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# Estimated Personal Soot Exposure Is Associated With Acute Myocardial Infarction Onset in a Case-Crossover Study

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**Abstract** The current study investigates the association of estimated personal exposure to traffic-related air pollution and acute myocardial infarction (AMI). Cases of AMI were interviewed in the Augsburg KORA Myocardial Infarction Registry from February 1999 through December 2003, and 960 AMI survivors were included in the analyses. The time-varying component of daily personal soot exposure (the temporally variable contribution due to the daily area level of exposure and daily personal activities) was estimated using a linear combination of estimated mean ambient soot concentration, time spent outdoors, and time spent in traffic. The association of soot exposure with AMI onset was estimated in a case-crossover analysis controlling for temperature and day of the week using conditional logistic regression analyses. Estimated personal soot exposure was associated with AMI (relative risk, 1.30 per 1.1 $m^{-1} \times 10^{-5}$ [95% confidence interval, 1.09-1.55]). Estimated ambient soot and measured ambient $PM_{2.5}$ particulate matter 2.5 $\mu$m and smaller in aerodynamic diameter were not significantly associated with AMI onset. Our results suggest that an increase in risk of AMI in association with personal soot exposure may be in great part due to the contribution of personal soot from individual times spent in traffic and individual times spent outdoors. As a consequence, estimates calculated based on measurements at urban background stations may be underestimations. Health effects of traffic-related air pollution may need to be updated, taking into account individual time spent in traffic and outdoors, to adequately protect the public. (Prog Cardiovasc Dis 2011;53:361-368)


*Keywords:* Soot; Personal exposure; Myocardial infarction; Trigger

Acute myocardial infarction (AMI) is a major cause of death in the Western world. Ambient particulate matter has been consistently associated with cardiovascular disease morbidity and mortality.[1] The hypothesis that ambient particulate air pollution exposure also may act as transient risk factor for AMI onset was supported by some studies[2-7] and not by others.[8-11] All of these studies relied on central

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**Abbreviations and Acronyms**

**AMI** = acute myocardial infarction

**CI** = confidence interval

**IQR** = interquartile range

**NO** = nitrogen oxide

**$PM_{2.5}$** = fine particulate matter/particulate matter 2.5 $\mu$m and smaller in aerodynamic diameter

**$R^2$** = coefficient of determination

**RR** = relative risk

monitoring data as the measure of exposure of the population. A study on personal black smoke exposure showed that individuals' exposure was higher for those living close to major roads and was also elevated by times spent outdoors and in transport.[12] In this study, personal exposure was predicted using central monitoring data and individual information.

We have shown earlier that exposure to traffic might trigger AMI within 1 hour.[13] In that investigation, we relied solely upon diary-based individual information on times spent in traffic. In the current study, we build on the same study, drawing cases from the KORA Myocardial Infarction Registry in Augsburg, Southern Germany. We used a diary to collect information on potential triggers of AMI during the 4 days before the onset of AMI symptoms including detailed information on time spent outdoors and in traffic hour by hour. The aim of the present study is to estimate personal exposure combining this individual information with central monitoring data and to then estimate its impact on the risk of AMI.

## Methods

### *Patient data*

Cases were drawn from the complete case series of the population-based KORA Myocardial Infarction Registry from February 1999 to December 2003. The details of the recruitment procedures and data collection have been described elsewhere.[14,15]

Briefly, hospitalized 24-hour survivors of AMI aged 25 to 74 years and resident in the study area were routinely entered. The diagnosis of AMI was confirmed by applying the criteria established within the MONItoring trends and determinants in CArdiovascular disease (MONICA) framework[16] based on symptoms, enzyme elevation, and electrocardiogram. Interviews were conducted by trained research nurses on the general ward as soon as possible after the event. Data on sociodemographic characteristics, medical history, and smoking status of the patients were collected. For this specific study, patients were additionally interviewed about their activities on the day of their AMI and the preceding 3 days using a standardized data collection form (diary interview). Patients were asked by the nurse to report time spent outdoors, means of transportation, and levels of activity while being awake. Patients were not informed of the hypothesized hazard period, and equal importance was given to the assessment of activity levels across the 4 days. The median time between event and interview was 8 days.

All patients gave written informed consent for participation; the research protocol was approved by the KORA review board. After the patient's discharge from hospital, clinical data were abstracted from the medical record according to a standardized protocol. The *time of onset of the AMI* was defined as the time of onset of chest pain with at least 20 minutes of duration or, in case of atypical symptoms, as the time of the severest symptoms.

### *Soot exposure estimation*

#### *Ambient soot concentrations*

Ambient soot was intermittently measured during the study period, whereas other particulate air pollution indicators as well as gases and meteorological parameters were measured continuously.

During the study period, mass concentration of particulate matter with aerodynamic diameters less than 2.5 $\mu$m ($PM_{2.5}$) was measured using a tapered element oscillating microbalance (TEOM) (formerly Rupprecht & Patashnick, German distributor: MLU, Essen, Germany; now Thermo Fisher Scientific Inc., Waltham, MA, USA) at a central background monitoring site in an orchard, located within the ancient walls of the city.

At the same site, 100 additional daily $PM_{2.5}$ samples were taken by means of a Harvard Impactor (Marple et al 1987)[17] between September 1999 and January 2001. Afterward, reflectance was measured on the collected Teflon filters using the M43D Smoke Stain Reflectometer (Diffusion Systems LTD, London, UK).[18] Values were transformed into an absorption coefficient using the formula according to ISO 9835 (ISO, 1993),[19] as a proxy for ambient soot, expressed in $m^{-1} \times 10^{-5}$.

Hourly measurements of nitrogen oxides (NOs), measured at a monitoring station close to the orchard site, and meteorology (temperature, relative humidity), from a regional background site, were obtained through the Bavarian Air Monitoring Network.

To obtain a continuous time series, we developed a linear prediction model of daily ambient soot concentrations using the reflectometer measurements from the $PM_{2.5}$ Harvard Impactor filters of 1999-2000 as outcome, and daily $PM_{2.5}$, nitrogen dioxide, NO, and relative humidity as explanatory variables. The resulting regression formula was as follows:

$$\begin{aligned}\text{Absorption coefficient} = {} & -0.96 + 0.062 \\ & \times PM_{2.5}(\text{TEOM}) + 0.0071 \\ & \times \text{relative humidity} + 0.029 \\ & \times \text{nitrogen dioxide} + 0.011 \\ & \times \text{NO}, R^2 = 0.76.\end{aligned}$$

To validate the prediction model, we applied the formula to a validation data set of hourly measurements

of black carbon taken with an Aethalometer (series 8100, Thermo Fisher Scientific Inc) in 2004-2005.[20] The comparison of observed and predicted values showed only a minimal drop in coefficient of determination (validation $R^2$ = 0.72). Based on this, hourly soot was estimated applying the coefficients of the prediction model to the entire study period. Running 24-hour means of estimated soot as well as of TEOM $PM_{2.5}$ and temperature were calculated for each hour.

*Personal soot exposure estimation*

Wichmann et al[12] developed a model that explains the personal level of exposure to soot with a spatial component characterized by closeness to outside sources (such as traffic density near the home), a personal component that defines sources at home, and a temporal component that is dependent on daily average level of soot as well as activities such as time spent in traffic or outdoors. We used this prediction model and estimated the time-varying component of personal soot exposure. The formula was developed using studies on elderly adults, hence likely applicable to our population. We used a linear combination of estimated 24-hour mean ambient soot concentration, reported number of hours spent outdoors, and number of hours spent in traffic over the 24 preceding hours as follows:

$$\begin{aligned}\mathrm{Soot_{it}} = {} & 0.87 \times \mathrm{Soot_t} + 0.14 \times \mathrm{h^{-1}} \times \mathrm{m^{-1}} \\ & \times 10^{-5} * \mathrm{Traffic_{it}} + 0.06 \times \mathrm{h^{-1}} \times \mathrm{m^{-1}} \\ & \times 10^{-5} * \mathrm{Outside_{it}},\end{aligned}$$

where $\mathrm{Soot_{it}}$ is the time-varying component of the estimated personal soot exposure, $\mathrm{Soot_t}$ is the estimated ambient soot exposure (expressed in $\mathrm{m^{-1}} \times 10^{-5}$), and $\mathrm{Traffic_{it}}$ and $\mathrm{Outside_{it}}$ are the personal number of hours spent in traffic and outside in the previous 24-hour period (expressed in hours). Whereas the original formula by Wichmann et al also included living in homes along busy roads and indoor exposure characteristics as predictors of personal exposures, here only the time-varying component of the regression equation was used for 2 reasons. First, only the time-varying component contributes to transient changes in exposure and can therefore act as trigger of AMI. Second, information on traffic near residence was available for only half of the patients.

### *Statistical analyses*

To investigate triggering of AMI onset by air pollution exposure, we used the case-crossover approach.[21] This approach contrasts exposure in the hazard period to exposure in referent periods within the same individual, using standard methods for matched case-control analysis. Cases serve as their own controls, eliminating potential confounding by time-invariant factors. For each case, we compared exposure during the hazard period immediately before onset of infarction symptoms with the same subjects' exposure during 2 referent periods 24 and 48 hours earlier, respectively. We used conditional logistic regression models controlling for temperature and day of the week and computed odds ratios as a measure of relative risk (RR).

The main air pollution exposure of interest was the estimated personal 24-hour mean soot exposure. We furthermore analyzed the association of estimated ambient 24-hour mean soot exposure and ambient 24-hour mean $PM_{2.5}$ exposure with AMI onset analogously.

To be in line with previous case-crossover investigations on air pollution effects, we repeated the analyses using ambient exposures of the same weekday and month as referent periods instead of the unidirectional design. This time-stratified approach is free of a bias due to trend,[22,23] but could not be used in the analyses of personal exposures because time-activity data collected by a diary are only valid for times before AMI onset.

## Results

### *Patient characteristics*

Between February 1999 and December 2003, 2882 confirmed 24-hour survivors of AMI were recorded. Of these, 2059 cases were available for interview. Initially, 1459 cases with known time of onset and diary information could be included. For the present analyses, those 1072 who provided complete diary information on times spent in traffic and times spent outdoors for at least the hazard period (1-24 hours before onset) and one referent period (25-48 or 49-72 hours before onset) were considered. Because air pollution concentrations were predicted based on measurements taken at a central site, we considered those 960 cases that spent more than two thirds of the 24-hour periods within the study area as eligible for the present analyses.

In Table 1, the main characteristics of all 1459 interviewed cases with diary data as well as those fractions included (n = 960) and excluded (n = 387) because of insufficient data and excluded because they were absent from the study area (n = 112) are presented. The patients who were included were younger and healthier than those 387 who were excluded because of insufficient data. On the other hand, the patients who were included were somewhat older and less healthy than those 112 who were excluded because of absence of the study area. Patients included in the analyses were predominantly male (76%), aged on average 61 years, and former or never smokers (64%). The number of cases per day ranged between 0 and 5, with a mean of 0.8 (Fig 1).

Table 1
Description of the AMI survivors (age, 25-74 years) recruited between February 1999 and December 2003 from the KORA Myocardial Infarction Registry, Augsburg, Germany

| | | | At Least 24-h Hazard Period and One 24-h Referent Period | | | Tests for Differences |
|---|---|---|---|---|---|---|
| | | | | Yes | Yes | |
| | | | | 2/3 of Observation Periods Within Study Area | | |
| | | All With Diary | No | No | Yes | *P* Value |
| | All | 1459 | 387 | 112 | 960 | |
| Age (y) | Mean | 60 | 63 | 53 | 61 | <.0001 |
| | 25-49 | 255 (17%) | 48 (12%) | 34 (30%) | 173 (18%) | |
| | 50-64 | 664 (46%) | 162 (42%) | 60 (54%) | 442 (46%) | |
| | 65-74 | 540 (37%) | 177 (46%) | 18 (16%) | 345 (36%) | <.0001 |
| Male | | 1119 (77%) | 289 (75%) | 100 (89%) | 730 (76%) | .0040 |
| German | | 1384 (95%) | 364 (94%) | 105 (94%) | 915 (95%) | .5493 |
| Employment status | Employed | 580 (40%) | 98 (25%) | 79 (71%) | 403 (42%) | |
| | Not employed | 879 (60%) | 289 (75%) | 33 (29%) | 557 (58%) | <.0001 |
| Education | Low education* | 1118 (77%) | 300 (78%) | 75 (67%) | 743 (77%) | |
| | High education† | 282 (19%) | 71 (18%) | 30 (27%) | 181 (19%) | .0802 |
| First AMI | | 1235 (85%) | 315 (81%) | 99 (88%) | 821 (86%) | .0391 |
| 28-d survival | | 1450 (99%) | 385 (99%) | 112 (100%) | 953 (99%) | 1.000 |
| STEMI | STEMI | 735 (50%) | 187 (48%) | 55 (49%) | 493 (51%) | |
| | NSTEMI | 625 (43%) | 173 (45%) | 52 (46%) | 400 (42%) | |
| | Other (BBB) | 68 (5%) | 18 (5%) | 4 (4%) | 46 (5%) | |
| | Missing | 31 (2%) | 9 (2%) | 1 (1%) | 21 (2%) | .7732 |
| Symptoms of AMI | Typical | 1377 (94%) | 369 (95%) | 106 (95%) | 902 (94%) | |
| | Atypical | 53 (4%) | 12 (3%) | 3 (3%) | 38 (4%) | |
| | Other | 29 (2%) | 6 (2%) | 3 (3%) | 20 (2%) | .8164 |
| Cardiovascular disease before onset | | | | | | |
| | Angina | 329 (23%) | 96 (25%) | 18 (16%) | 215 (22%) | .1471 |
| | Hypertension | 1048 (72%) | 304 (79%) | 68 (61%) | 676 (70%) | .0005 |
| | Diabetes | 397 (27%) | 101 (26%) | 24 (21%) | 272 (28%) | .2537 |
| | Neither | 295 (20%) | 58 (15%) | 34 (30%) | 203 (21%) | .0008 |
| Smoking status | Smoker | 531 (36%) | 133 (34%) | 47 (42%) | 351 (37%) | |
| | Nonsmoker | 489 (34%) | 132 (34%) | 32 (29%) | 325 (34%) | |
| | Former smoker | 439 (30%) | 122 (32%) | 33 (29%) | 284 (30%) | .6179 |

*Abbreviations:* STEMI, ST-elevation myocardial infarctions; NSTEMI, non–ST-elevation myocardial infarctions; BBB: bundle-branch blocks.
* Eight to 11 years.
† More than 11 years.

### *Exposure*

Daily estimated ambient soot concentrations ranged between 0.2 and 7.1 $m^{-1} \times 10^{-5}$, with a mean of 1.9 $m^{-1} \times 10^{-5}$ (Table 2, Fig 1). Daily ambient fine particle concentrations were moderate, with a mean of 17 $\mu g/m^3$ (correlation Pearson $r = 0.88$ of soot and $PM_{2.5}$). The time-varying component of daily estimated personal soot concentrations had a mean of 1.9 $m^{-1} \times 10^{-5}$ and ranged between 0.2 and 6.6 $m^{-1} \times 10^{-5}$ in hazard and referent periods. Correlation of the time-varying component of daily estimated personal soot concentrations and estimated ambient soot was high (Pearson $r = 0.94$). Patients spent 0 to 15 hours in traffic per day and 0 to 14 hours outdoors. Distributions of times spent outdoors, times spent in traffic, and the time-varying component of daily estimated personal soot concentrations are shown in Fig 2. It illustrates that more time was spent in traffic and outside on the case day than on referent days and that the time-varying component of daily estimated personal soot concentrations was somewhat higher on the hazard day than on the referent days.

### *Case-crossover analyses*

Case-crossover analyses of the association of the time-varying component of daily estimated personal soot exposure with AMI resulted in an RR of 1.30 per interquartile range (IQR) of 1.1 $m^{-1} \times 10^{-5}$ (95% confidence interval [CI], 1.09-1.55) (Table 3). When considering the effects of estimated ambient soot, hours spent outdoors, and hours spent in traffic simultaneously in one model—as personal soot from these 3 sources—exposure to soot due to times spent in traffic (RR, 1.41; 95% CI, 1.22-1.64 per IQR [2 hours, equivalent to 0.28 $m^{-1} \times 10^{-5}$]) and outdoors (RR, 1.26; 95% CI,

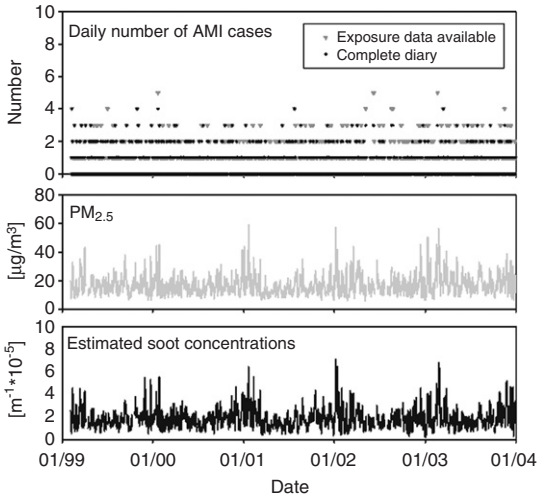


Fig 1. Daily number of AMI cases (black dots, with 72-hour complete diary data, n = 960; gray triangles, with $PM_{2.5}$ concentration exposure data, n = 1411), $PM_{2.5}$, and estimated soot concentrations.

1.12-1.42 per IQR [2 hours equivalent to 0.12 $m^{-1} \times 10^{-5}$]) dominated the association, whereas the effect for estimated ambient soot was smaller (RR, 1.025; 95% CI, 0.87-1.21 [per 0.95 $m^{-1} \times 10^{-5}$ personal soot equivalent to 1.09 $m^{-1} \times 10^{-5}$ ambient soot]). In comparison, ambient estimated soot alone was similarly weakly associated with AMI onset (RR, 1.041; 95% CI, 0.88-1.23 per 1.09 $m^{-1} \times 10^{-5}$). This was reflected in sensitivity analyses with weak associations when including more subjects or using the time-stratified approach instead of a unidirectional approach. In addition, ambient $PM_{2.5}$ was not significantly associated with AMI onset, with unstable point estimates and wide confidence intervals in each of the control selection strategies.

## Discussion

In the present study, we showed a transient increase in risk of AMI onset by 30% (95% CI, 9.1-55%) per 1.1 $m^{-1} \times 10^{-5}$ increase in estimated daily personal soot concentration. The contribution of personal soot from individual times spent in traffic and individual times spent outdoors was far more significant to this increase in risk than the estimated ambient soot exposure. We did not find a statistically significant association of AMI with ambient fine particulate air pollution.

Previous studies showed an increase in risk for AMI onset using central monitoring data,[2-6] whereas others did not.[8-11] We found no association of $PM_{2.5}$ or estimated ambient soot when only using central site data in this study. But when applying a prediction model developed in an exposure assessment study,[12] which also weighed in times spent outdoors as well as in traffic, we found a clear association of estimated personal soot exposure with AMI onset. This was due to the higher effects associated with time spent in traffic and outdoors, significant contributors to personal exposure. This suggests that using personal exposure assessment instead of ambient measurements may be more suitable to estimate the health burden due to traffic exposure. Traffic particles are more toxic than general ambient particles even when soot is used as an exposure metric. Soot represents primary combustion particles, including traffic, but also wood burning and industrial sources. Furthermore, people are more active outdoors and while in traffic compared with being indoors and hence inhale more air. Alternatively, time spent in traffic and outdoors includes the impact of other stressors than air pollution, for example, noise.

It is important to note that the study had no power to detect the small effect size previously reported for centrally monitored $PM_{2.5}$. In a previous study, we observed an association between exposure to traffic and AMI onset 1 hour later (odds ratio, 2.92; 95% CI, 2.22-3.83; $P<.001$).[13] The present study can be regarded as an extension of that study and a way of rescaling the RR to the air pollution concentrations related to the exposure "times spent in traffic."

Time spent outdoors was a risk factor per se[13] that had not been expected a priori. In that study the risk of outdoor activities carried an RR of 2.21 (95% CI, 1.61-3.03). Time spent outdoors was also an effect modifier for the association of exertion and AMI onset. Strenuous exertion outside was associated with a 4-fold larger RR of AMI symptom onset than exertion performed indoors.[24] The estimates provided here for soot exposure due to times spent outdoors may hint at interplay of various factors combined in the diary entry "times spent outdoors."

The exposure assessment in this study used estimations in 2 levels. First, ambient soot was estimated using a prediction model from parallel daily measurements of fine

Table 2
Exposure distribution calculated for 24-hour periods

| Variable | Time | N | Min | 25th Pctl | Mean | Median | 75th Pctl | Max |
|---|---|---|---|---|---|---|---|---|
| Time-varying component of daily personal soot ($m^{-1} \times 10^{-5}$) | Hazard and referent periods | 2622 | 0.19 | 1.27 | 1.89 | 1.79 | 2.35 | 6.61 |
| Time spent in traffic (h) | Hazard and referent periods | 2622 | 0 | 0 | 1.27 | 1 | 2 | 15 |
| Time spent outdoors (h) | Hazard and referent periods | 2622 | 0 | 0 | 1.45 | 1 | 2 | 14 |
| $PM_{2.5}$ (mean) ($\mu g/m^3$) | Study period (2/99-12/03) | 1744 | 5.7 | 11.9 | 17.0 | 15.6 | 20.4 | 59.0 |
| Estimated soot ($m^{-1} \times 10^{-5}$) | Study period (2/99-12/03) | 1719 | 0.20 | 1.25 | 1.86 | 1.71 | 2.29 | 7.11 |
| Temperature (°C) | Study period (2/99-12/03) | 1788 | −12.8 | 4.0 | 10.1 | 10.3 | 16.7 | 27.7 |

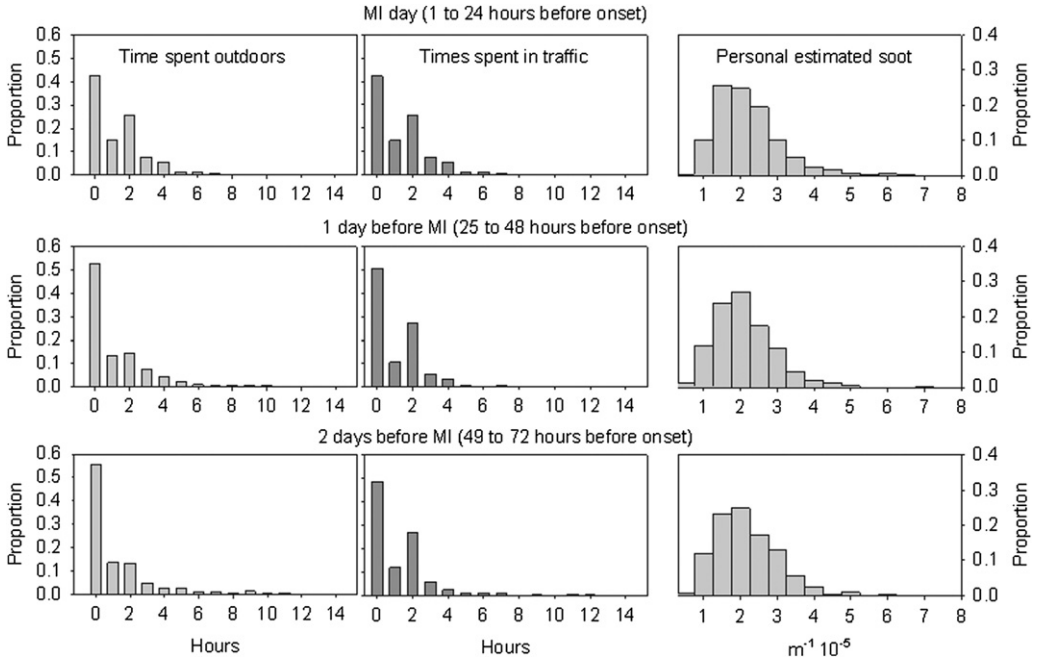


Fig 2. Distribution of times spent outdoors and in traffic in hazard and referent periods.

particulate air pollution and filter reflectance that were conducted during part of the study period. Although this procedure certainly entailed many assumptions, it may be acceptable for the present purpose, given that the predictions from the final model had a relatively good agreement with the measured values ($R^2$ = 0.76) and a similarly good agreement with an hourly validation data set of Aethalometer measurements ($R^2$ = 0.72). In the next level, to obtain estimates of personal exposure to soot, we applied a prediction model developed previously.[12] This linear regression model included a y-intercept, ambient soot, the characteristic of residence being close to a major road, and personal activities. Because we decided to use only time-varying and statistically significant components in this equation (ie, ambient soot, times spent outdoors, and times spent in traffic), sufficient to determine transient risk factors, we could not perform analyses that would require absolute values for personal exposure as analyses of the exposure response function. Living close to busy roads as effect modifier of the personal soot and AMI

Table 3
Case-crossover results adjusting for ambient temperature and day of the week

| Exposure | Referent Selection | N | Per IQR | RR (95% CI) | *P* Value |
|---|---|---|---|---|---|
| Personal estimated soot (24-h mean) | Unidirectional | 960 | 1.10 $m^{-1} \times 10^{-5}$ | 1.3 (1.091-1.55) | .0034 |
| *Multivariate model including predictors for personal estimated soot* | | | | | |
| Personal soot from ambient soot | Unidirectional | 960 | 0.95 $m^{-1} \times 10^{-5}$ | 1.025 (0.866-1.212) | .7772 |
| Personal soot from time spent outdoors | | | 2 h (≈0.12 $m^{-1} \times 10^{-5}$) | 1.262 (1.124-1.418) | <.0001 |
| Personal soot from time spent in traffic | | | 2 h (≈0.28 $m^{-1} \times 10^{-5}$) | 1.413 (1.220-1.636) | <.0001 |
| *Estimated ambient soot (24-h mean)* | | | | | |
| | Unidirectional | 960 | 1.09 $m^{-1} \times 10^{-5}$ | 1.041 (0.8818-1.229) | .6343 |
| | Unidirectional† | 1390* | 1.09 $m^{-1} \times 10^{-5}$ | 1.011 (0.8898-1.149) | .8647 |
| | Time stratified† | 960 | 1.09 $m^{-1} \times 10^{-5}$ | 1.015 (0.9263-1.113) | .7463 |
| | Time stratified† | 1396* | 1.09 $m^{-1} \times 10^{-5}$ | 1.035 (0.9596-1.115) | .3755 |
| *Ambient $PM_{2.5}$ (24-h mean)* | | | | | |
| | Unidirectional | 960 | 8 $\mu g/m^3$ | 1.019 (0.876-1.185) | .804 |
| | Unidirectional† | 1407* | 8 $\mu g/m^3$ | 1.044 (0.929-1.174) | .465 |
| | Time stratified† | 960 | 8 $\mu g/m^3$ | 1.006 (0.928-1.09) | .889 |
| | Time stratified† | 1411* | 8 $\mu g/m^3$ | 1.022 (0.957-1.091) | .521 |

* All subjects with ambient exposure data out of 1459 independent of whereabouts.
† Hazard and/or referent periods may not have been spent within study area.

association could also not be investigated because we were lacking this information for half of the cases.

We used a formula derived for elderly adults in the city of Amsterdam to estimate personal exposure for our study subjects.[12] Two other studies conducted in different populations of elderly adults[25,26] also found significant effects of time spent in traffic and outdoors on 24-hour average personal soot exposure, supporting the use of the current model. Each hour spent in traffic was associated with a 12%, 13%, and 9% increase in 24-hour personal exposure to soot in adults living in Utrecht,[26] Amsterdam, and Helsinki,[25] respectively. Each hour spent outdoors was associated with a 3%, 2%, and 5% increase in 24-hour personal exposure to soot in adults living in Utrecht,[26] Amsterdam, and Helsinki,[25] respectively.

For the case-crossover analyses, we selected referent periods previous to the onset of AMI by design. This has the potential of bias due to trend,[27] but referent periods of personal activities after the event would not represent the usual frequencies. Because ambient exposures are not affected by individuals' activities, we could use the time-stratified approach when we investigated those exposures.[22,23] The estimates did not show a systematic difference between unidirectional and time-stratified approach and were all rather imprecise.

## Conclusions

Our results suggest that an increase in risk of AMI in association with personal soot exposure may be in great part due to the contribution of personal soot from individual times spent in traffic and individual times spent outdoors. As a consequence, estimates calculated based on measurements at urban background stations may be underestimations. Health effects of traffic-related air pollution may need to be updated, taking into account individual time spent in traffic and outdoors, to adequately protect the public.

## Statement of Conflict of Interest

All authors declare that there are no conflicts of interest.

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## References

1. Brook RD, Rajagopalan S, Pope III CA, et al: Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation 2010; 121:2331-2378.
2. Peters A, Dockery DW, Muller JE, et al: Increased particulate air pollution and the triggering of myocardial infarction. Circulation 2001;103:2810-2815.
3. Pope III CA, Muhlestein JB, May HT, et al: Ischemic heart disease events triggered by short-term exposure to fine particulate air pollution. Circulation 2006;114:2443-2448.
4. D'Ippoliti D, Forastiere F, Ancona C, et al: Air pollution and myocardial infarction in Rome: a case-crossover analysis. Epidemiology 2003;14:528-535.
5. von Klot S, Peters A, Aalto P, et al: Ambient air pollution is associated with increased risk of hospital cardiac readmissions of myocardial infarction survivors in five European cities. Circulation 2005;112:3073-3079.
6. Zanobetti A, Schwartz J: The effect of particulate air pollution on emergency admissions for myocardial infarction: a multi-city case-crossover analysis. Environ 2005, doi:10.1289/ehp.7550 available via http://dx.doi.org/ [Online 16 March 2005].
7. Rich DQ, Kipen HM, Zhang J, et al: Triggering of transmural infarctions, but not nontransmural infarctions, by ambient fine particles. Environ Health Perspect 2010;118:1229-1234.
8. Berglind N, Ljungman P, Moller J, et al: Air pollution exposure–a trigger for myocardial infarction? Int J Environ Res Public Health 2010;7:1486-1499.
9. Sullivan J, Sheppard L, Schreuder A, et al: Relation between short-term fine-particulate matter exposure and onset of myocardial infarction. Epidemiology 2005;16:41-48.
10. Peters A, von Klot S, Heier M, et al: Particulate air pollution, personal activities and the onset of myocardial infarction—a case-crossover study. 124 Part I. 2005. Health Effects Institute Research Report. Ref Type: report.
11. Mann JK, Tager IB, Lurmann F, et al: Air pollution and hospital admissions for ischemic heart disease in persons with congestive heart failure or arrhythmia. Environ Health Perspect 2002;110: 1247-1252.
12. Wichmann J, Janssen NAH, van der Zee S, et al: Traffic-related differences in indoor and personal absorption coefficient measurements in Amsterdam, the Netherlands. Atmospheric Environment 2005;39:7384-7392.
13. Peters A, von Klot S, Heier M, et al: Exposure to traffic and the onset of myocardial infarction. N Engl J Med 2004;351:1721-1730.
14. Kuch B, Heier M, von Scheidt W, et al: 20-year trends in clinical characteristics, therapy and short-term prognosis in acute myocardial infarction according to presenting electrocardiogram: the MONICA/KORA AMI Registry (1985-2004). J Intern Med 2008;264:254-264.

15. Lowel H, Meisinger C, Heier M, et al: The population-based acute myocardial infarction (AMI) registry of the MONICA/KORA study region of Augsburg. Gesundheitswesen 2005;67(Suppl 1):S31-S37.
16. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, et al: Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. Circulation 1994;90:583-612.
17. Marple VA, Rubow KL, Turner W, et al: Low flow rate sharp cut impactors for indoor air sampling: Design and calibration. JAPCA 1987;37:1303-1307.
18. Cyrys J, Heinrich J, Hoek G, et al: Comparison between different traffic-related particle indicators: elemental carbon (EC), PM2.5 mass, and absorbance. J Expo Anal Environ Epidemiol 2003;13: 134-143.
19. ISO: Ambient air-determination of a black smoke index. International Organization for Standarization. International Standard 1993 (E):9835.
20. Pitz M, Schmid O, Heinrich J, et al: Seasonal and diurnal variation of PM2.5 apparent particle density in urban air in Augsburg, Germany. Environ Sci Technol 2008;42:5087-5093.
21. Maclure M: The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol 1991; 133:144-153.
22. Janes H, Sheppard L, Lumley T: Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology 2005;16:717-726.
23. Mittleman MA: Optimal referent selection strategies in case-crossover studies: a settled issue. Epidemiology 2005;16:715-716.
24. von Klot S, Mittleman MA, Dockery DW, et al: Intensity of physical exertion and triggering of myocardial infarction: a case-crossover study. Eur Heart J 2008;29:1881-1888.
25. Lanki T, Ahokas A, Alm S, et al: Determinants of personal and indoor PM2.5 and absorbance among elderly subjects with coronary heart disease. J Expo Sci Environ Epidemiol 2007;17:124-133.
26. Van Roosbroeck S, Hoek G, Meliefste K, et al: Validity of residential traffic intensity as an estimate of long-term personal exposure to traffic-related air pollution among adults. Environ Sci Technol 2008; 42:1337-1344.
27. Bateson TF, Schwartz J: Selection bias and confounding in case-crossover analyses of environmental time-series data. Epidemiology 2001;12:654-661.