DAILY NON-EXTERNAL MORTALITY EFFECTS OF OUTDOOR AIR POLLUTION 1999-2001, BANGKOK, THAILAND: CASE-CROSSOVER STUDY

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ABSTRACT: There have been many time series and case-crossover (CCO) studies of short-term ambient air pollution effects on daily mortality and morbidity. To the best of our knowledge, no CCO studies of such effects in Thailand have been published previously. We conducted a CCO study to assess effects of ambient air pollution on non-external (non-accidental) mortality in Bangkok during 1999-2001 (total 3 years). We assessed associations of daily non-external mortality with ambient air pollutant concentrations in Bangkok from 1999 through 2001. Pollutant metrics assessed were 24-hour average particulate matter of diameter ≤10 μm (PM_{10}), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2), and 8-hour average ozone (O_3) from 10:00 AM to 6:00 PM. Data were analyzed with stratified conditional logistic regression. There was one stratum for each of the 102,522 deaths included in analysis. In each stratum, the case day was the day on which a given death occurred. The crossover (control) days were all matched days of week in the same month as the case day (time-stratified analysis). Two-day moving average levels of each pollutant were assessed in separate analyses (single-pollutant models). For each pollutant, unadjusted effects and effects adjusted for same-day average temperature and previous-day average relative humidity, were modeled. Air pollution effects were assessed overall, by year, and by gender. The study revealed that pollutant concentrations were consistently positively associated with mortality from non-external causes. Unadjusted associations were statistically significant ($p<0.05$) for O_3, SO_2, and PM_{10}. Adjusted associations were significant for NO_2 and PM_{10}. Adjusted pollutant effects were weaker than unadjusted ones for all pollutants but NO_2. Associations of air pollution with mortality varied considerably by year, and were generally strongest in 2001. Associations were significantly stronger in females than males. Conclusions, these findings suggest that in Bangkok, daily non-external mortality increases with increasing short-term exposure to ambient air pollution, especially PM_{10}. Findings are qualitatively consistent with those of previous studies of air pollution and daily mortality. Further research is needed to develop optimal strategies for adjusting analytical models for weather, to evaluate the generalizability of these findings across times and across locations in Asia, to advance understanding of observed temporal and gender differences in air pollution effects, and to assess the relative importance of different pollutants (e.g., airborne particulate and gaseous pollutants) in promoting increased mortality.

Keywords: ambient air pollution, non-external mortality, case-crossover, Bangkok

BACKGROUND

Human activities release chemicals and particulates into the indoor and outdoor atmospheres. Some of these pollutants can cause problems for humans, animals, plants, and environment [1]. Exposure to both indoor and outdoor air pollutants has been associated with increased morbidity and mortality in humans [2, 3]. Major sources of ambient (outdoor) air pollution include automotive traffic and industry. Numerous studies to date have assessed human health effects of the ambient air pollutants ozone (O_3) [4], nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and particulate matter of diameter ≤10 μm (PM_{10}) [5, 6]. Short-term and long-term exposures to these and other air pollutants have been associated with a variety of harmful effects [7 - 9], including mortality [10].

To date, most research on health effects of short-term and long-term ambient air pollution exposure has been conducted in western countries [11 - 14]. Fortunately, the body of related evidence from Asian countries has increased substantially in recent years. For example, the Health Effects Institute, Boston, MA, USA, has sponsored a series of studies of short-term air pollution exposure and daily mortality in Thailand, China, and India. Despite the recent increase in air pollution health effects studies

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in Asia, similarities and differences in air pollution health effects between Asian and western countries are not yet fully understood [15].

To date, most studies of short-term air pollution effects have employed the time series design or the case-crossover (CCO) design [14]. In the former, daily counts of a health-related event, such as mortality or hospitalization, are analyzed in relation to short-term ambient air pollution concentrations, generally with adjustment for meteorology and personal characteristics such as age and gender. In the CCO design, the short-term air pollution concentration for the day of each event (the "case day") is compared to concentrations for other, matched days on which the event did not occur ("control days") [16]. Evaluation of these comparisons over a large number of events gives an overall estimate of the air pollution effect on occurrence of the event [17]. In these studies, adjustment is usually made for meteorology, which can vary between case and control days. Personal characteristics such as age and gender are matched in the analysis, and thus do not require adjustment.

To supplement the data base in Thailand, we conducted a case-crossover (CCO) study of short-term ambient air pollution effects on mortality from non-external causes, that is, from causes other than accident, injury, and poisoning. This study considers mortality in Bangkok, and covers the 3-year period 1999-2001. To the best of our knowledge, this is the first peer-reviewed published report of a CCO study of air pollution health effects in Thailand.

DATA AND METHODS

Mortality Data

Information on deaths occurring in Bangkok from January 1, 1999, through December 31, 2001, was provided by Thailand's Ministry of Public Health. Causes of death were coded according to the International Classification of Disease, Tenth Revision (ICD-10) [18]. All deaths due to non-external causes (causes other than accident, injury, and poisoning, ICD-10 ranging from A00 to R99) were eligible for analysis. Data for each death included ICD-10 code, date of death, gender, and age.

Air pollution and meteorological data

Ambient air pollutant concentrations were provided by the Pollution Control Department (PCD), Ministry of Natural Resources and Environment. PCD operated 5 stationary ambient air pollution monitoring stations in Bangkok during the study period. Three gaseous air pollutants, ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2), were considered in analysis. Particulate matter of diameter $\leq$10 μm (PM_{10}) was also considered. Ambient concentrations of these pollutants were measured by ultraviolet absorption, chemiluminescence, ultraviolet fluorescence, and beta gauge, respectively. These methods are either US EPA designated reference methods or equivalent methods. Quality control of monitoring instruments was performed once per month. 24-hour average concentrations of NO_2, SO_2, and PM_{10} were used in analysis. For O_3, the 8-hour average concentration from 10:00 AM to 6:00 PM was used, because maximum O_3 levels occur during the daylight hours [19], and because this averaging time has generally been used for O_3 in previous research on short-term ambient air pollution health effects [20]. Within each station, each pollutant was excluded from analysis on all days during which at least 75% of hourly measurements were not available ($\geq$6 hours for O_3 and $\geq$18 hours for the other pollutants). Also, for each pollutant, a station's measurements were omitted entirely from analysis unless measurements of that pollutant were available for $\geq$75% of all study days at that station. To reduce bias in study findings, the analysis included only days for which these requirements were satisfied for all pollutants (total 1091/1096 days, or 99.5% of all possible days).

Daily 24-hour average levels of ambient temperature, relative humidity, and barometric pressure in Bangkok were obtained from the Department of Meteorology.

DATA ANALYSIS

This was a time-stratified case-crossover study. For each death, a unique stratum was constructed. This consisted of the day of that death, along with all corresponding days of week in the month during which that death occurred [21]. (Thus, for example, the SO_2-related stratum for a death on Thursday, June 14, 2001, consisted of the SO_2 levels on that day and on the Thursdays June 7, 21, and 28, 2001.) This type of stratification has been shown to minimize bias in analytical results [22].

The data were analyzed with conditional logistic regression [23], employing the Cox modeling routine in SPSS. The analyses were stratified as described above. This procedure yielded an odds ratio (OR) of each pollutant for non-external mortality. In this report, ORs are presented per 10-μg/cubic meter ($\mu g/m^3$) increment in pollutant concentration. (As an example, an OR of 1.0094 for NO_2 would indicate a modeled percentage increase of 0.94% in mortality per 10-$\mu g/m^3$ increment in

Table 1 Descriptive statistics for daily deaths from non-external causes, age at death, ambient air pollutant concentrations, temperature, and relative humidity, Bangkok, 1999 through 2001

Metric	N*	Mean	SD	Minimum	Maximum
Daily deaths	102,522	94.1	12.3	29	147
Age at death (yrs)	102,522	58.3	22.2	0**	117
8-hr O_3, 10:00 AM to 6:00 PM†	1096	54.4	27.8	6.8	179.1
24-hr NO_2†	1096	43.7	17.0	7.0	119.3
24-hr SO_2†	1096	15.3	5.9	2.2	62.1
24-hr PM_{10}†	1091§	52.8	21.7	20.2	166.3
24-hr temperature (°C)	1096	28.9	1.7	18.6	32.9
24-hr relative humidity (%)	1096	72.5	8.4	39.0	95.7

* Number of deaths for daily deaths and age, number of days otherwise.

** Age zero denotes infancy, the first year of life.

† All pollutant concentrations are expressed in $\mu g/m^3$.

§ PM_{10} concentrations were missing for 5 days in 2001.

NO_2 concentration.)

Many previous studies of ambient air pollution and daily mortality have assessed pollutant concentrations as the moving average of concentrations on the day of death and the previous day (mv01). We also chose this as the analyzed metric for each pollutant. Pollutant effects were assessed without adjustment and with adjustment for meteorological parameters. To decide on a specific adjustment, 24-hour averages of daily temperature, relative humidity (RH), and barometric pressure (BP) were examined. For each of these, the measurement on the day of death (lag 0), the measurement one day before death (lag 1) and the moving average of these two measurements (mv01) were considered. Each of these 9 metrics was analyzed separately in relation to daily mortality. Modeled effects of temperature and RH, for which Wald chi-square statistics ranged from 15.6 to 43.5 ($p<0.001$ in all cases), were clearly stronger than those of BP, for which chi-squares ranged from only 0.9 to 6.3 ($p\geq0.012$). All two-way combinations of temperature and RH metrics were then examined (total 6 combinations). The largest model chi-square was observed for the combination of same-day temperature (temperature lag 0) and previous-day RH (RH lag 1). Each BP metric was entered separately with this combination. The modeled effect of BP never approached statistical significance ($p\geq0.617$). Thus, modeled effects of air pollutants were adjusted for temperature lag 0 and RH lag 1.

Air pollution effects on non-external daily mortality were modeled as overall effects, and were also modeled by year and by gender.

RESULTS

The analysis included 102,522 deaths from non-external causes. These constituted 91.2% of all deaths recorded in Bangkok during the study period. Of these, 33,440 (32.6%), 33,933 (33.1%), and 35,149 (34.3%) occurred in 1999, 2000, and 2001, respectively. 57,998 deaths (56.6%) occurred in males. There was a total of 348,572 control days, for a total of 451,094 observations in the analytical dataset and an average of 3.4 control days per case day.

Descriptive statistics for daily deaths, age, air pollutant concentrations, temperature, and RH are shown in Table 1. The mean daily number of deaths was 94.1 (range 29 to 147). Mean age at death was 58.3 years. Not surprisingly, among gaseous pollutants, the highest mean concentration was observed for 8-hr average O_3 (54.4 $\mu g/m^3$). Mean PM_{10} concentration was 52.8 $\mu g/m^3$. Pollutant concentrations were consistently positively and statistically significantly correlated with each other during the study period ($p<0.001$); the highest and lowest Pearson correlation coefficients were 0.717 (NO_2 with PM_{10}) and 0.228 (O_3 with SO_2).

Unadjusted and adjusted modeled effects of ambient air pollutants on daily mortality from non-external causes are shown in Table 2. PM_{10} was the only pollutant for which unadjusted and adjusted effects were both significant ($p<0.001$ and $p=0.035$, respectively). Unadjusted effects were positive for all pollutants (OR>1), and significant for all but NO_2. The largest and smallest unadjusted ORs were 1.0186 (for SO_2) and 1.0054 (for NO_2), respectively.

Modeled pollutant effects were quite sensitive to adjustment for weather. After adjustment, ORs remained positive, but were smaller than unadjusted ones for all pollutants except NO_2. For example, the unadjusted OR for PM_{10} was 1.0098, in contrast to the adjusted OR of 1.0057. ORs for O_3 and SO_2 lost statistical significance after adjustment. The largest

Table 2 Modeled unadjusted and adjusted odds ratios, 95% confidence intervals, and p-values for non-external mortality, per 10-µg/m3 increment in 2-day moving average ambient air pollutant concentrations*, Bangkok, 1999-2001

Pollutant	Unadjusted			Adjusted†		
	OR	**95% CI**	***p-value***	**OR**	**95% CI**	***p-value***
8-hr O_3	1.0068	1.0033, 1.0103	<0.001	1.0012	0.9970, 1.0054	0.574
24-hr NO_2	1.0054	0.9993, 1.0114	0.082	1.0069	1.0004, 1.0134	0.038
24-hr SO_2	1.0186	1.0048, 1.0325	0.008	1.0068	0.9928, 1.0209	0.342
24-hr PM_{10}	1.0098	1.0050, 1.0147	<0.001	1.0057	1.0004, 1.0111	0.035

* Moving average of pollutant concentrations on the day of death (lag 0) and the previous day (lag 1).
† Adjusted for Temperature lag 0 and Humidity lag 1.

Table 3 Modeled unadjusted and adjusted odds ratios for non-external mortality, per 10-µg/m3 increment in 2-day moving average ambient air pollutant concentrations, by year, Bangkok, 1999-2001

Pollutant and year	Unadjusted			Adjusted*		
	OR	**95% CI**	***p-value***	**OR**	**95% CI**	***p-value***
8-hr O_3						
1999	1.0055	0.9991, 1.0119	0.091	0.9990	0.9922, 1.0057	0.761
2000	1.0072	1.0017, 1.0126	0.010	1.0031	0.9971, 1.0090	0.313
2001	1.0075	1.0012, 1.0139	0.020	1.0009	0.9942, 1.0076	0.796
24-hr NO_2						
1999	1.0021	0.9896, 1.0148	0.740	0.9981	0.9854, 1.0110	0.772
2000	1.0078	0.9981, 1.0176	0.116	1.0076	0.9973, 1.0180	0.146
2001	1.0049	0.9951, 1.0147	0.329	1.0112	1.0012, 1.0213	0.028
24-hr SO_2						
1999	1.0197	0.9913, 1.0489	0.176	0.9984	0.9701, 1.0276	0.916
2000	1.0159	0.9968, 1.0354	0.104	1.0104	0.9913, 1.0298	0.290
2001	1.0230	0.9955, 1.0512	0.102	1.0068	0.9795, 1.0348	0.628
24-hr PM_{10}						
1999	1.0101	1.0021, 1.0181	0.013	1.0039	0.9956, 1.0123	0.355
2000	1.0058	0.9984, 1.0132	0.122	1.0030	0.9952, 1.0108	0.457
2001	1.0175	1.0070, 1.0281	0.001	1.0138	1.0032, 1.0245	0.011

* Adjusted for temperature lag0 and humidity lag1.

adjusted OR, 1.0069, was observed for NO_2, and this was statistically significant (p=0.038, in contrast to p=0.082 for unadjusted NO_2). The magnitudes of unadjusted and adjusted ORs for SO_2 were relatively large, although the p-values for SO_2 were relatively small.

Unadjusted and adjusted modeled effects of ambient air pollutants on non-external mortality are shown, by year, in Table 3. Modeled effects on mortality were generally largest in 2001. For pollutants other than O_3, magnitudes of unadjusted and adjusted effects differed considerably from year to year (although these differences were not statistically significant). For example the unadjusted modeled percentage increase in mortality per 10 $\mu g/m^3$ increment in PM_{10} varied from 0.58% in 2000 to 1.75% in 2001, a 3-fold difference in effect between these 2 years. Similarly, the corresponding increase for adjusted SO_2 varied from -0.16% in 1999 to 1.04% in 2000, for about a 6-fold year-to-year difference. The adjusted modeled effects of NO_2 were smaller than the unadjusted effects in 1999 and 2000; the opposite was true in 2001.

Unadjusted and adjusted modeled effects of ambient air pollutants on mortality are shown, by gender, in Table 4. Effects were consistently stronger in females than in males. Gender differences in pollutant effects were significant for SO_2 (p=0.010 for both unadjusted and adjusted effects), but not for other pollutants ($p \geq 0.257$).

DISCUSSION

In the current study, as in many previous studies in Bangkok and elsewhere, short-term ambient air pollution concentrations were positively associated with daily mortality from non-external causes [20]. PM_{10} was the only pollutant for which both unadjusted and adjusted associations with mortality from non-external causes were statistically significant [15]. In this sense, PM_{10} was the pollutant most consistently associated with daily mortality [24]. On balance, these results increase confidence that regulation of ambient air pollution concentrations benefits public health.

Table 4 Modeled unadjusted and adjusted odds ratios for non-external mortality, per 10-µg/m3 increment in 2-day moving average ambient air pollutant concentrations, by gender, Bangkok, 1999-2001

Pollutant and gender	Unadjusted			Adjusted*		
	OR	**95% CI**	***p-value***	**OR**	**95% CI**	***p-value***
8-hr O_3						
Males	1.0050	1.0004, 1.0097	0.032	0.9994	0.9943, 1.0046	0.831
Females	1.0090	1.0038, 1.0144	0.001	1.0035	0.9977, 1.0092	0.234
24-hr NO_2						
Males	1.0031	0.9951, 1.0112	0.443	1.0046	0.9963, 1.0130	0.278
Females	1.0083	0.9991, 1.0175	0.078	1.0098	1.0003, 1.0194	0.043
24-hr SO_2						
Males	1.0027	0.9846, 1.0211	0.770	0.9906	0.9728, 1.0094	0.334
Females	1.0394	1.0182, 1.0610	<0.001	1.0276	1.0064, 1.0492	0.010
24-hr PM_{10}						
Males	1.0079	1.0015, 1.0143	0.015	1.0039	0.9971, 1.0107	0.261
Females	1.0123	1.0050, 1.0197	0.001	1.0082	1.0005, 1.0159	0.036

* Adjusted for temperature lag 0 and humidity lag 1.

The outcome measure for this report was mortality from non-external causes. This includes, but is not limited to, mortality from cardiovascular and respiratory causes. We chose to analyze this outcome for two reasons. First, it has been analyzed in many previous studies of short-term effects of ambient air pollution exposure. Second, an unusually high proportion of deaths in Bangkok (37,291 deaths, 36.9% of all deaths) was attributed to unclassified causes (ICD-10 code R). Of these, 14,424 deaths (38.7% of unclassified causes and 14.1% of all deaths) were attributed to "senility." At the same time, only 21,891 deaths (21.4%) were attributed specifically to cardiovascular or respiratory causes. We believe that a large proportion of unclassified deaths must actually have been attributable to cardiovascular or respiratory causes, and therefore that findings regarding cardiovascular and respiratory causes could have been subject to substantial bias [25, 26].

We adjusted air pollution effects for weather by entering same-day temperature and previous-day humidity into the conditional logistic regression models. As mentioned above, this combination gave the largest likelihood-ratio chi-square statistics for analytical models. This, together with our observation of generally larger pollution effects in unadjusted models, suggests that our modeling strategy may have been conservative with respect to modeled pollution effects. Actual pollution effects on mortality could conceivably have been somewhat larger than effects reported here. Also, it is not yet clear why adjusted modeled effects of O_3, SO_2, and PM_{10} were weaker than unadjusted ones, whereas the reverse was true for NO_2. Further research is needed to evaluate the influence of different adjustment strategies on modeled air pollution effects, and to ascertain which specific strategies give the most accurate estimates of actual air pollution effects.

There were considerable year-to-year differences in modeled effects of most air pollutants on mortality. For example, modeled adjusted percentage increases in mortality, per 10 $\mu g/m^3$ increase in PM_{10} concentration, ranged from 0.30% in 2000 to 1.38% in 2001 (table 3). Reasons for this temporal variation are not yet understood. Means of pollution concentrations, temperature, and humidity varied significantly from year to year ($p \leq 0.026$), and this might partly explain the observed year-to-year variation in modeled air pollution effects on mortality. Further research is needed on this issue. For example, more comprehensive comparison of year-to-year modeled pollutant effects in different locations, and during different time periods, would be useful in addressing this issue. Such comprehensive comparison is beyond the scope of this report.

Associations of ambient air pollution levels with daily mortality from non-external causes in Bangkok have been reported previously for the 5-year period 1999 through 2003 [15, 20]. Three of these years, 1999 through 2001, overlap with the time period assessed in the present report. Reported mean air pollutant levels were generally similar between the two studies, and mean daily death counts were very similar (94.8 in the previous study and 94.1 in the present study). Estimated ambient pollutant effects were generally higher in the previous study. For the 4 studied pollutants, the average increase in modeled mortality risk in the previous study was 48.5% higher than the average increase in unadjusted risk in the present study. The corresponding difference between the previous study and adjusted risk in the present study was 90.0%. The differences in modeled air pollution effects might be partly attibutable to the fact that the

studies covered different time periods, and to the fact that the studies employed different designs. Specifically, the previous study employed the time series design, whereas the present study employed the case-crossover design.

The current analysis covered the 3-year period 1999-2001. It is not certain whether these findings are generalizable to other time periods. One purpose of the present study, in addition to providing estimates of air pollution effects on mortality in Bangkok, is to provide a reference point for future research that compares pollutant effects during different time periods. Also, detailed assessment of the relative importance of different pollutants in promoting daily mortality is beyond the scope of this report. Such assessment will be presented subsequently.

CONCLUSION

Air pollution level in Bangkok was related to an increased daily non-external mortality. We found an association between short-term exposure to PM_{10} and daily mortality from non-external causes. Further research is needed to advance understanding of health effects of short-term air pollution exposures in Bangkok, and to assess the relative merits of the case-crossover design and the time series design as tools for analyzing such effects.

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