SOURCES OF UNCERTAINTY IN CALCULATING MORTALITY AND MORBIDITY ATTRIBUTABLE TO AIR POLLUTION

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ABSTRACT

Assessing and quantifying the burden of illness and mortality from air pollution exposure relies on statistical estimates and other assumptions that have inherent uncertainties. Through an intensive study in Hamilton, Canada, this study illustrates for policymakers the sensitivity of health effect estimates to a wide range of possible uncertainties. Dose-response relationships were derived based on pooled and averaged estimates published in the scientific literature from 1997 to 2001. These estimates were applied to local air pollution, mortality and hospital admissions data for the years 1995-1999. The data were adjusted to reflect uncertainties in the current state of knowledge, including: (1) baseline pollution, (2) single versus multipollutant effects, (3) local or pooled estimates, and (4) chronic effects. The estimates of mortality ranged from 96-374 annual deaths, while admissions ranged from 139-607 respiratory and 479-2000 cardiovascular admissions. Chronic fine particle exposure resulted in 232 annual deaths. Conclusions: First, there should be an effort to reach a consensus on reporting scientific findings from air pollution studies using standardized study designs and reporting formats. Second, given the sensitivity of the estimates to underlying assumptions, an immediate need exists for widely accepted burden of illness and mortality estimation conventions. Third, many areas of air pollution research require considerable refinement before complete estimates can be ascribed.

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INTRODUCTION

Adverse health outcomes due to exposure to ambient air pollution exposure are a major public health issue. Assessing and quantifying these impacts, however, requires the application of estimations and uncertainties. By conducting an intensive analysis within one study location, we aim to illustrate the sensitivity of health effect estimates to a wide range of possible assumptions.

Specifically, we estimate mortality and morbidity associated with ambient air pollution exposure in Hamilton, Canada. Currently, Hamilton has some of the highest ambient air pollution in Canada, exceeding government objectives on about 20 days per year. The reasons for these high exposures include the following: (1) proximity to the Ohio River Valley, where coal-fired generating stations emit pollutants that travel hundreds of kilometres to Hamilton; (2) the Nanticoke coal-fired generating station located on the northern shore of Lake Erie, which also contributes considerably to local pollution; (3) increasing transportation emissions that result from automobile and truck traffic in and around the city; (4) local point source emissions from one of the largest industrial areas in Canada; and (5) topographic and meteorological conditions that often keep the pollution close to ground level (Jerrett et al., 2001; HAQI, 1997). All of these factors elevate ambient air pollution exposures and make the issue of health effects particularly important in Hamilton, thus making this a good location to assess the uncertainties in health effects assessments.

Clean Air Hamilton (CAH), a multi-stakeholder group tasked with advising Hamilton City Council on air pollution policy, requested an update on estimates of mortality and morbidity attributable to air pollution in the City previously prepared by Pengelly et al. (1997). The updated findings were calculated using the most recent research and data available at the time. Quantitative information from this new assessment can help local decision-makers to understand the size of the health effects from air pollution and to take action to improve population health in Hamilton. This paper summarizes our findings from this update, but more broadly gives policymakers elsewhere an appreciation of the challenges that underlie the estimation of mortality and morbidity attributable to air pollution exposure.

METHODS

Overview

To promote comparison with the Pengelly work, we followed a similar methodology. The methodology used in this paper followed a series of four sequential steps: (1) Identification of pollutants of interest through consultation with local officials and the scientific literature; (2) review of published results to identify risk coefficients for specific pollutants and conversion into comparable values; and (3) acquisition of relevant air quality and health outcome data; (4) estimation of the burden of illness. After completion of the basic burden calculations, we completed extensive sensitivity analyses, which are detailed below.

Identification of Pollutants of Interest

Based on consultations with the Health and Environmental Impacts Working Group for Clean Air Hamilton (CAH), we utilized the criteria pollutants that were indicated in the Hamilton-Wentworth Air Quality Initiative (HAQI) report in 1997. Specifically, we included particulate matter (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3). Pengelly et al. (1997) also applied this methodology to Toronto data in 2000 (i.e., using the same pollutants except for the air toxics). In addition, we estimated the mortality attributable to fine particles (i.e., $PM_{2.5}$) because these have received increasing attention in the scholarly literature as particularly harmful to pulmonary function (Pope, 2000).

Literature Review

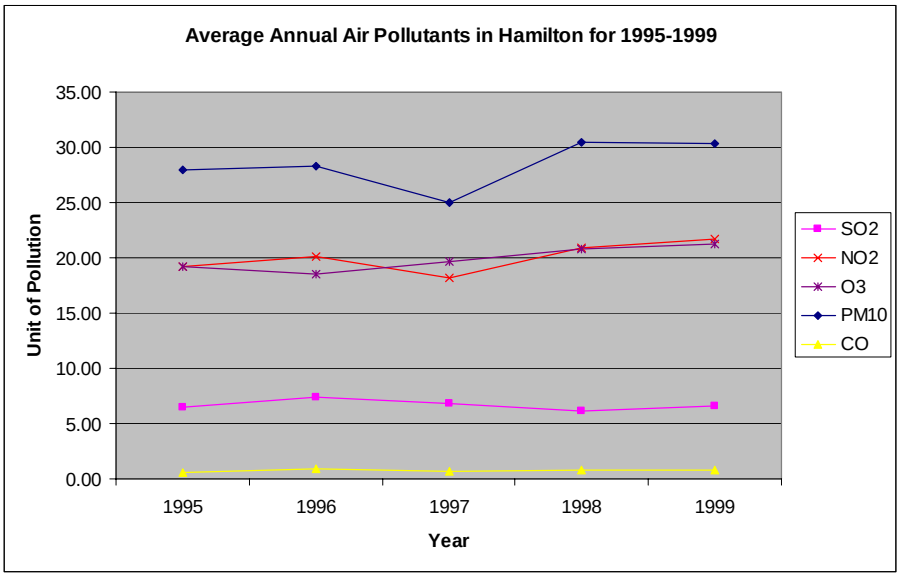
We conducted our literature review using the Medline and PubMed search engines. We searched combinations of the words "air pollution" with the following keywords – mortality, morbidity, health effects, time-series – for articles dated 1997 and onwards, until the beginning of October, 2001. Using Medline, 2067 related articles were identified, while the search in PubMed revealed about 6900 articles.

Subsequent review and selection of the articles was based on relevance, suitability of outcome measure, and significance of findings. We excluded articles that were not related to mortality or hospital admissions; those that focused on indoor air pollutants and tobacco smoke; those in languages other than English or French; and those that specifically identified elderly or infants as study groups. Articles that made use of multipollutant models were given priority to provide maximum control for co-pollutants. While findings from single pollutant models and significant associations with the elderly population were present and included in the literature review, they were not included in the average calculations. Studies including random effects and meta-analysis of previous studies as a comparative metric were selected. Research that used Hamilton estimates in particular was emphasized.

Chronic studies were also included in this analysis. Based on the limited number available, this literature review included a search as far back until 1993 when the earlier chronic effect literature was published. Recent reanalyses of these articles were included in the literature review. Additionally, the literature review was updated based on the recent discoveries of previously undetected problems in the statistical software used to apply generalized additive models (GAM) in time-series studies (Ramsey et al., 2003).

Air Quality Data

Annual averages for the identified pollutants were available for multiple locations in Hamilton, courtesy of the Ministry of Environment's monitoring network. Regional arithmetic averages from all the available stations were calculated to derive the city-wide average. Figure 1 illustrates the general trends in ambient pollution for the period 1995-99.



Note: SO_2, NO_2, and O_3 expressed in parts per billion (ppb), CO expressed in parts per million (ppm) and PM_{10} expressed in $\mu g/m^3$

Figure 1. Change of average annual air pollutants in Hamilton, 1995-1999.

Health Outcome Data

Annual morbidity and mortality data for Hamilton were supplied by the Central West Health Planning Information Network. The data were extracted from the Ontario "data warehouse," available through the Government of Ontario Network (GONET). The ICD-9 codes used were those indicated by the Pengelly studies, covering the area of the City of Hamilton. Complete mortality data sets were only available for 1995 to 1997, while hospital admissions data were available for a longer period (i.e., 1995 to 1999).

We observed a marked increase in the number of hospital admissions, especially for cardio-vascular (CV) admissions, between 1995 and 1996 (Table 1). We checked the acquired data for internal errors, but the difference seems to be due to other factors not reported by the Ministry of Health.

Table 1. Mortality and morbidity data for Hamilton used in the analysis.

	Non-traumatic mortality			**Morbidity**			
	All	CV	Resp	All	CV	CHF	Resp
1995	3,730	1,445	370	39,854	5,612	814	2,249
1996	3,694	1,422	367	41,149	7,702	1,123	3,085
1997	3,868	1,419	353	39,420	7,468	1,176	2,738
1998				40,044	7,322	1,108	3,266
1999				39,993	7,572	1,031	3,330
Average	3,764	1,429	363	40,092	7,135	1,050	2,934

NT= non-traumatic, CV = cardiovascular, CHF = congestive heart failure, Resp = respiratory

Estimating the Mortality and Hospital Admissions Associated with Air Pollution

Following the methodology set by the Pengelly et al. (1997 and 2000), we computed the relationship to estimate health outcomes as follows:

$$HO = B * \Delta H\% * P$$

where:

HO = annual health outcome
B = base number of outcomes per year
ΔH% = percent change in health outcome per unit increase of pollutant
P = annual pollution average

Similar methods have been used by Kunzli et al. (2000) and Mindel and Joffe (2004).

Example Calculation

The following data were utilized to calculate the premature mortality attributable to particulates (PM_{10}) for the year 1995:

- Total non-traumatic deaths in Hamilton for 1995 = 3730 deaths per year
- Percent increase in non-traumatic mortality for PM_{10}, averaged from literature values, per unit increase = 0.076 increase in deaths per 1 $\mu g/m^3$ increase in PM_{10} * 1/100
- Annual average of PM_{10} for Hamilton for 1995 = 27.9 $\mu g/m^3$

$$HO = 3730 \frac{deaths}{year} \times 0.076 \frac{deaths}{\mu g/m^3} \text{ per } 100 \text{ deaths} \times 27.9\ \mu g/m^3 = 79.09 \frac{deaths}{year}$$

The sample equation shows that the units cancel each other out to leave deaths per year as the final unit of analysis. Thus, following normal rounding rules, 79 premature deaths are associated with an increase of 10 $\mu g/m^3$ PM_{10} exposure in Hamilton for the year 1995.

Estimate Adjustments

Three adjustments were conducted on the original estimates based on the literature review and methods outlined above. The first involves a recent discovery of a statistical limitation in one of the software packages used in time-series analyses. The second adjustment pertains to an achievable baseline pollution estimate. The third adjustment was the application of both of the previous adjustments.

The time-series studies summarized in this paper typically have used GAM in their statistical analysis, as these models allow for control of time-varying factors through the incorporation of non-parametric smoothers of weather and other confounders. The findings from these studies are now in question due to recent research identifying a programming limitation in the statistical software used in these analyses (Ramsey et al., 2003). The statistical software provided biased risk estimates because it neither adequately accounted for concurvity nor assured convergence of its iterative estimation procedure. The Health Effects Institute's (HEI) Special Report summarized the reanalysed findings of 21 time-series analyses that were conducted using GAM models, and concluded that changes in estimates varied between less than 10% to above 40% (HEI, 2003). The reanalysis of the National Morbidity, Mortality and Air Pollution Study (NMMAPS) data, one of the largest pooled data sets in the U.S., revealed that the risk estimates have been overestimated by 36 - 42% (Dominici et al., 2002). These reanalyses showed that positive associations still exist, although in some cases they become insignificant.

Adjustments were made on the summarized findings of the average dose-response estimates in this paper. The values were adjusted to account for the maximum overestimation of 42%. This model is referred to as the "adjusted" model. We have also utilized recently published random effect estimates derived from meta-analyses (Stieb et al., 2003) overestimates resulting from the GAM estimation problems.

The second adjustment considers that in calculating risk estimates, the impacts are often sensitive to the range of values chosen to estimate population exposure. The World Health Organization (WHO) suggests that this sensitivity be quantified by conducting the analysis of health impacts under various exposure levels (WHO, 2001). The choice of range to use depends on realistic policy options, and can include theoretical zero concentrations, non-zero 'acceptable' levels, and up to concentrations determined by air quality standards. Estimates are often calculated in terms of comparison to the zero pollution level, which is considered to be unattainable and overly idealistic. We chose a more achievable estimate of a baseline of 20% of current pollution concentrations to emphasize this sensitivity. A separate estimate was calculated using annual pollution values of the mean minus the lower quintile, based on daily averages. These were calculated for 1997 to provide a comparison estimate. This adjustment is referred to as "baseline 20% model." Calculation of this 20% estimate required additional compilation of daily pollution data for a representative year (1997) to assess those in the lowest quintile.

Hamilton-specific Estimates

We also calculated estimates of studies conducted in Hamilton, using the research of Burnett et al. (1998a) for gaseous air pollutants and Jerrett et al. (2003) for the particulate metric, measured with the coefficient of haze (CoH). For these estimates, multipollutant models were used for the gaseous air pollutants, while single pollutant models were available for the particulate measures. The percent risks at the mean value for relevant years were computed.[2]

[2] Because the Poisson regression takes a log-linear form, we computed the risk estimates for each criteria pollutant as follows:

$$e^{(\beta \bar{x})}$$

where: e is the exponential function, β is the regression coefficient estimating the average increase in mortality associated with a unit increase in pollution, and $\bar{x}$ is the average of the air pollutant.

Random Effects Estimates

We also attempted to estimate pooled effects with a random effects model (Dersimonian and Laird, 1984). The relative risks (RR's) were extracted from the articles and reported as change in mortality/morbidity associated with an increase of 10 units of pollutant (except for CO, which was calculated per 1 unit for pollutant). Standard errors, 95% confidence intervals or t-ratios of the regression parameters were also extracted when available. As differences exist in reporting methods between authors, the same data was not present in every paper. Thus conversions between RR's and regression coefficients, and 95% confidence intervals and standard errors were applied to have comparable value formats.

The following two equations were used where required:
1. $RR = e^{(\Delta conc \times \beta)}$
2. $95\%\ CI = e^{[\Delta conc \times (\beta +/- 1.96 \times SE)]}$

where:
Δ conc = change in concentration of pollutant
CI = confidence interval
SE = standard error associated with estimate

RESULTS

Results of the Literature Review

A narrative and summary of our findings from this search is presented in Appendix 1. While single pollutant analyses are included in our commentary, they were not included in the calculations for final estimates. The detailed tables containing the literature review results are presented in Appendix 2. The tables include the study location, the modeled pollutants and the key results in a standardized format.

Results of Estimated and Adjusted Calculations

To calculate the final averages of the risk estimates from the literature, only multipollutant models were used. A simple averaging method for correlation studies was used to compute the overall effect from the literature (see Wolf, 1986). As well, the low and high ends of the findings are noted, as there are considerable differences in estimates of dose-response. Adjusted values were applied to the mean values. Recent pooled random effect estimates (Stieb et al., 2003) and estimates from chronic studies (Pope et al., 2002) were also included.

Notation in the following tables includes 'P1997' as the original HAQI report, Pengelly et al. (1997); 'P2000' as the City of Toronto report, Pengelly et al. (2000); 'CAH' as the current reanalysis of HAQI conducted for Clean Air Hamilton; 'Adjusted' as the current results with adjustment of 42% overestimate; 'M-min' (mean minus minimum 20%) represents the baseline 20% model; and 'M-min adj' indicates the baseline model adjusted for the 42% overestimate.

Relatively wide ranges can be observed within the estimated percent changes from increases in pollutants (Table 2). For a 10 $\mu g/m^3$ increase in PM_{10}, there was an increase ranging from 0.43% to 1.07% in non-traumatic deaths; 0.7-3.5% for respiratory admissions; and 0.5-2.3% in cardiovascular admissions. In the case of SO_2, the increase per 10 ppb resulted in a range of 0.84-3.89% increase in mortality; 1.3-6.1% for respiratory admissions; and 0.2-2.1% in cardiovascular admissions. The other pollutants follow similar ranges, with the higher ranges existing for morbidity results and lower ranges in mortality estimates. Adjusted mean values were slightly higher than the low end of the estimates, except for the association between O_3 and non-traumatic mortality.

Table 3 compares the average values for the risk estimates found in the literature after 1997 with the literature findings from the two previous studies and the adjusted values. This identifies the trends in literature values for the estimates. Current estimates were consistently higher than the 1997 estimates, except for PM_{10} estimates for non-

traumatic mortality and CO estimates for cardiovascular admissions. Adjusted values were lower than initial estimates for PM_{10} and O_3, but higher for SO_2, NO_2, and CO.

Table 2. Summary of percent changes per 10 units of pollutant: low, mean, high, and 42% adjusted mean estimates of calculated values.

Pollutant	NT mortality[a] (change per 10 units pollutant) range of estimates				Respiratory admissions[b] (change per 10 units pollutant) range of estimates				CV admissions[b] (change per 10 units pollutant) range of estimates			
	low	mean	high	adj mean	low	mean	high	adj mean	low	mean	high	adj mean
PM_{10} ($\mu g/m^3$)	0.43	0.76	1.07	0.44	0.7	2.1	3.5	1.22	0.5	1.4	2.3	0.8
$PM_{2.5}$(μ/m^3)	1.68	2.88	4.46	1.67								
SO_2 (ppb)	0.84	2	3.89	1.16	1.3	3.7	6.1	2.15	0.2	1.1	2.1	0.6
NO_2 (ppb)	1.5	1.9	2.3	1.10	1	4.9	9	2.84	4.4	6.55	8.7	3.8
CO (1 ppm)	2	3.68	4.95	2.13					0.4	1.95	2.5	1.1
O_3 (ppb)	0.94	1.38	1.7	0.80	1.5	2.8	4.9	1.62	1.6	4.5	7.5	2.6

NT= Non-traumatic; CV = cardiovascular;
[a] = Mortality values were calculated on the basis of 2 or 3 estimates
[b] = Morbidity values were calculated on the basis of 1 or 2 estimates; in the case of one estimate, 95% confidence intervals were used as the low and high range of estimates
adj mean = Mean estimate adjusted for 42% overestimate
Note: Because the ranges of data vary among pollutants, the 10-unit change is not directly comparable as a metric of severity in effects. For pollutants with a smaller range such as CO, a 10-unit change is proportionately larger than for PM_{10}, which has a larger range.

Table 3. Summary of percent changes per 10 units of pollutant, comparing average estimates of studies, adjusted and pooled estimates.

Pollutant	NT mortality (change per 10 units pollutant) average of estimates					Respiratory admissions (change per 10 units pollutant) average of estimates				CV admissions (change per 10 units pollutant) average of estimates			
	P1997	P2000	CAH	Adj	Pooled	P1997	P2000	CAH	Adj	P1997	P2000	CAH	Adj
PM_{10}	1	0.8	0.76	0.46	0.32	0.7	1.7	2.1	0.99	0.6	2.3	1.4	1.3
$PM_{2.5}$			1.9	1.10									
SO_2	0.6	2.25	2	1.16	0.85	0.4	2.76	3.7	1.60			1.1	0.0
NO_2	1.15	1.19	1.9	1.10	0.2	0.4	2.49	4.9	1.44		3.9	6.55	2.3
CO	1.1	3.48	3.68	2.13	0					5	6	1.95	3.5
O_3	0.3	0.4	1.38	0.80	0.3	0.8	1.1	2.8	0.64		4.52	4.5	2.6

Pooled = Pooled random effect model estimates (Stieb et al., 2003)
Adj = Mean CAH estimate adjusted for 42% overestimate

Table 4 presents the calculated mortality and morbidity estimates as incidences per year, using low, mean, high and adjusted risk estimates. Values ranged as in Table 2. Totals for all pollutants ranged from 248 to 567 annual deaths (using PM_{10} as a particulate estimate), to between 236 to 1252 respiratory and 993 to 3036 cardiovascular deaths. Adjusted mean totals were higher than the lower end estimates for all total counts.

Table 4. Summary of low, mean, high, and adjusted mean in the mortality and morbidity counts averaged for available years in current study.

Pollutant	NT mortality (incidences/year) calculated estimates				Respiratory admissions (incidences/year) calculated estimates				CV admissions (incidences/year) calculated estimates			
	low	mean	high	adj mean	low	mean	high	adj mean	low	mean	high	adj mean
PM_{10}	44	77	109	45	59	176	293	102	101	284	466	165
$PM_{2.5}$	108	185	286	107								
SO_2	22	51	100	30	30	72	140	42	10	52	100	30
NO_2	108	137	166	79	59	290	532	168	629	937	1244	543
CO	6	10	14	6					26	126	162	73
O_3	68	119	178	69	88	164	287	95	227	638	1064	370
Total	248	394	567	229	236	702	1252	407	993	2037	3036	1181
Total *	312	502	744	291								

* = total has been calculated with $PM_{2.5}$ instead of PM_{10}

Table 5 compares the estimates taken from the three studies and adjusted values, calculated on current air quality and health outcome data. Detailed calculations for these estimates can be found in Appendix 3. This table shows the differences in estimated mortality and morbidity counts according to the respective study values. The adjusted estimate is lower than any of the studies for mortality, at 229 annual deaths, but higher than the initial Pengelly study for morbidity at 407 annual respiratory and 1239 cardiovascular admissions.

Table 5. Summary and comparison of the mortality and morbidity counts using the average dose-response calculated in the three studies with adjusted values, applied to current Hamilton data.

Pollutant	NT mortality (average incidences/year) average of estimates				Respiratory admissions (incidences/year) average of estimates				CV admissions (incidences/year) average of estimates			
	P1997	P2000	CAH	Adjusted	P1997	P2000	CAH	Adjusted	P1997	P2000	CAH	Adjusted
PM_{10}	102	81	77	45	59	142	176	102	122	466	384	223
SO_2	15	58	51	30	22	81	72	42		629	52	30
NO_2	83	86	137	79	24	147	290	168	135	338	937	543
CO	3	10	10	6					20	50	126	73
O_3	97	29	119	69	53	66	164	95		641	638	370
Total	300	264	394	229	158	436	702	407	277	2124	2137	1239

Table 6 compares the original study, the current study, adjusted risk estimate values, baseline 20% adjustments, and application of both adjustments, all calculated for 1997 values. As the values show, there is a substantial difference in total mortality and morbidity counts, depending on the assumptions underlying the calculations. Our most conservative estimate, the application of both the 42% adjustment and the baseline 20% model, estimated 96 deaths in 1997 due to PM_{10}, compared to HAQI initial estimate of 298, our initial estimate of 374, and 217 deaths if the GAM discrepancy is taken into consideration. For respiratory admissions, the most conservative estimate is only a few admissions lower than HAQI estimates (139 compared to 144, respectively), while the highest estimate stands at 607 admissions. The highest estimate for cardiovascular admissions is our initial estimate of 2000 admissions, while the most conservative estimate is 479 admissions, still higher than the 257 admissions estimated by HAQI in 1997.

Table 6. Summary of the mortality and morbidity counts using the average dose-response in HAQI, CAH and both adjustments; applied to 1997 Hamilton data.

Pollutant	NT mortality (average incidences/year) average of estimates					Respiratory admissions (incidences/year) average of estimates					CV admissions (incidences/year) average of estimates				
	P1997	CAH	Adj	M-min	M-min adj	P1997	CAH	Adj	M-min	M-min adj	P1997	CAH	Adj	M-Min	M-Min adj
PM_{10}	97	73	43	24	14	48	144	83	46	27	112	280	157	84	49
SO_2	16	53	31	27	16	28	69	40	35	20		56	31	45	26
NO_2	81	134	78	46	27	20	244	142	83	48	125	888	497	303	176
CO	3	10	6	6	3						20	118	66	65	38
O_3	102	105	61	62	36	48	150	87	75	44		659	369	329	191
Total	298	374	217	119	96	144	607	352	239	139	257	2000	1120	826	479

M-min = Mean minus the minimum 20% (baseline 20% model). M-min adj = Adjusted value of M-min, for overestimate of 42%

Results of Hamilton-Specific Estimates

Hamilton-specific estimates revealed that, for NO_2 and CO, the values were comparable to the lower ranges of the literature estimates. For SO_2, estimates were slightly higher than the mean count from literature estimates, and Hamilton-specific O_3 estimates were at the higher end of the calculations (Table 7). Because the CoH estimate was derived from a non-GAM model, adjustments were not applied. For the remaining Hamilton-specific estimates, applying the adjustments brought their values closer to the mean of the literature estimates; however, the totals were not directly comparable to the remaining calculations because of the CoH component.

Table 8 summarizes all available calculations performed for non-traumatic mortality estimates.

Table 7. Comparison of the range of mortality counts using current estimates with averaged Hamilton-specific estimates and adjustments.

Pollutant	NT mortality (incidences/year) range in estimates						
	low	mean	high	Hamilton	Adj	$M\text{-}min_{1997}$	M-min adj
PM_{10}	44	77	109				
CoH				256	256	256	256
SO_2	22	51	100	73	42	37	21
NO_2	108	137	166	108	63	45	26
CO	6	10	14	5	3	4	2
O_3	68	119	122	122	71	81	47
Total	248	394	511	564	435	423	352

CoH= coefficient of haze (estimated from Jerrett (2003), using a non-GAM based model).

Table 8. Summary and comparison of mortality counts estimated for all available models, based on 1997 Hamilton pollution values.

Pollutant	NT mortality (average incidences/year) average of estimates								
	P1997	CAH	Adj	M-min	M-min adj	Pooled	Hamilton	Chronic	Chronic (M-min)
PM_{10}	97	73	43	24	14	31			
$PM_{2.5}$		110	64					348	140
CoH							256		
SO_2	16	53	31	27	16	22	73		
NO_2	81	134	78	46	27	14	108		
CO	3	10	6	6	3	0	5		
O_3	102	105	61	62	36	23	122		
Total	298	374	217	119	96	90		348	140
Total **		411	238				564		

Pooled = Pooled random effect model estimates (Stieb et al., 2003)
Hamilton = Hamilton-specific dose-response estimates
Chronic = Estimates based on chronic exposures to fine particulates (Pope et al., 2002)
CoH= Coefficient of haze (estimated from Jerrett (2003), using a non-GAM based model)
Total ** = Totals calculated with $PM_{2.5}$ or CoH as particulate measure

Results of Random Effects Models

Because there were no pooled estimates of morbidity analogous to the Stieb et al. (2003) article, we attempted to apply a random effects model to morbidity studies. In adhering to the constraints set in our literature review, with the emphasis placed on multipollutant models, we were only able to include two to three estimates per pollutant and outcome category. A random effects model was applied to outcomes with three estimates. The model reached convergence for only one of the pollutants (PM_{10} mortality), and this was run for estimates conducted before GAM adjustments. The model applied to morbidity estimates did not reach convergence, probably due to the small number of estimates and variability between them.

We also attempted to run the random effects model to include both respiratory and cardiovascular admissions to increase the number of estimates per category. These models reached convergence and had significant parameters. When calculating attributable morbidity, using 1997 data as the tables above, the results were comparable for PM_{10}, 28% lower for NO_2 and 21% lower for O_3 (Table 9).

Table 9. Comparison of combined morbidity counts estimated for initial and random effects models, based on 1997 Hamilton pollution values.

Pollutant	Combined morbidity (average incidences/year) average of estimates				Pooled RE estimates for combined morbidity (average incidences/year) average of estimates			
	CAH	Adj	M-Min	M-Min adj	CAH	Adj	M-min	M-min adj
PM_{10}	424	240	130	75	434	252	126	73
SO_2	125	71	80	46				
NO_2	1132	639	386	224	886	514	277	161
CO	118	66	65	38				
O_3	809	456	404	234	548	318	319	185

Combined morbidity = Respiratory and cardiovascular morbidity estimates. RE = Random effects model

DISCUSSION

This study has estimated mortality and hospital admissions associated with ambient air pollution in Hamilton, a mid-sized industrial city at the western tip of Lake Ontario. Dose-response relationships were derived based on exposure estimates published in the peer-reviewed literature. These estimates were applied to recent air pollution and health outcomes data available through routinely-gathered governmental sources.

Recent scientific discoveries identified software limitations in the GAM models used in time-series modeling. Applying the adjustments to account for a 42% overestimate lowered the average annual mortality rate to 229 from 394, respiratory admissions to 407 from 702, and cardiovascular admissions to 1181 incidences from 2137.

If further assumptions are taken into account by using the baseline 20% model of 1997 pollution values, annual mortality rates drop to 119 from 374, respiratory admissions to 239 from 607, cardiovascular admissions to 826 from 2000. Applying the 42% adjustment to these values revealed even lower mortality counts of 96 from 374, respiratory admissions at 139 from 607, and cardiovascular admissions at 479 from 2000. Similar baseline model adjustments and scenarios have been researched by Mindell and Joffe (2004). Differences in predicted premature deaths were estimated by applying four different theoretical models for pollution reduction in Westminster, England. Reductions to annual mean PM_{10} objectives to 24-hour PM_{10} objectives (current and 2009) as well as the effects of reducing PM_{10} to a zero-pollution level were considered. Adjustments to baseline pollution levels are important examples in emphasizing to policy-makers the sensitivities and uncertainties involved in the estimation of air pollution related health effects.

The Hamilton-specific estimates resulted in 352 annual deaths. This revealed that the total estimates of non-traumatic mortality were initially at the higher end of the range found in our literature review. With the adjustments, the values remained elevated but were not directly comparable to our other estimates due to differences in the particle metrics.

Pooled random effects model estimates from Stieb et al. (2003) resulted in 90 deaths, comparable to the 96 estimated by applying both GAM model and baseline 20% adjustments. Random effects models combining cardiovascular and respiratory morbidity estimates were also derived. These estimates revealed findings comparable for particulates, but lower than adjusted findings for the gaseous pollutants. The Dominici et al. (2002) and Stieb et al. (2003) GAM-adjusted findings were included in our mortality estimates for comparative purposes to cover the available range of model estimates. In future research, we will include the HEI (HEI, 2003) findings by incorporating updated morbidity and mortality estimates. Similar applications of random effects model estimates in calculating summaries for the effects of O_3 on a range of health outcomes have been utilized by the WHO (2003).

Chronic estimates of $PM_{2.5}$-related mortality produced an estimate of 348 deaths, and 110 using the baseline 20% adjustment. Both these values were higher than the adjusted acute-exposures summed for all other pollutants, despite being estimated for a single pollutant. Kunzli et al. (2001) have noted the likely pathways toward mortality burden from air pollution. Long-term exposure may contribute to the development of chronic disease that may occur through complex inflammatory and oxidative pathways over many years, such as the formation of atherosclerosis (Kunzli et al., 2004). Others work through the acute mechanisms, which may be more severe in susceptible individuals, who have underlying conditions that may or may not have been attributable to air pollution health effects. Thus the observation of chronic mortality effects probably represents both types of chronic and acute effects, some operating over many years and potentially leading to chronic conditions such as IHD or lung cancer, while others prey upon susceptible individuals with diseases such as diabetes. Thus, the larger chronic estimates reported here fit within the expected physiopathology of expected health effects.

Chronic estimates based on cohort studies are considered to be the “gold standard” for assessing health effects related to air pollution, due to their ability to assess life expectancy and incidence, course and remission of disease (Kunzli and Tager, 2000). The cohort study design provides the most accurate and comprehensive estimates of true health impacts as well as average reductions in lifespan due to pollution exposure. Thus, it captures the effects from both short-term and long-term outcomes, resulting in larger estimates (WHO, 2001). While researchers agree that time-series and cohort studies are methodologically different approaches for addressing the health effects of

exposure to pollution, disagreement still exists on how the results can best be used for estimations of total health burdens.

McMichael et al. (1998) suggest that time-series analyses are often inappropriately used to estimate longer-term effects. The time-series analyses report results of short-term exposures of individuals, not for sustained periods of exposure. Thus, the calculation of annual average mortality outcomes based on regression coefficients from the acute studies is criticized. The reason for this criticism stems from the notion that some of the deaths, while premature, may have occurred during the same year regardless of pollution exposure. This short-term displacement of deaths is also known as the harvesting effect. Following this reasoning, annual mortality may be overestimated due to the use of short-term estimates.

On the other hand, other researchers (Schwartz, 2000, 2001; Zeger et al., 1999), investigating the effect of harvesting on mortality estimates, found that time-series analyses often underestimate the exposure effect because the time lag usually employed did not account for effects occurring more than a few days after exposure. Kunzli et al. (2001) agree that time-series analyses underestimate the mortality attributable to air pollution exposure and that the results from cohort studies should be used instead. The WHO also maintains that time-series results are robust, both in terms of potential confounders and measurement error in exposure classification, and are able to provide estimates of premature mortality due to some recent exposure (WHO, 1996). Nevertheless, the time-series method still does not result in an accurate quantification of deaths due to air pollution exposure, and likely underestimates the total effects of air pollution (WHO, 2001, 2003). Thus, we caution that when interpreting results from our study (and similar studies), these limitations should be considered.

In our calculations, we did not include studies that concentrated on specific susceptible populations groups, nor did we attempt to incorporate inequalities in health. In Canada, we have evidence suggesting that persons with pre-existing conditions, such as diabetes (Goldberg et al., 2000) and persons of lower educational attainment may be more susceptible to the acute effects of ambient air pollution exposure (Jerrett et al., 2004). Estimates from different zones in Hamilton revealed effect modification by neighbourhood educational status and manufacturing employment. When these zonal estimates were pooled, however, the effects of the pooled model equalled those of a city-wide estimate (Jerrett et al., 2004). This may suggest that these effect modifiers have scale dependencies that negate the influence of susceptible populations in health effects assessments conducted at city-wide scales. For the estimates in this paper, we have assumed homogeneous susceptibilities across different strata of the population. Further research is needed to assess these heterogeneities in survival experience as they relate to air pollution exposure (Burnett et al., 2003).

A caveat is required with respect to the totals calculated in this paper and other similar efforts. They should be interpreted as general aids to decision-making rather than exact counts of death and illness. Researchers are often cautioned to avoid adding estimates of individual pollutants derived from single-pollutant models (WHO, 2001). If specific pollutants are not correlated, then adding single-pollutant effects may be justified; however, this must be done cautiously as pollutants often act in synergistic or antagonistic manners. As numbers of pollutants studied in multipollutant models increase, the estimates may become unstable due to collinearity (Samet et al., 1997).

Although we used multipollutant models to derive estimates, we used significant findings from estimates where collinearity between pollutants was accounted for. Some models, however, did not control for all criteria pollutants simultaneously. The uncontrolled confounding of co-pollutants may also influence the totals. In addition, each study may contain estimation error that is not accounted for in our simple averages of effect. Therefore, our totalled mortality estimates could exceed the actual number of deaths associated with air pollution and should be viewed with caution. Despite the limitations discussed, we summed the estimated effects to provide a direct comparison with the original Pengelly et al. (1997) document.

For an appreciation of the size of the uncertainties associated with the concept of summing estimates, we chose to separately assess several markers of independent aspects of the air pollution mixture. SO_2 can serve as a marker for localized industrial pollution, while NO_2 and CO are markers for traffic (Fenger, 1999). $PM_{2.5}$ accounts for long-range transportation and secondary sulfates from power plants (Brook et al., 2004; Burnett et al., 1997), while O_3 represents regional effects and reflect increases in the secondary photochemical pollution mixture (Bell et al., 2004).

Localized industrial pollution would then contribute 16 out of the 96 estimated total deaths, traffic indicators would result in 30 deaths, long range transportation would result in 22 deaths and the marker for secondary regional effects would produce approximately 36 deaths. Similar patterns were observed for respiratory and cardiovascular admissions. Thus, by estimating the separate markers, it appears that the largest contribution to adverse health outcomes is due to regional pollution effects, namely ozone exposure.

An alternative estimation would be to not sum pollutants that are known to be more correlated than others. Both O_3 and SO_2 (Bell et al., 2004; Katsouyanni et al., 2001; Gauderman et al. 2004) have been shown to be relatively uncorrelated with particulate matter, while NO_2 and CO have been identified as potential confounders due to high correlations (Burnett et al., 1997; Sarnat et al., 2001). This would indicate that perhaps effects of O_3, SO_2 and PM_{10} could be summed as they do not confound each other, but summing CO and NO_2 would be inappropriate. If we were to use our most conservative estimates, this would lead to 66 deaths, 91 respiratory admissions and 266 cardio-vascular admissions, compared to 96, 139 and 479 respectively, an average 37% decrease in total health estimates. These two applications again show the sensitivity of assessing health outcomes relating to the complex mix of pollutions in ambient air pollution exposure.

While we have adjusted for the GAM problem, which was a major statistical discovery that left scientists and policymakers questioning the magnitude of associations between acute exposures to air pollution and health, some continued uncertainty remains. Many time-series studies employed this method in their analysis, leading to many research groups reanalyzing their data in light of the new findings (e.g. Atkinson, 2004; Dominici et al., 2002). Reanalysis of both multi-city and single-city studies revealed that for the majority, the health effects of air pollution were still significant, but that the effects were slightly to substantially smaller. The WHO reported that an unpublished meta-analysis at the St. George Medical School (England) of 26 studies not using the GAM in their analysis averaged an increase of 0.4% per 10 $\mu g/m^3$ of PM_{10} (WHO, 2003). This was similar to both the lower end of our range of estimates (0.43%), and to our adjusted mean calculation (0.44%). This supports the use of our adjustment of the 42% decrease in observed effect (Dominici et al., 2002) to highlight the potential uncertainties that exist within the air pollution and health research. The close correspondence of our estimates with the new meta-analysis study by Stieb et al. (2003) lends further support to the validity of the 42% adjustment.

Another source of uncertainty is the "file drawer" problem, otherwise known as publication bias. Published research generally favours significant findings, while insignificant findings are rarely reported, leading to overestimates in the air pollution effect (Levy et al. 2000; WHO, 2004). While publication bias is a common problem in the general research culture (Simes, 1986; Begg and Berlin, 1989), it is only relatively recently being discussed specifically in the air pollution and health field (Anderson et al., 2002; Peacock et al., 2002). Since our study relies on published articles, there may be a bias in favour of positive findings and consequently inflated estimates.

Other considerations suggest our study may underestimate the total burden of illness due to air pollution in Hamilton. Our estimates only include mortality and acute health effects from air pollution. Other important health effects such as the development and exacerbation of asthma (Tenias et al., 1998; Yu et al., 2000), reproductive abnormalities (Bobak and Leon, 1999; Wang et al., 1997), elevated cancer rates (Beeson et al., 1998; Cohen, 2000) and less serious respiratory conditions such as infectious respiratory diseases (Kim et al., 1996) are excluded from this analysis.

As a final caveat, we emphasize that the different ways that the estimates were derived, calculated and discussed were to document and highlight the sensitivities and sources of uncertainty that exist in assessing air pollution health effects. While the literature review for our discussion is current, the original review for calculating the health effect estimates had to be limited to the end of 2001 with minor adjustments for later meta-analyses. These earlier estimates informed the policy process for air quality management in the City of Hamilton report. Thus, further updates would be needed to utilize this information for current policy making.

CONCLUSIONS

Four main points of concern arose from our research. First, there are no standardized methods for reporting the results from air pollution and health studies. This makes it difficult for individuals and groups working outside of academic structures to analyze the multitude of scientific findings. There are well-known limitations and difficulties

often associated with the interpretation of epidemiological studies (WHO, 1996, 2001). The necessity for thorough evaluation, accurate interpretation and appropriate presentation of uncertainties involved in impact estimates are especially highlighted. For example, the medical field utilizes the CONSORT (Consolidated Standards for Reporting Trials) statement to improve the quality of reporting results of a randomized control trial (Begg et al., 1996). This statement is a widely adopted requirement for medical journals such as JAMA, BMJ and The Lancet (Moher et al., 2001). While the WHO has developed a suggested protocol for conducting health impact assessments that calls for clear specifications and descriptions of purpose, approach, assumptions, methods, metrics and estimations, it does not specifically apply to reporting results (WHO, 2000). We recommend a standardized format for reporting of health effects that includes full disclosure of regression coefficients, standard errors, and significance tests. Such standardizations will ease the process of compiling and updating estimates.

Second, there are no widely accepted standards or conventions for dealing with important assumptions such as pollution baselines. In related fields such as economic and environmental accounting, conventions for dealing with normative issues have evolved through professional consensus (Jerrett et al., 1999). The calculations involved in estimating health effects attributable to air pollution can be compared to "health accounting" systems, where accepted conventions are utilized. To develop these conventions, accepted norms must be formalized to account for these uncertainties and limitations.

Third, a wide gap exists in the communication between scientists and policymakers. We repeatedly cautioned policymakers in Hamilton about the problem of summing estimates that may not have adequately controlled for co-pollutants. Yet the members of the CAH committee and policy representatives from the City emphasized the importance of "bottom line" estimates that could be used to inform the policy process and track ongoing progress. These differences can cause potentially complicated situations for users of scientific literature outside of the academic structure, such as policymakers and public health officials. Additionally, it indicates that much work remains in making scientific reporting formats more suitable and accessible to non-academic groups.

Fourth, we have learned that the over-reliance of scientific research on one method may result in situations similar to the GAM findings, in which results can change by as much as 42% literally overnight. While not all analyses of the acute effects of air pollution used this method, we feel that the impact was still significant enough to document as a source of uncertainty. In avoiding the dangers that exist in placing importance on one type of method or one type of estimate, we suggest that future studies should also incorporate a plurality of study research designs as well as methods, such as case control, cohort, ecologic and panel studies. Other gaps include the limited number of chronic effects studies, especially for morbidity, though this number is increasing both in European and North American contexts (e.g. Hoek et al., 2002; McConnell et al., 2002; Finkelstein et al., 2004; Nafstad et al., 2004).

Based on our analysis and experience with advising policymakers, we conclude with three suggestions for future research. First, there should be an effort to reach a consensus to report scientific findings using standardized or comparable methods. Second, given the sensitivity of the estimates to underlying assumptions, an immediate need exists for widely accepted health accounting conventions, particularly related to the baseline pollution level. Third, many areas of air pollution research require considerable work before complete estimates can be ascribed. Priority areas include studies on the chronic health effects of air pollution, multipollutant studies, and on health outcomes that are likely to have large population health impacts.

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APPENDIX I

Carbon Monoxide (CO)

Non-traumatic mortality

Three studies have found significant associations between CO and non-traumatic mortality since the HAQI study in 1997. Burnett et al. (1998a, 1998b) and Gywnn et al. (2000) found an increase of 4.7%, 2.0%, and 4.13% per 1 ppm increase, respectively. The studies all used multipollutant models.

Respiratory hospital admissions

None of the literature reported significant associations between respiratory hospital admissions and CO.

Cardiac hospital admissions

CO was related to cardiac hospital admissions, specifically for hospitalization for congestive heart failure. Schwartz (1997) examined data for Tucson, US, and reported an increase of 1.4% in admissions per 1 ppm increase. Burnett et al. (1997c) calculated congestive heart failure admissions specifically for Hamilton and reported a 2.5% increase. Interestingly, the Toronto-specific estimate by the same researchers was comparatively higher at 6%.

Sulfur Dioxide (SO_2)

Non-traumatic mortality

Recent research shows a range of dose-response estimates for sulfur dioxide and total non-traumatic mortality. Garcia-Aymerich et al. (2000) found that in Barcelona, Spain, a 10 ppb increase in SO_2 led to a 4.2% increase in total mortality. Saez et al. (2001) found a 1.1% increase for three Spanish cities using a multipollutant model. In Madrid, Spain, Diaz et al. (1999) found a 2.1% increase in non-traumatic mortality with a single pollutant model. Taking 12 European countries into account, Katsouyanni et al. (1997) found an increase of 1.1%. Kelsall et al. (1997) considered a multipollutant model for Philadelphia, US, and found a 0.84% relative increase to the 10 ppm increase. Burnett et al. (1998a) studied SO_2 effects for 11 cities in Canada, using multipollutant models, and obtained a 3.89% increase in non-traumatic mortality for Hamilton.

Respiratory hospital admissions

Gywnn et al. (2001) associated an increase of 3.7% per 10 ppb increase in SO_2 in terms of respiratory hospital admissions. No other studies investigated this association.

Nitrogen Dioxide (NO_2)

Non-traumatic mortality

NO_2 has recently been significantly associated with non-traumatic mortality in a number of studies. In Rome, Italy, Michelozzi et al. (1998) found a 1.54% increase in a 10 ppb increase, while in Barcelona, Spain, Garcia-Aymerich et al. (2000) reported a 2.9% increase. Morgan (1998b) in Sydney, Australia indicated the value was closer to 1.5%. However, the latter study did not take multipollutant modeling into account. Burnett et al. (1998a) revealed a 1.5% increase in non-traumatic mortality associated with a 10 ppb increase in NO_2, specifically for Hamilton, while a 2.3% increase was estimated for Toronto.

Respiratory hospital admissions

Burnett et al. (1997a) found a 4.87% increase in respiratory admissions for Hamilton for a 10 ppb increase in NO_2.

Cardiac hospital admissions

Three studies found significant associations between NO_2 and cardiac hospital admissions. Burnett et al. (1997a) found an 8.7% increase for the 10 ppb increase in NO_2. Morgan et al. (1998a) found a lower value of 4.4%. However, a multipollutant model was not taken into account for this study. Moolgavkar (2000), in Los Angeles County, US, found a 1.7% increase, with a two-pollutant model (i.e., SO_2 and NO_2).

Ozone (O_3)

Non-traumatic mortality

There has been an increasing amount of research in ozone-related mortality. Recent studies showed significant associations between O_3 and non-traumatic mortality. Garcia-Aymerich et al. (2000) in Barcelona, Spain, estimated a 0.95% increase in non-traumatic mortality, while Gouveia et al. (2000) in Sao Paulo, Brazil, identified a 0.43% increase. In Philadelphia, US, Kelsall et al. (1997) found the relative risk to be at 0.94%, while in Santa Clara

County, California, US, Fairley (1999) estimated a much higher risk at 2.47%. Thurston and Ito (2001) calculated this value at 0.56% in a meta-analysis study based on 12 published estimates.

Respiratory hospital admissions

Moolgavkar et al. (1997) found a 4% increase in respiratory hospital admissions associated with a 10 ppb increase of ozone, while using a multipollutant model. Burnett et al. (1997b) found an increase of 1.5%; however, in his 1998 article (Burnett et al., 1998b), this value was estimated to be 4.9%. Gywnn et al. (2000) found this value closer to 2.0%.

Cardiac hospital admissions

Only one study, Burnett et al. (1997b) tested the ozone-admission association. They reported a 4.5% increase for cardiac hospital admissions. As this is the only study to find significant associations at such high values, this estimate should be considered preliminary.

Particulates

Non-traumatic mortality

Numerous studies have calculated the percent increase in daily mortality per 10 $\mu g/m^3$ increase in particulate matter, in the form of TSP, PM_{10}, $PM_{2.5}$, and SO_4^{2-}.

TSP: Alberdi Odriozola et al. (1998) and Diaz et al. (1999) conducted studies in Madrid, Spain, and found a 0.6% and 0.72% increase, respectively. In Rome, Italy, Michelozzi et al. (1998) calculated a comparable 0.66% increase. Neas et al. (1999) found a 0.56% increase in Philadelphia using a single pollutant study. Goldberg et al. (2001) calculated increases in non-traumatic mortality in Montreal and reported a value of 0.65% for a 10 $\mu g/m^3$ in TSP in single pollutant analysis. Kelsall et al. (1997) found a 0.3% increase in Philadelphia using a multipollutant model.

PM_{10}: Burnett et al. (1998b) estimated a 0.7% increase in non-traumatic deaths in Hamilton taking into account other pollutants, while in Montreal, Goldberg et al. (2001) calculated an increase of 0.69% in a single pollutant analysis.

In a meta-analysis, Daniels et al. (2000) found a 0.54% increase in non-traumatic deaths in 20 US cities. Samet et al. (2000) reported a 0.51% increase for 20 US cities considered. In their reanalysis of Schwartz et al. (1996) article on particulates in six US cities, Klemm et al. (2000) found a 0.8% increase associated with PM_{10}. Katsouyanni et al. (1997) reported non-traumatic mortality for PM_{10} increases equal 0.4% for the 12 European countries studied.

Primarily in European research, black smoke (BS) values were used as approximations to PM_{10} values. Saez et al. (2001) calculated a 0.64% increase for the three Spanish cities in the study, while Garcia-Aymerich et al. (2000) found this value closer to 1.1% in their single-pollutant analysis.

$PM_{2.5}$: Goldberg et al. (2001) found a 1.96% increase in non-traumatic mortality related to the increase in $PM_{2.5}$ in Montreal. Fairley (1999) calculated a 4.46% in Santa Clara County, US. Klemm et al. (2000) estimated this increase as 1.3% in a study of six US cities. In Mexico City, Mexico, Borja-Aburto et al. (1998) recorded a 1.68% in non-traumatic mortality associated with the fine particulates. Burnett et al. (1998b) reported a 2.5% increase in Hamilton.

Respiratory hospital admissions

PM_{10}: Moolgavkar et al. (1997) found a 1.7% increase in respiratory hospital admissions in Los Angeles County, US. Burnett et al. (1997b) calculated the relative risk at 2.1% in Hamilton, while Gywnn et al. (2000) found this value to be closer to 2.2% in New York, US.

$PM_{2.5}$: There were no studies that report significant associations within our literature time-frame and search specifications, mainly due to the concentration of studies reporting findings related to specific subpopulations of children and elderly.

SO_4^{2-}: Gywnn et al. (2000) estimated this to be 0.5% in New York, while Burnett et al. (1997b) reported 2.7% for Hamilton.

Cardiac hospital admissions

PM_{10}: Burnett et al. (1999) found a 0.5% increase in cardiac admissions in Toronto, Canada, while Morgan et al. (1998a) found this value closer to 0.76% in Sydney, Australia.

$PM_{2.5}$: Burnett et al. (1999) calculated a 0.75% increase. Again, this was the only study that found significance in our review, and it should be considered preliminary.

Appendix 2: Detailed Literature Summary Tables

Table A-1. Comparison of % increases in non-traumatic deaths in relation to increases of 10 units per pollutant.

			% change in daily mortality for each 10 unit increase in pollutant				
Reference	**Location**	**Multi Pollutant models**	**Particulates ($\mu g/m^3$)**	**SO_2 (ppb)**	**NO_2 (ppb)**	**CO (1 ppm)**	**O_3 (ppb)**
Borja-Aburto et al. (1998)	Mexico City, Mexico	$PM_{2.5}$, O_3, NO_2 (4 day lag)	$PM_{2.5}$ = 1.68 % (0.2, 3.14)				
Burnett et al. (1998a)	Estimates derived for Hamilton, Canada	CO, NO_2, SO_2, O_3		2.2%	1.5%	2.0%	1.7%
Burnett et al. (1998b)	Toronto	CO	PM_{10}= 1.5% (1.1,1.9) $PM_{2.5}$=2.5% (1.7,3.3)	3.89% (2.9, 4.86)	2.3% (1.6, 2.8)	4.95% (3.8, 6.1)	1.5% (1.2, 1.9)
Gwynn et al. (2000)	Buffalo, US	PM_{10}, CO	PM_{10} = 1.07% (0.02, 2.1)			4.1% (CI) (1.0, 7.2)	
Fairley (1999)	Santa Clara County, CA, USA	CO, NO_2, O_3, NO_3	$PM_{2.5}$ = 4.46%				2.47%
Kelsall et al. (1997)	Philadelphia, USA	TSP, SO_2, NO_2, O_3	TSP = 0.31% (0, 0.61)	0.84% (0.11. 1.57)			0.94% (0.35, 0.15)
Morgan et al. (1998)	Sydney, Australia	PM_{10}, NO_2, O_3	PM_{10}= 0.8%(0.0, 1.6)				
Saez et al. (2001)	3 Spanish Cities	SO_2, BS	BS= 0.64% (0.2, 1.1)	1.1% (0.2, 1.9)			
Chronic:							
Dockery et al. (1993)	6 US cities	yes	$PM_{2.5}$: 0.68% (0.5, 0.8)				
Reanalysis of 6 cities			$PM_{2.5}$: 0.69% (0.6, 0.8)				
Pope et al. (1995) ACS study	151 US cities	yes	$PM_{2.5}$: 0.48% (0.44, 0.51)				
Reanalysis of ACS (2000)		yes	$PM_{2.5}$: 0.48% (0.45, 0.52)				
Not used in the calculation of current estimate:							
Pengelly et al. (2000)	Toronto, Canada	depending on average calculation	PM_{10}= 0.8% $PM_{2.5}$= 1.5% (0.85, 2.2)	2.2%	1.19%	3.48% (24 hr)	0.4%

Table A-2. Comparison of % increases in non-traumatic deaths in relation to increases of 10 units per pollutant for studies using single-pollutant models and meta-analysis studies.

		% change in daily mortality for each 10 unit increase in pollutant				
Reference	**Location**	**Particulates ($\mu g/m^3$)**	**SO_2 (ppb)**	**NO_2 (ppb)**	**CO (1 ppm)**	**O_3 (ppb)**
Alberdi Odriozola et al. (1998)	Madrid, Spain	TSP = 0.6%				
Diaz et al.(1999)	Madrid, Spain	TSP = 0.72%	2.1%			
Garcia-Aymerich et al. (2000)	Barcelona, Spain	BS = 1.1% (0.5, 1.7)	4.2% (2.2, 6.1)	2.9% (0.7, 5.1)		0.95% (0.2, 1.6)
Goldberg et al. (2001)	Montreal	TSP = 0.65% $PM_{2.5}$= 1.96%				
Gouveia et al. (2000)	Sao Paulo, Brazil	PM_{10} = 0.51% (0.1, 0.9)	4.5 % (1.1, 7.9)			0.43% (0.00, 0.85)
Katsouyanni et al. (1997)	12 European cities	PM_{10}= 0.44% (0.2, 0.6)	1.1% (0.8, 1.3)			
Michelozzi et al. (1998)	Rome, Italy	TSP = 0.66% (0.31, 1.02)		1.54% (0.14, 2.97)		
Morgan et al. (1998)	Sydney, Australia			1.5% (0.2, 2.1)		0.7% (0.0,1..3)
Neas et al. (1999)	Philadelphia, USA	TSP= 0.56% (0.27, 0.86)				
Meta-analysis articles:						
Daniels et al. (2000)	20 US cities	PM_{10} = 0.54% (0.33, 0.76)				
Klemm et al. (2000)	6 US cities (reanalysis)	PM_{10}=0.8% $PM_{2.5}$=1.3% $SO_4^=$=1.6% (0.5, 1.1) (0.9, 1.7) (0.9, 2.4)				
Samet et al. (2000)	20 US cities	PM_{10} = 0.51% (0.07, 0.93)				
Thurston & Ito (2001)	Combined analysis					0.56% (0.32, 1.08)

Table A-3. Comparison of % increases in indicated morbidity values in relation to 10 unit increase per pollutant

				% change in daily morbidity for 10 unit increase in pollutant				
Reference	**Location**	**Multi-pollutants**	**Measure**	**Particulates ($\mu g/m^3$)**	**SO_2 (ppb)**	**NO_2 (ppb)**	**CO (1 ppm)**	**O_3 (ppb)**
Ballester et al. (2001)	Valencia, Spain	single pollutant	*card hosp adm*		1.1% (0.2, 2.1)			
Burnett et al. (1997a)	Hamilton	O_3, CO	*resp hosp adm*					1.5% (0.7, 2.2)
Burnett et al. (1997b)	Toronto	T, DP for PM_{10}, +SO_2, O_3 for NO_2 + PM, NO_2, CO for O_3	*card hosp admin* *resp hosp admin*	2.3% (0.3, 4.4) 2.1% (0.9, 3.3)		8.7% (3.2, 14.5) 4.9% (1.0, 9.0)	2.5% (0.2, 4.9)	4.5% (1.6, 7.5) 4.9% (2.7, 7.1)
Burnett et al. (1999)	Toronto	gaseous pollutants	*card hosp adm*	PM_{10}=0.50% $PM_{2.5}$=0.75%				
Gywnn et al. (2000)	Buffalo, NY	each gas against particulates	*resp hosp adm*	PM_{10} = 2.1% (0.7, 3.5) SO_4^{2-}= 0.5% (0.3, 0.7)	3.7% (1.3, 6.1)			2.0% (0.9, 3.0)
Morgan et al. (1998)	Sydney	single pollutant	*card hosp adm*	PM_{10} = 0.7 (0.2-1.3)		4.4% (3.06-5.8)		
Morris et al. (1998)	Chicago	PM_{10}, NO_2, SO_2, O_3	*chf hosp adm*				2.6% (1.0-3.9)	