

ADDENDUM 2 TO COMEAP/2008/05

COLLATION OF SEPARATE COEFFICIENTS FOR MEN AND WOMEN FROM THE AMERICAN CANCER SOCIETY STUDY AND THE SIX CITIES STUDY

1. A series of tables are attached that collect together in one place various coefficients given separately for men and women in the HEI Reanalysis of the American Cancer Society (ACS) study and Six Cities study¹ and the later follow-up of the ACS study (Pope *et al* 2002). This is intended mainly for reference but it is being circulated at this stage because of its relevance to the discussion of the study by Miller *et al* (2007). Coefficients given separately for men and women in other cohort studies will be added at a later stage. Ultimately this collation will assist in judging whether or not there is consistent evidence of a different size of effect in men and women.
2. This page extracts the information most relevant to the discussion of the study by Miller *et al* (2007) – the coefficients for cardiopulmonary mortality (no separate coefficients for men and women were available for cardiovascular mortality). Results are not given here for subdivisions amongst men and women (e.g. smokers and non-smokers) but these are in the attached tables.
3. The coefficient for women for cardiopulmonary mortality was almost twice that for men in the HEI reanalysis of the ACS study. The relative risks for a 19.9 µg/m³ increase in sulphate were 1.42 (1.25-1.62) in women and 1.20 (1.08-1.31) in men (Table 1 attached). For a 24.5 µg/m³ increase in fine particles, the relative risks were 1.45 (1.22-1.71) for women and 1.24 (1.08-1.41) for men (Table 2 attached).
4. However, the coefficient for women for cardiopulmonary mortality was only slightly greater than for men in the longer follow-up in Pope *et al* (2002). The relative risks for a 10 µg/m³ increase in fine particles were 1.063 (1.009-1.12) for women and 1.05 (1.004-1.099) for men.
5. The coefficient for men and women for cardiopulmonary mortality was very similar in the HEI reanalysis of the 6 cities study. The relative risk for an 18.6 µg/m³ increase in fine particles was 1.33 (0.92-1.90) for women and 1.34 (1.03-1.75) for men (Table 6 attached).
6. Thus, although there is some indication from these key cohort studies that women are more affected than men, this is not entirely consistent.

Secretariat
February 2008

¹ Published results on later follow-up of the 6 cities study do not give results separately for men and women. A paper by Villeneuve *et al* (2002) does give results separately but the dataset used is more or less that used for the HEI reanalysis. Although the results differ slightly from those in the HEI reanalysis, the qualitative comparisons between the results for men and women are the same.

References

Health Effects Institute. (2000) *Re-analysis of the Harvard Six Cities Study and the American Cancer Society Study of Air Pollution and Mortality*. Cambridge, MA: Health Effects Institute. Available at (accessed April 2007): <http://pubs.healtheffects.org/getfile.php?u=273>

Miller, K.A., Siscovick, D.S., Sheppard, L., Shepherd, K., Sullivan, J.H., Anderson, G.L. and Kaufman, J.D. (2007) 'Long-term exposure to air pollution and incidence of cardiovascular events in women.' *New Eng. J. Med.* 356(5):447-458.

Pope, C.A. III, Burnett, R.T., Thun, M.J., Calle, E.E., Krewski, D., Ito, K., and Thurston, G.D. (2002) 'Lung cancer, cardiopulmonary mortality and long-term exposure to fine particulate air pollution' *JAMA* 287(9):1132-1141.

Villeneuve P.J., Goldberg M.S., Krewski D., Burnett R.T. and Chen Y. (2002) 'Fine particulate air pollution and all-cause mortality within the Harvard Six-Cities study: Variations in risk by period of exposure.' *Ann. Epidemiol.* 12: 568-576.

Table 1. Adjusted mortality risk ratios for the most-polluted areas compared with the least-polluted areas for deaths from all causes, lung cancer, and cardiopulmonary disease by gender and smoking status for sulphate (19.9 µg/m³): Reanalysis results for the ACS Study based on the Revised ACS Cohort (Table taken from pg 87 (Table 26c) of the HEI Reanalysis Report, 2000)^a

Study Group	All Causes	Lung Cancer	Cardiopulmonary disease
All combined	1.16 (1.10-1.23)	1.36 (1.13-1.65)	1.28 (1.19-1.40)
Women	1.20 (1.10-1.30)	1.22 (0.87-1.70)	1.42 (1.25-1.62)
Men	1.14 (1.05-1.22)	1.43 (1.13-1.81)	1.20 (1.08-1.31)
Never-smokers	1.19 (1.08-1.30)	1.87 (0.95-3.69)	1.37 (1.20-1.56)
Women	1.21 (1.08-1.36)	2.17 (0.96-4.88)	1.42 (1.20-1.67)
Men	1.14 (0.97-1.34)	1.36 (0.40-4.66)	1.28 (1.03-1.58)
Ever smokers	1.15 (1.07-1.24)	1.33 (1.09-1.62)	1.23 (1.12-1.34)
Women	1.18 (1.04-1.35)	1.09 (0.75-1.57)	1.44 (1.17-1.78)
Men	1.14 (1.05-1.23)	1.44 (1.13-1.83)	1.17 (1.05-1.32)

^a. Values are risk ratios (95% CIs) which have been adjusted for age, sex, race, cigarette smoking, exposure to passive cigarette smoke, body mass index, drinks per day of alcohol, education, and occupational exposure.

Table 2. Adjusted mortality risk ratios for the most-polluted areas compared with the least-polluted areas for deaths from all causes, lung cancer, and cardiopulmonary disease by gender and smoking status for fine particles (24.5 µg/m³): Reanalysis results for the ACS Study based on the Revised ACS Cohort (Table taken from pg 89 (Table 27c) of the HEI Reanalysis Report, 2000)^a

Study Group	All Causes	Lung Cancer	Cardiopulmonary disease
All combined	1.18 (1.10-1.27)	1.02 (0.80-1.30)	1.32 (1.19-1.46)
Women	1.19 (1.06-1.33)	0.89 (0.59-1.34)	1.45 (1.22-1.71)
Men	1.18 (1.07-1.29)	1.10 (0.81-1.48)	1.24 (1.08-1.41)
Never-smokers	1.24 (1.10-1.40)	0.73 (0.30-1.80)	1.43 (1.20-1.70)
Women	1.25 (1.07-1.45)	0.87 (0.30-2.52)	1.54 (1.24-1.92)
Men	1.24 (1.00-1.54)	0.49 (0.09-2.66)	1.24 (0.93-1.66)
Ever smokers	1.15 (1.05-1.26)	1.04 (0.81-1.34)	1.25 (1.10-1.42)
Women	1.12 (0.95-1.32)	0.88 (0.56-1.39)	1.32 (1.01-1.72)
Men	1.16 (1.05-1.29)	1.12 (0.83-1.52)	1.23 (1.06-1.43)

^a. Values are risk ratios (95% CIs) which have been adjusted for age, sex, race, cigarette smoking, exposure to passive cigarette smoke, body mass index, drinks per day of alcohol, education, and occupational exposure.

Table 3. Adjusted mortality relative risk ratio associated with 10- $\mu\text{g}/\text{m}^3$ differences of $\text{PM}_{2.5}$ concentrations (Table constructed from data provided in Pope *et al* (2002) in a follow up to the ACS study and by data personally provided from Professor Pope to the Secretariat

Study Group	All-Cause	Cardiopulmonary	Lung cancer	All other cause
Men	1.056 (1.016-1.097)	1.05 (1.004-1.099)	1.13 (1.037-1.232)	1.027 (0.98-1.075)
Women	1.016 (0.978-1.056)	1.063 (1.009-1.120)	0.991 (0.896-1.096)	0.980 (0.934-1.028)

Table 4. Relative risks of mortality from all causes associated with an increase in fine particles for gender and education level in the Six Cities Study (extracted from Table 5, page 140 of the HEI Reanalysis Report, 2000)

Gender	High School or Less		More than High School	
	<i>n</i>	All-cause mortality	<i>n</i>	All-cause mortality
Male	2,330	1.48 (1.16-1.87)	1,341	1.07 (0.70-1.63)
Female	3,027	1.29 (0.97-1.7)	1,413	0.81 (0.49-1.36)

Table 5. Relative risks of all-cause mortality in the Six Cities Study from Poisson Regression of time-varying covariates^a (Table taken from page 148 (Table 13) of the HEI Reanalysis Report, 2000)

Variable	All subjects	Men	Women
Current smoker	1.37 (0.98-1.87)	1.79 (1.05-2.86)	1.16 (0.73-1.74)
< 10 pack years ^b	1.0	1.0	1.0
10-30 pack years	1.57 (1.13-2.24)	1.35 (0.83-2.31)	1.74 (1.12-2.82)
> 30 Pack years	1.87 (1.36-2.64)	1.56 (0.99-2.63)	1.93 (1.24-3.15)
Former smoker	1.23 (0.99-1.52)	1.21 (0.88-1.63)	1.30 (0.95-1.75)
< 10 Pack years ^b	1.0	1.0	1.0
10-25 Pack years	0.96 (0.73-1.27)	0.96 (0.67-1.36)	1.12 (0.70-1.78)
> 25 Pack years	1.47 (1.17-1.86)	1.54 (1.15-2.07)	1.73 (1.09-2.76)
Less than high school education	1.26 (1.13-1.41)	1.29 (1.12-1.49)	1.22 (1.03-1.45)
Body mass index ^c			
4 th Quartile ^b	1.0	1.0	1.0
3 rd Quartile	0.85 (0.74-0.98)	0.91 (0.77-1.09)	0.74 (0.59-0.93)
2 nd Quartile	0.78 (0.67-0.90)	0.80 (0.66-0.97)	0.75 (0.59-0.93)
1 st Quartile	0.82 (0.70-0.96)	0.98 (0.79-1.22)	0.69 (0.56-0.87)
City ^d			
Portage	1.0	1.0	1.0
Topeka	1.01 (0.82-1.24)	1.04 (0.79-1.36)	0.96 (0.69-1.31)
Harriman	1.16 (0.96-1.39)	1.20 (0.94-1.51)	1.06 (0.78-1.43)
Watertown	1.06 (0.89-1.27)	0.98 (0.77-1.24)	1.13 (0.86-1.49)
St Louis	1.13 (0.95-1.35)	1.16 (0.92-1.45)	1.07 (0.81-1.41)
Steubenville	1.32 (1.11-1.57)	1.39 (1.11-1.74)	1.22 (0.93-1.61)

^aRisks have been adjusted for age, sex, and all other variables listed in this table

^bOther relative risks in this category are expressed in relation to this table

^cBody mass index was categorized into quartiles based on the 8,111 subjects at baseline. Cutpoints in kg/m² were ≤ 22.7, 25.26, 28.21 and > 28.21

Table 6. Relative risks of mortality from all causes, cardiopulmonary disease, and lung cancer associated with an increase in fine particles in various subsets of the population using the original model + dirtiness + lung carcinogens in the Reanalysis of the Six Cities Study^a (Table is taken from page 143 (Table 8) of the HEI Reanalysis Report, 2000)

Group	All Cause	Cardiopulmonary disease	Lung cancer
All subjects	1.26 (1.08-1.48)	1.34 (1.08-1.65)	1.30 (0.75-2.27)
Females	1.19 (0.92-1.53)	1.33 (0.92-1.90)	0.67 (0.22-2.08)
Males	1.31 (1.07-1.61)	1.34 (1.03-1.75)	1.64 (0.85-3.16)
Never-smokers	1.24 (0.92-1.66)	1.39 (0.93-2.10)	3.88 (0.44-34.18) ^b
Females	1.16 (0.80-1.67)	1.21 (0.70-2.08)	4.06 (0.46-36.12) ^b
Males	1.25 (0.77-2.04)	1.61 (0.85-3.06)	NA ^c
Ever-smokers	1.33 (1.10-1.61)	1.37 (1.07-1.76)	1.40 (0.80-2.46)
Females	1.29 (0.90-1.84)	1.56 (0.96-2.54)	0.52 (0.13-2.10)
Males	1.38 (1.11-1.73)	1.33 (0.99-1.78)	1.82 (0.97-3.43)

^aRelative risks were calculated for a change in the pollutant of interest equal to the difference in mean concentration between the most-polluted city and the least-polluted city; in the Six Cities Study, this difference for fine particles was 18.6 $\mu\text{g}/\text{m}^3$. The Original Model included the following covariates: PM_{2.5}, indicators of current- and former-smokers, current smoker pack-years, a two-level indicator of education level, occupational exposure to dust or fumes, and body mass index. "Dirtiness" is a continuous occupational variable; "lung carcinogens" is a binary variable for occupations with exposure to lung carcinogens and was used only in the analyses for lung cancer. Data are RRs with 95% CIs.

^bThe large upper confidence limit is due to the small number of deaths (8) in this group.

NA^c = no deaths in that group.