mass concentration level

The steepest $PM_{2.5}$-effect slopes were observed below the ~80-$\mu g/m^3$ $PM_{2.5}$ level for EDV and hospital admissions, and below the ~100-$\mu g/m^3$ $PM_{2.5}$ level for mortality (Figure 2A–C), consistently with a previous study.[15] As we have published previously, concentration-weighted trajectories (CWTs), $PM_{2.5}$ pollution rose and conditional bivariate probability function analyses have provided supportive evidence that high-pollution days (>100 $\mu g/m^3$) were dominated by transboundary crop-burning pollution, whereas the <100-$\mu g/m^3$ days are instead dominated by more local sources,[17] so we also performed a hinge analysis evaluating $PM_{2.5}$ health impacts of >100 $\mu g/m^3$ vs <100 $\mu g/m^3$. These results confirmed that there was significant decrease in the CVD-effect size per $\mu g/m^3$ $PM_{2.5}$ mass when the $PM_{2.5}$ concentration was >100 $\mu g/m^3$ (Figure 3). During <100-$\mu g/m^3$ pollution days, the effect sizes per 10 $\mu g/m^3$ in $PM_{2.5}$ were 0.74% (0.27% to 1.20%) for ED visits, 0.92% (0.35% to 1.48%) for hospital admissions and 2.09% (1.00% to 3.18%) for mortality (Figure 3). In contrast, the effect sizes per 10-$\mu g/m^3$ increase in $PM_{2.5}$ during >100-$\mu g/m^3$ pollution days were all non-significant: 0.05% (–0.21% to 0.31%) for ED visits, 0.15% (–0.16% to 0.46%) for hospital admissions and 0.25% (–0.46% to 0.96%) for mortality (Figure 3).

Supplementary Figure 5A, Supplementary Appendix B, available as Supplementary data at *IJE* online, documents that sulphur in the air, predominantly from fossil-fuel combustion, levelled off during the extremely high-pollution episodes, even though $PM_{2.5}$ levels were rising. Thus, we found that there was not significantly more fossil-fuel-associated $PM_{2.5}$ during the extreme $PM_{2.5}$ pollution days, but there was, instead, more of the biomass-burning-related $PM_{2.5}$, contributing strongly to the mass on the highest-$PM_{2.5}$ days (Supplementary Figure 5B, Supplementary Appendix B, available as Supplementary data at *IJE* online) and coincident with the lowered PM toxicity per unit mass during the highest-pollution days.

$PM_{2.5}$–health-effect modification by composition and source

In order to further characterize the lower $PM_{2.5}$ mass-effect estimates per $\mu g/m^3$ of the three CVD health outcomes during crop-burning periods (i.e. during high-pollution episodes) as a function of $PM_{2.5}$ source, we also conducted analyses comparing CVD health-effects estimates for the predominantly fossil-fuel sulphur-associated $PM_{2.5}$ vs for the biomass-associated adjusted potassium $PM_{2.5}$. In contrast to the $PM_{2.5}$ mass E–R curves, the E–R curves for sulphur–PM with all three health outcomes showed a much more linear relationship (Supplementary Figure 6, Supplementary Appendix B, available as Supplementary data at *IJE* online), without 'bending over' during higher-concentration days. A 10-$\mu g/m^3$ increase in fossil-fuel $PM_{2.5}$ was associated with 0.79% (–0.01% to 1.59%) at lag-0, 1.44% (0.45% to 2.45%) at lag-0 and 3.06% (0.97% to 5.20%) at lag-0 excess risk for EDV, hospital admissions and mortality, respectively (Figure 1). In contrast, the biomass-burning-related $PM_{2.5}$ mass-effect estimates for EDV, hospital admissions and mortality were 0.58% (0.18% to 0.97%) at lag-0, 0.72% (0.20% to

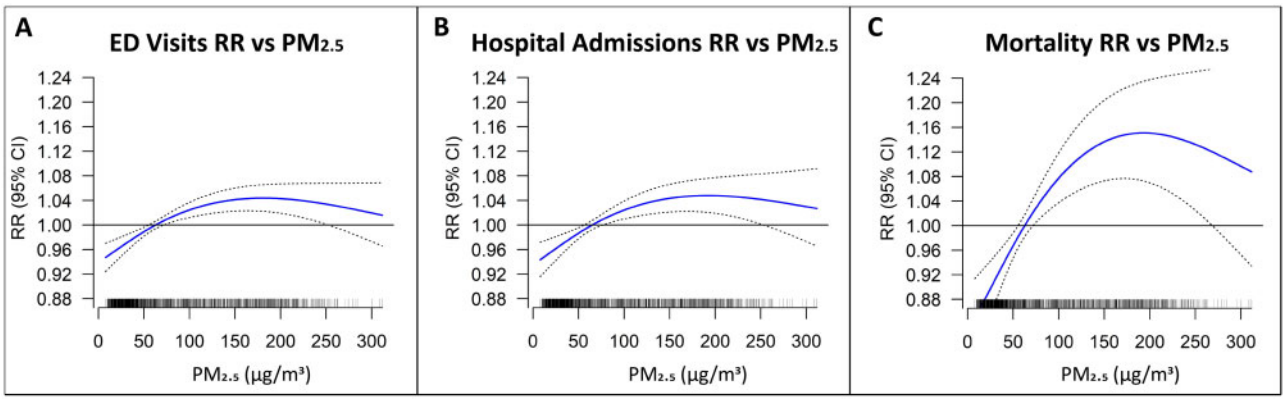

Figure 2 (A–C) The exposure–response (E-R) curves with 3df for cardiovascular emergency visits (lag-0), hospital admissions (lag-0) and mortality (lag-1), respectively, against PM2.5 for full study period adjusted for temporal trends, holidays, Ramadan, blockade days, day-of-week, temperature and relative humidity. ED, emergency department; PM2.5, fine particulate matter with an aerodynamic diameter of ≤2.5 μm; RR, relative risk.

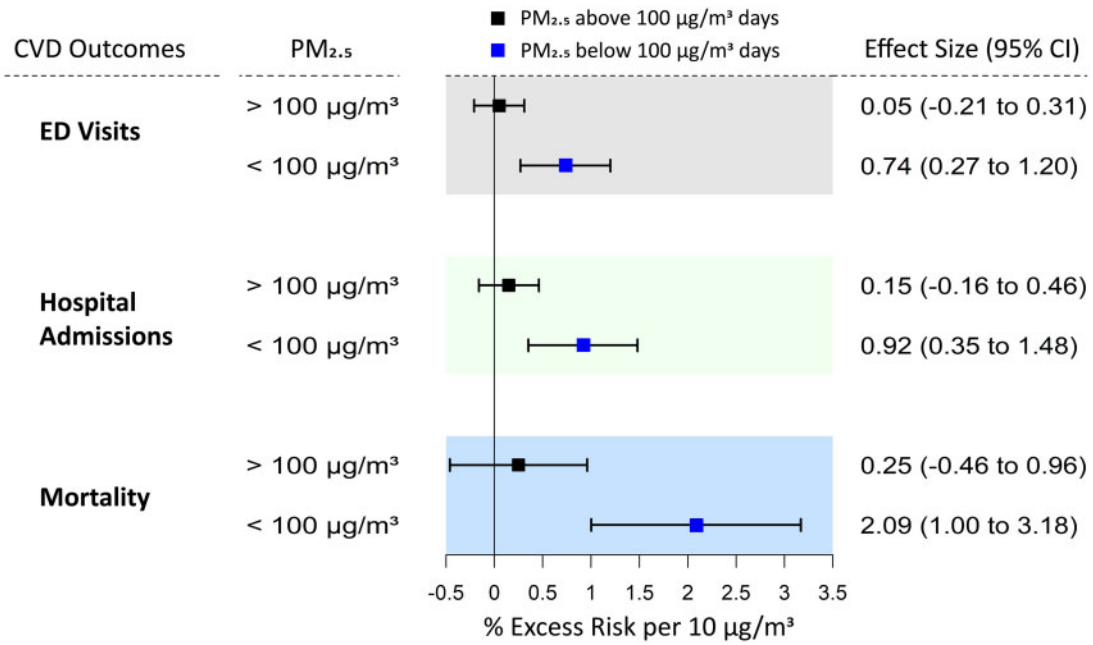

Figure 3 Comparison of the effect sizes per 10 μg/m^3 increase in PM2.5 mass concentration with all three cardiovascular health outcomes during all year, when PM2.5 was <100 μg/m^3 (total 1019 days), and when PM2.5 was >100 μg/m^3 (total 564 days). PM2.5 associations with emergency department visits and hospital admissions were at lag-0, and with mortality was at lag-1. The model was adjusted for long-term trends and seasonality, day-of-week, Ramadan, blockade days, holidays and the effect of temperature and relative humidity. CVD, cardiovascular disease; ED, emergency department; PM2.5, fine particulate matter with an aerodynamic diameter of ≤2.5 μm.

1.25%) at lag-0 and 0.75% (–0.42% to 1.94%) at lag-1, respectively, per 10-μg/m^3 (Figure 1). We also evaluated associations by residual $PM_{2.5}$ (i.e. 'other $PM_{2.5}$') with CVD health outcomes. A 10-μg/m^3 increase in residual $PM_{2.5}$ was associated with 0.29% (–0.08% to 0.66%) at lag-1, 0.34% (–0.14% to 0.82%) lag-0 and 1.04% (–0.09% to 2.19%) at lag-1 increased risk of CVD EDV, hospital admissions and mortality, respectively. The season-specific models also provided a larger effect size for fossil-fuel $PM_{2.5}$, but the wide confidence interval gets wider during monsoon season due to fewer $PM_{2.5}$ samples.

The E–R relationship curves for EDV, hospital admissions and mortality with fossil-fuel-associated and biomass-associated $PM_{2.5}$ are shown in Figure 4A–C, respectively. These curves indicate that the mortality and hospital admissions slope is steepest for the fossil-fuel-combustion-associated $PM_{2.5}$ mass and much lower for the biomass-associated-$PM_{2.5}$ mass, which is strongly impacted by crop burning at those times.

Sensitivity analyses indicated that the results were not sensitive to changes in df for the smooth functions of time, temperature and relative humidity, or to adding a lag-1- to lag-3-day moving average of temperature and relative humidity with different degrees of freedom (Supplementary Tables 1–3, Supplementary Appendix C, available as Supplementary data at *IJE* online).

Discussion

Our results are consistent with an effect of $PM_{2.5}$ air pollution on CVD morbidity and mortality in Dhaka. In addition, our results further found that the $PM_{2.5}$ impacts on the CVD health outcomes considered varied, depending on the composition and source of the $PM_{2.5}$. CVD outcomes were most adversely impacted by the fossil-fuel-related-$PM_{2.5}$ air pollution (primarily from diesel traffic and coal-burning brick kilns in Dhaka) per μg/m^3 $PM_{2.5}$.

The excess risk of acute cardiovascular events varies between 1% and 3% in developed-country studies.[14,19,30,33,35–43] Our estimated overall $PM_{2.5}$ mass–CVD-effect sizes are lower than generally found in those studies. This is likely because the $PM_{2.5}$ air pollution in developed counties was more dominated by fossil-fuel-combustion sources (~70–80%),[44–46] whereas the contribution of fossil-fuel sources on total $PM_{2.5}$ mass in Dhaka was only 21.6%. Dhaka $PM_{2.5}$ mass was more dominated by biomass-burning $PM_{2.5}$.[17] It is important to note that we found comparable effect sizes with developed-country-study effect sizes by our fossil-fuel-burning-associated $PM_{2.5}$ mass [1.44% (0.45% to 2.45%) for hospital admissions; and 3.07% (0.96% to 5.22%) for mortality] and by our <100-μg/m^3 pollution days [0.92% (0.35% to 1.48%) for hospital admissions and 2.09% (1.00% to 3.18%) for mortality]. This indicates that the fossil-fuel-combustion-

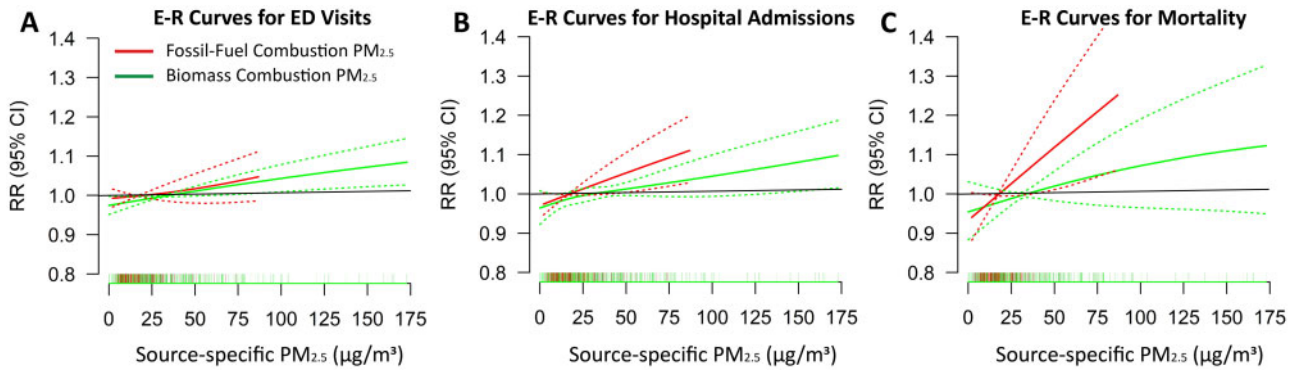

Figure 4 The exposure–response (E-R) relationship curves with 3df for cardiovascular emergency department visits, hospital admissions and mortality with fossil-fuel combustion-related PM2.5 mass and biomass combustion-related PM2.5 mass. The strongest single-day fossil-fuel PM2.5 associations with cardiovascular emergency department visits and hospital admissions were at lag-0, and with mortality was at lag-1. The strongest single-day biomass PM2.5 associations with cardiovascular emergency department visits and hospital admissions were at lag-0, and with mortality was at lag-1. The model was adjusted for long-term trends and seasonality, day-of-week, Ramadan, blockade days, holidays and the effect of temperature and relative humidity. ED, emergency department; E-R, exposure–response; PM2.5, fine particulate matter with an aerodynamic diameter of ≤2.5 μm.

related $PM_{2.5}$ in Dhaka has similar health risks to particles in the developed world, which are more similar in composition to this component of Dhaka $PM_{2.5}$.

As found in several prior developing-world studies,[10,11,13] the relative risk (RR) response to $PM_{2.5}$-exposure curves for all three health outcomes exhibited non-linear relationships, flattening out at higher concentrations during pollution episodes, indicating a lower population health impact per $\mu g/m^3$ by the $PM_{2.5}$ pollution added on high-$PM_{2.5}$ days. These episodes usually occurred during the rice-paddy-residue crop-burning period from November to February,[17,47] as well as during the wheat-residue crop-burning in April–May.[1] The 'levelling-off' of adverse CVD effects seen at high $PM_{2.5}$ (Figure 2) could result from two possible factors: (i) composition changes as $PM_{2.5}$ goes up; or (ii) there is a depletion of susceptible individuals by more moderate levels as they rise, so that there are fewer especially susceptible people left to be affected when the highest levels subsequently occur.[48] But, the fact that neither the fossil-fuel-$PM_{2.5}$ health-effects curves nor the biomass-$PM_{2.5}$ health-effects curves bend over (Figure 4) like the $PM_{2.5}$ curves do is inconsistent with a depletion in the population pool of susceptible individuals. If that form of 'harvesting' were happening, then the biomass- and the fossil-fuel-associated mortality and morbidity would also bend over at high levels, just like the $PM_{2.5}$ curves do. Thus, it is indicated that a 'depletion' in susceptible individuals is not happening and that the bending-over is a result of lower-toxicity biomass particles dominating the $PM_{2.5}$ exposures during the highest-$PM_{2.5}$ days. In addition, comparisons between the overall fossil-fuel-$PM_{2.5}$ vs biomass-$PM_{2.5}$ mean effects on CVD health outcomes also indicate that the fossil-fuel-combustion-related $PM_{2.5}$ mass is more responsible than the biomass-related $PM_{2.5}$ for the overall adverse $PM_{2.5}$–CVD health associations. When compared on an acute effect per $\mu g/m^3$ mass basis, our results revealed that fossil-fuel-combustion-related $PM_{2.5}$ mass had a roughly four times greater effect on CVD mortality and two times greater effect on CVD hospital admissions vs Biomass-combustion-related $PM_{2.5}$ mass.

Although the acute health effects of biomass PM on acute respiratory health have been well documented,[49–51] the CVD toxicity of biomass $PM_{2.5}$ has also been indicated to be lower than PM from fossil-fuel combustion in the USA.[21] This apparently lower CVD effect by biomass-combustion $PM_{2.5}$ per unit mass is further supported by studies of indoor biomass burning, which experience very high $PM_{2.5}$ exposures, but it has been found in biomass-cooking studies to have lower CVD-mortality effects per unit $PM_{2.5}$ mass than found for respiratory effects.[52]

The biological mechanism for the apparently much higher CVD impact from fossil-fuel-combustion-related $PM_{2.5}$ mass is not completely understood, but recent research indicates that it could be due to the enrichment of these particles in both transition metals and sulphur, and these constituents' combined enhancement of $PM_{2.5}$ oxidative-stress potential in the body. Oxidative stress and its associated inflammation are thought to be a major driving force in the adverse health effects of $PM_{2.5}$ exposures.[53–55] Whereas research has indicated that exposure to biomass-burning $PM_{2.5}$ can add oxidative potential, comparisons have found the co-presence of sulphur with transition metals in fossil-fuel-combustion particles giving them much greater bioavailability and resulting oxidative-

stress impacts, consistently with our results.[56–58] The greater CVD impact of fossil-fuel particles, which are more enriched in oxidant transition-metal species and sulphur than biomass particles,[58,59] is therefore consistent with a role by oxidative stress induced by transition metals in the effects of $PM_{2.5}$. For example, burning coal in brick-kiln operations, which are common in the Dhaka area, results in the production of primary acidic sulphate, which can function as a ligand to mobilize the transition metals and consequent oxidative stress.[56,57,60] Recent research also indicates that a diet rich in anti-oxidants is protective against the CVD-mortality effects of $PM_{2.5}$, which is consistent with the importance of the oxidative-stress mechanism in $PM_{2.5}$ cardiac health effects.[61,62] Thus, there is a strong body of toxicological evidence consistent with the greater CVD toxicity that we find in fossil-fuel-combustion $PM_{2.5}$ vs Biomass-combustion $PM_{2.5}$, per mass basis.

Strengths and limitations

Our study also has multiple unique strengths, especially in the consideration of trace-element constituents and source health impacts in our $PM_{2.5}$–health effects analyses, as well as providing research in an understudied area. However, we did not have detailed personal information for patients' socio-economic status, status of home air-conditioning use (likely $<1\%$) and status of using cooking stoves, but these characteristics should not change from day to day and are unlikely to confound our time-series analyses.[63] Some other individual-level factors such as age and sex can be of importance, but were not able to be considered in this analysis. Also, we were unable to calculate the percentage of the population served by this hospital, as the electronic health data were not available from other hospitals in Dhaka. However, this percentage should not change from day to day and is unlikely to affect the results of the time-series analyses we conducted. Also, since we only had total daily CVD hospital counts, we also did not have count information for specific cardiovascular admission diagnoses on a daily basis or an ability to exclude scheduled hospital admissions, which may introduce error or ascertainment bias. Future research with more detailed health data should investigate these remaining issues. We were also not able to estimate the cumulative effect from distributed-lag models for $PM_{2.5}$ constituents and sources, as those samples were not collected daily, and only sampled at most twice each week. Future work would benefit from daily $PM_{2.5}$ chemical-characterization sampling at multiples sites within Dhaka.

Finally, a notable and novel strength of this research is that it provides $PM_{2.5}$ health-impact estimates that are source-specific and therefore more generalizable than prior total $PM_{2.5}$ mass health-effect estimates. In the past, $PM_{2.5}$ health impacts have employed health-effect estimates that inherently assume that all $PM_{2.5}$ mass has the same toxicity, irrespective of differences over time and locality in source mix and composition. In contrast, source-specific estimates, such as we provide here, can more appropriately be applied to other locations, once source-specific $PM_{2.5}$ impacts are calculated, allowing the application of health-effect estimates of $PM_{2.5}$ mass that more properly address $PM_{2.5}$ source-mix changes over space and time.

Conclusion

This study provides confirming evidence of the detrimental CVD health effects of exposure to $PM_{2.5}$ air pollution in a region where the PM is dominated by crop-burning air pollution. However, it also indicates that the CVD toxicity of $PM_{2.5}$ mass varies with composition and source, and that greater adverse health impacts are from fossil-fuel-combustion-derived $PM_{2.5}$ than from biomass-combustion-derived $PM_{2.5}$, when compared on a per-unit-mass-exposure basis. These findings not only add to our overall scientific understanding of the role of PM and its composition in impacting cardiovascular health; they can also guide governments and healthcare professionals to adopt source- and composition-specific strategies to maximize the public-health benefits of $PM_{2.5}$-mitigation actions.

Supplementary Data

Supplementary data are available at *IJE* online.

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Author Contributions

M.M.R. and G.D.T. conceived of the study and contributed to the study design. M.M.R. and K.N. collected and cleaned the health data, air-pollution data and meteorological data. B.A.B. and P.K.H. collected $PM_{2.5}$ samples for elemental analysis. M.M.R. did the statistical analysis and wrote the first draft. G.D.T., K.N., B.A.B., J.N. and P.K.H. helped to revise the manuscript, commented on the manuscript and contributed to discussion. G.D.T. contributed in interpreting the results and added intellectual content to the manuscript. All authors read and approved the manuscript.

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Conflict of interest

None declared.

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