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Fine Particulate Air Pollution and Total Mortality Among Elderly Californians, 1973–2002

James E. Enstrom

Jonsson Comprehensive Cancer Center, University of California, Los Angeles, California, USA, and Scientific Integrity Institute, Los Angeles, California, USA

Fine particulate air pollution has been associated with increases in long-term mortality in selected cohort studies, and this association has been influential in the establishment of air quality regulations for fine particles ($PM_{2.5}$). However, this epidemiologic evidence has been questioned because of methodological issues, conflicting findings, and lack of an accepted causal mechanism. To further evaluate this association, the long-term relation between fine particulate air pollution and total mortality was examined in a cohort of 49,975 elderly Californians, with a mean age of 65 yr as of 1973. These subjects, who resided in 25 California counties, were enrolled in 1959, recontacted in 1972, and followed from 1973 through 2002; 39,846 deaths were identified. Proportional hazards regression models were used to determine their relative risk of death (RR) and 95% confidence interval (CI) during 1973–2002 by county of residence. The models adjusted for age, sex, cigarette smoking, race, education, marital status, body mass index, occupational exposure, exercise, and a dietary factor. For the 35,789 subjects residing in 11 of these counties, county-wide exposure to fine particles was estimated from outdoor ambient concentrations measured during 1979–1983 and RRs were calculated as a function of these $PM_{2.5}$ levels (mean of 23.4 $\mu g/m^3$). For the initial period, 1973–1982, a small positive risk was found: RR was 1.04 (1.01–1.07) for a 10-$\mu g/m^3$ increase in $PM_{2.5}$. For the subsequent period, 1983–2002, this risk was no longer present: RR was 1.00 (0.98–1.02). For the entire follow-up period, RR was 1.01 (0.99–1.03). The RRs varied somewhat among major subgroups defined by sex, age, education level, smoking status, and health status. None of the subgroups that had significantly elevated RRs during 1973–1982 had significantly elevated RRs during 1983–2002. The RRs showed no substantial variation by county of residence during any of the three follow-up periods. Subjects in the two counties with the highest $PM_{2.5}$ levels (mean of 36.1 $\mu g/m^3$) had no greater risk of death than those in the two counties with the lowest $PM_{2.5}$ levels (mean of 13.1 $\mu g/m^3$). These epidemiologic results do not support a current relationship between fine particulate pollution and total mortality in elderly Californians, but they do not rule out a small effect, particularly before 1983.

Many observational epidemiological studies have reported associations between air pollution from combustion sources and human health (Lipfert, 1994). During past severe air pollution events, such as the 1952 London fog incident (Logan & Glasg, 1953), extremely high concentrations of particulate air pollution were accompanied by major increases in coincident mortality. In more recent years, health effects have also been associated with much lower concentrations of particulate air pollution (Pope & Dockery, 1999). While much of the recent research has focused on short-term exposures, several studies suggest that long-term exposures may be more important. In particular, results from two major cohorts (Dockery et al., 1993; Pope et al., 1995, 2002) have shown significant mortality associations with outdoor concentrations of fine particles ($PM_{2.5}$, median aerodynamic diameter

less than 2.5 μm). Other cohort studies have also examined mortality associations with $PM_{2.5}$ and other pollutants (McDonnell et al., 2000; Lipfert et al., 2000, 2003), with somewhat different findings.

The major cohort studies have been used to support new national ambient air quality standards for fine particles issued by the U.S. Environmental Protection Agency (U.S. EPA, 1997). These standards are specific with respect to particle size, but not with respect to chemical composition. $PM_{2.5}$ is a variable mixture, rather than a defined chemical compound as in the case of gaseous air pollutants. Fine particles are generated mainly by combustion processes and their atmospheric sequelae, and all such particles measured by the approved methods are considered equally harmful. However, the chemical composition of airborne particulate matter varies appreciably across the nation and within metropolitan areas. Although national ambient air quality standards are intended to apply throughout the nation, it is not clear that the selected epidemiological studies on which those standards are based are equally applicable nationwide.

The associations of particulate air pollution with long-term mortality remain controversial (Phalen, 2002; Moolgavkar, 2005; Kaiser, 2005). This is in large part because the epidemiologic studies that have examined these health effects are subject to a number of methodological limitations (Greenbaum et al., 2001; Moolgavkar, 1996; Gamble, 1998; Krewski et al., 2000; Lipfert, 2003). Actual exposures to air pollution are difficult to determine accurately in large cohorts. Indeed, the exposure of each individual has not been directly measured in these studies, but has been assumed to equal the ambient outdoor $PM_{2.5}$ concentration for the individual's county or metropolitan area of residence. Also, one national cohort study has found largely negative associations between $PM_{2.5}$ and mortality (Lipfert et al., 2000, 2003).

California is a large, diverse state that has long been concerned about the health effects of air pollution and that has recently issued new stricter ambient $PM_{2.5}$ standards (CARB, 2003), based in large part on the national standards. However, no previous cohort study has focused on mortality with respect to measured $PM_{2.5}$ levels in California. This article used a large cohort of elderly Californians to examine in detail the relationship between $PM_{2.5}$ levels measured during 1979–1983 and mortality from all causes during 1973–2002.

METHODS

California Cancer Prevention Study

The California Cancer Prevention Study (CA CPS I) is the extended follow-up of the 118,094 California subjects from the original Cancer Prevention Study (CPS I) of 1,078,894 adults from 25 states. CPS I was initiated by the American Cancer Society (ACS) beginning in 1959, and CA CPS I has been independently conducted at the University of California, Los Angeles (UCLA), since 1991, as described in detail elsewhere (Enstrom

& Heath, 1999; Enstrom & Kabat, 2003). The conduct of CA CPS I has been approved by the UCLA, Office for Protection of Research Subjects during this entire period. The subjects in this prospective cohort study were enrolled from October 1959 through February 1960 using a detailed four-page questionnaire. Surviving cohort members completed short questionnaires in late 1961, 1963, 1965, and 1972, and a two-page questionnaire in mid 1999. Deaths through 1972 were identified primarily by surviving study subjects and were confirmed with death certificates. The later deaths were identified primarily from computerized and manual matches with the California death file and the nationwide Social Security Death Index, using name and other identifying variables (Enstrom & Heath, 1999; Enstrom & Kabat, 2003). About 86% of the later deaths were identified on the California death file and the remainder were identified on the Social Security Death Index file. The only prior analysis of the CPS I cohort with respect to air pollution found no relationship between suspended particulate matter and lung cancer mortality during the 1960s and had no $PM_{2.5}$ data (Hammond, 1972; Hammond & Garfinkel, 1980).

This article analyzes those CA CPS I subjects who reported their cigarette smoking status in both the 1959 and 1972 questionnaires and who were alive as of January 1, 1973. Respondents to both questionnaires were traced more easily than those who responded only to the 1959 questionnaire. The 1972 questionnaire updated their cigarette smoking status, the most important confounding variable. The early years of follow-up (January 1, 1960–December 31, 1972) have not been included in this article because there are no statewide $PM_{2.5}$ data before 1979. Results for this early period and for the entire follow-up period since 1960 will be presented in a subsequent article dealing with other air pollutants. This analysis is limited to the 25 counties with the largest number of CA CPS I subjects, which ranged from 325 to 17,340 per county. About 95% of the CA CPS I subjects resided in these 25 counties. There were 49,975 traceable subjects alive as of January 1, 1973, of whom 39,846 died as of December 31, 2002. There were 35,789 traceable subjects alive as of January 1, 1983 in the 11 counties with $PM_{2.5}$ data, of whom 28,441 died as of December 31, 2002. An additional 2,735 subjects in these counties lost since January 1, 1973 (7.64%), have been omitted from further analysis.

The 1999 addresses for most of the traceable subjects alive as of January 1, 1999, were determined from a match with California driver's license (DL) identifying information, and about 33% of the subjects responded to a two-page smoking and lifestyle questionnaire that was mailed in mid 1999 to their DL address (Enstrom & Heath, 1999; Enstrom & Kabat, 2003). Based on the questionnaire information in late 1972, the 1999 DL address information, and the death information, the county of residence and county of death were determined for most subjects as of late 1972 and early 1999. The residential mobility of subjects was assessed by calculating the percentage of subjects who lived or died in the same county from 1972 to 1999.

1979–1983 PM$_{2.5}$ Data and 1973–2002 Mortality Data

The independent variable in this analysis is PM$_{2.5}$, as measured during 1979–1983 in 11 California counties by the EPA as part of the Inhalable Particulate Network (IPN) (Hinton et al., 1984, 1986), also known as the Inhalable Particle Monitoring Network (IPMN) (Sune, 1999; Pope et al., 2002). These data have been used in several previous epidemiological studies (Ozkaynak et al., 1987; Lipfert et al., 1988, 2000, 2003; Pope et al., 1995, 2002). In this article, the PM$_{2.5}$ data for each county were averaged over time and across the available monitoring stations, and are assumed to indicate the average long-term exposure level for all subjects in the county. No routinely measured PM$_{2.5}$ data in California exist before 1979 or during 1984–1998; routine statewide measurements in California were resumed in 1999. The average county-level PM$_{2.5}$ value was assigned to the traceable subjects alive as of January 1, 1973, based on their county of residence as of late 1972. This analysis was based on the deaths from January 1, 1973, to December 31, 2002, a 30-year follow-up period that includes the 5-yr period of the 1979–1983 PM$_{2.5}$ data. Additional analyses have been done for

deaths from January 1, 1973, to December 31, 1982, and from January 1, 1983, to December 31, 2002. This latter period is roughly the same as the period (September 1, 1982–December 31, 1998) used in the recent national cohort study (Pope et al., 2002).

Analysis by Proportional Hazards Regression

The age- and sex-adjusted relative risk of death (RR) and 95% confidence interval (CI) were calculated using Cox proportional hazards regression, specifically the SAS PHREG procedure (SAS, 2004), including age at baseline in 1-yr intervals and sex, as a function of PM$_{2.5}$ level in units of 10 μg/m^3. This type of analysis is similar to the one used recently (Pope et al., 2002). Fully adjusted relative risks were calculated using a Cox model that includes age, sex, and eight potential confounding variables at baseline: cigarette smoking status (never, former as of 1959 and 1972, 1–9, 10–19, 20, 21–39, 40+ cigarettes per day as of 1972), race (white, nonwhite), education level (<12, 12, >12 yr), marital status (married, widowed, single, separated, divorced), body mass index (<20, 20–22.99, 23–25.99,

TABLE 1

Demographic and lifestyle characteristics in 1959 for California CPS I male subjects as of 1/1/1973 who resided in the 11 counties having 1979–1983 PM$_{2.5}$ measurements and who provided 10/1/1972 cigarette smoking status

Characteristic	1959 value (11 PM$_{2.5}$ counties)	1959 value (2 highest PM$_{2.5}$ counties)	1959 value (2 lowest PM$_{2.5}$ counties)	1959 value for 1999 respondents	1999 value for 1999 respondents
Mean level of 1979–1983 PM$_{2.5}$ (μg/m^3)	23.4	36.1	13.1		
Number of subjects alive as of 1/1/1973	16,296	1043	1040		
Lost to follow-up since 1/1/1973 (%)	4.432	2.987	4.840		
Number of subjects alive 1/1/1973 and not lost since 1/1/1973	15,574	1012	990	1314 (alive 1999)	1314 (alive 1999)
Age as of 1/1/1973 (mean, years)	65.7	67.1	64.5	58.4	58.4
Age as of 1/1/1983 (mean, years)	73.8	74.9	72.4	68.4	68.4
Race (% white)	98.4	99.0	97.5	98.5	98.0
Marital status (% married)	97.3	97.4	98.0	96.3	75.6
Education (% ≥12 yr)	71.8	70.7	79.8	90.3	92.6
Height (mean, inches)	69.4	69.5	69.9	69.9	69.3
Weight (mean, pounds)	173.0	172.7	174.5	172.9	168.9
History of serious diseases (% yes)	9.7	12.7	7.5	4.6	
Cancer	4.6	6.9	3.8	3.1	42.5
Heart disease	4.6	4.6	3.5	1.2	
Stroke	0.6	1.2	0.2	0.3	
Sick at the present time (% yes)	6.8	6.8	5.4	6.2	25.9
Occupation (% professional)	10.5	11.9	9.8	17.5	
Residence location (% urban)	98.1	99.2	98.6	98.1	
Exercise (% moderate or heavy)	72.5	73.9	76.1	67.1	61.7
Cigarette smoking (% current in 1959)	41.5	40.5	45.3	41.9	1.8
Cigarette smoking (% current in 1972)	23.3	24.2	25.9	14.9	1.8
Fruit/fruit juices (7+ times/week)	63.2	60.6	63.7	66.2	59.0

Note. Values in 1959 and 1999 for male subjects in 11 counties who responded to 1999 questionnaire.

TABLE 2

Demographic and lifestyle characteristics in 1959 for California CPS I female subjects as of 1/1/1973 who resided in the 11 counties having 1979–1983 PM$_{2.5}$ measurements and provided 1972 cigarette smoking status

Characteristic	1959 value (11 PM$_{2.5}$ counties)	1959 value (2 highest PM$_{2.5}$ counties)	1959 value (2 lowest PM$_{2.5}$ counties)	1959 value for 1999 respondents	1999 value for 1999 respondents
Mean level of 1979–1983 PM$_{2.5}$ (μg/m^3)	23.4	36.1	13.1		
Number of subjects alive or lost as of 1/1/1973	22,228	1491	1313		
Lost to follow-up since 1/1/1973 (%)	9.058	9.276	10.252		
Number of subjects alive 1/1/1973 and not lost since 1/1/1973	20,215	1353	1178	2877 (alive 1999)	2877 (alive 1999)
Age as of 1/1/1973 (mean, years)	64.9	66.3	64.0	57.1	57.1
Age as of 1/1/1983 (mean, years)	72.9	74.3	72.0	67.1	67.1
Race (% white)	98.3	99.3	97.9	98.1	97.7
Marital status (% married)	83.1	81.8	86.3	90.0	32.3
Education (% $\geq$12 yr)	76.8	76.6	82.6	89.9	93.3
Height (mean, inches)	63.8	63.8	64.0	64.1	63.5
Weight (mean, pounds)	137.1	138.4	135.3	133.0	137.4
History of serious diseases (% yes)	9.9	10.6	9.8	5.5	
Cancer	5.9	7.0	6.0	3.8	36.8
Heart disease	3.5	3.0	3.1	1.5	
Stroke	0.5	0.6	0.7	0.2	
Sick at the present time (% yes)	8.4	8.1	5.6	7.2	22.0
Occupation (% professional)	15.9	21.4	16.0	18.6	
Residence location (% urban)	97.7	99.1	98.0	96.9	
Exercise (% moderate or heavy)	80.2	82.8	83.3	77.9	63.4
Cigarette smoking (% current in 1959)	32.5	28.7	40.4	31.1	3.6
Cigarette smoking (% current in 1972)	22.8	19.6	29.1	19.8	3.6
Fruit/fruit juices (7+ times/week)	74.1	75.4	74.3	74.8	60.1

Note. Values in 1959 and 1999 for female subjects in 11 counties who responded to 1999 questionnaire.

26–29.99, >30 kg/m^2), male occupational exposure (no, yes), exercise (none/slight, moderate, heavy), and fruit/fruit juice intake (0, 1, 2, 3, 4, 5, 6, 7 days/wk). One additional variable, health status at entry (good, fair, poor, ill, sick/cancer/CHD/stroke), was evaluated in a sensitivity analysis. The confounding variables are defined at original entry into study in late 1959, except for cigarette smoking status, which was updated in late 1972. All of the confounding variables were measured again in a large sample of survivors during 1999.

Subgroup analyses were done by sex, year of birth (1873–1907, 1908–1929, representing ages 43–64 and 65–99 as of January 1, 1973), education level (<12, 12, 12+ yr), cigarette smoking status (never, former, current as of October 1, 1972), and health status (healthy, unhealthy as of October 1, 1959), as well as by decade of follow-up (January 1, 1973–December 31, 1982, January 1, 1983–December 31, 1992, January 1, 1993–December 31, 2002). In addition, the relative mortality rates by county of residence were calculated using PHREG as an alternative method to assess the influence of different county-wide

pollution levels. The Los Angeles county subjects are used as the referent group in estimating the fully-adjusted RRs during 1973–2002, 1973–1982, and 1983–2002 for each of the other 24 counties.

RESULTS

Demographic Characteristics and 1979–1983 PM$_{2.5}$ Data

The late 1959 demographic and lifestyle characteristics of the CA CPS I subjects in the 11 counties with 1979–1983 PM$_{2.5}$ data (mean of 23.4 μg/m^3) are shown in Table 1 for 15,574 males and in Table 2 for 20,218 females. These tables also show the corresponding characteristics for the subjects in the two counties (Kern and Riverside) with the highest PM$_{2.5}$ levels (mean of 36.1 μg/m^3) and in the two counties (Contra Costa and Santa Barbara) with the lowest PM$_{2.5}$ levels (mean of 13.1 μg/m^3). The characteristics of subjects are quite similar, irrespective of their mean pollution levels. The mean age of the subjects alive as of January 1, 1973, was 65.7 yr for males and 64.9 yr for

TABLE 3

Fully adjusted relative risk of death from all causes (RR and 95% CI) during 1/1/1973–12/31/2002 and 1/1/1983–12/31/2002 for both sexes, by county of residence relative to Los Angeles county for the 25 counties with the most California CPS I subjects, based on 10/1/1972 county of residence

County of residence as of 10/1/1972	1973–2002 Deaths/ 1973 subjects	Percent alive or dead same co in 1999	Fully adjusted 1973–2002 RR(95% CI)	Fully adjusted 1973–1982 RR(95% CI)	Fully adjusted 1983–2002 RR(95% CI)
Alameda	3380/4294	60.7	0.962 (0.926–0.999)	0.948 (0.886–1.015)	0.967 (0.924–1.012)
Butte	462/534	73.1	0.999 (0.910–1.096)	0.899 (0.763–1.060)	1.051 (0.939–1.176)
Contra Costa	1260/1652	60.1	0.999 (0.943–1.058)	0.989 (0.890–1.100)	1.004 (0.937–1.076)
Fresno	840/1085	80.0	0.935 (0.872–1.002)	0.896 (0.786–1.021)	0.951 (0.876–1.033)
Humboldt	424/507	79.3	0.992 (0.900–1.092)	0.985 (0.830–1.168)	0.992 (0.882–1.115)
Kern	630/790	79.5	0.944 (0.872–1.023)	0.950 (0.824–1.096)	0.941 (0.854–1.036)
Marin	641/805	57.2	0.939 (0.867–1.016)	1.006 (0.875–1.158)	0.908 (0.825–1.000)
Napa	500/627	73.4	0.949 (0.868–1.038)	0.817 (0.687–0.972)	1.006 (0.906–1.117)
Orange	2453/3050	65.1	0.990 (0.948–1.034)	0.962 (0.891–1.038)	1.003 (0.952–1.056)
Riverside	1311/1575	59.6	0.959 (0.906–1.015)	1.022 (0.928–1.064)	0.926 (0.863–0.993)
Sacramento	1370/1721	77.2	0.998 (0.944–1.055)	0.960 (0.867–1.064)	1.013 (0.948–1.083)
San Bernardino	1340/1622	63.5	0.992 (0.938–1.049)	0.932 (0.841–1.033)	1.018 (0.951–1.088)
San Diego	2958/3615	84.4	0.992 (0.954–1.033)	0.911 (0.847–0.979)	1.028 (0.981–1.078)
San Francisco	1597/2043	48.3	0.963 (0.914–1.014)	0.985 (0.899–1.080)	0.952 (0.894–1.014)
San Joaquin	248/325	71.9	0.925 (0.816–1.049)	0.847 (0.670–1.071)	0.965 (0.832–1.120)
San Mateo	1403/1789	58.0	0.949 (0.899–1.003)	0.897 (0.808–0.997)	0.971 (0.910–1.035)
Santa Barbara	411/516	67.4	0.968 (0.878–1.068)	0.832 (0.690–1.003)	1.030 (0.918–1.156)
Santa Clara	1851/2345	63.5	0.955 (0.910–1.003)	0.961 (0.880–1.049)	0.954 (0.900–1.012)
Santa Cruz	295/372	64.7	0.890 (0.793–0.999)	0.980 (0.805–1.193)	0.849 (0.736–0.979)
Solano	402/505	59.8	0.901 (0.815–0.995)	0.823 (0.685–0.989)	0.934 (0.830–1.051)
Sonoma	482/581	75.7	0.968 (0.884–1.060)	0.919 (0.781–1.082)	0.987 (0.885–1.102)
Stanislaus	551/691	83.7	0.984 (0.904–1.072)	0.981 (0.841–1.144)	0.981 (0.885–1.087)
Tulare	921/1117	78.7	1.047 (0.979–1.119)	1.031 (0.918–1.158)	1.054 (0.972–1.144)
Ventura	369/474	69.1	0.967 (0.872–1.072)	0.774 (0.629–0.951)	1.053 (0.935–1.187)
Los Angeles	13,747/17,340	64.4	1.000	1.000	1.000
Total	39,846/49,975	66.4			
Chi-square test of homogeneity (24 degrees of freedom)			$\chi^2 = 27.48\ p = .283$	$\chi^2 = 32.21\ p = .122$	$\chi^2 = 30.70\ p = .163$

TABLE 4

Fully adjusted relative risk of death from all causes (RR and 95% CI) by county of residence relative to Los Angeles county, during 1973–2002 and 1983–2002 for both sexes, for the 35,789 California CPS I subjects in rank order of 1979–1983 $PM_{2.5}$ level for the 11 counties and groups of these counties

County of residence as of 10/1/1972	1/1/1973 subjects	Fully adjusted 1973–2002 RR(95% CI)	Fully adjusted 1973–1982 RR(95% CI)	Fully adjusted 1983–2002 RR(95% CI)	$PM_{2.5}$ ($\mu g/m^3$) 1979–1983	Rank
Santa Barbara	516	0.968 (0.878–1.068)	0.832 (0.690–1.003)	1.030 (0.918–1.156)	10.6	1
Contra Costa	1652	0.999 (0.943–1.058)	0.989 (0.890–1.100)	1.004 (0.937–1.076)	13.9	2
Alameda	4294	0.962 (0.926–0.999)	0.948 (0.886–1.015)	0.967 (0.924–1.012)	14.4	3
Butte	534	0.999 (0.910–1.096)	0.899 (0.763–1.060)	1.051 (0.939–1.176)	15.5	4
San Francisco	2043	0.963 (0.914–1.014)	0.985 (0.899–1.080)	0.952 (0.894–1.014)	16.4	5
Santa Clara	2345	0.955 (0.910–1.003)	0.961 (0.880–1.049)	0.954 (0.900–1.012)	17.8	6
Fresno	1085	0.935 (0.872–1.002)	0.896 (0.786–1.021)	0.951 (0.876–1.033)	18.4	7
San Diego	3615	0.992 (0.954–1.033)	0.911 (0.847–0.979)	1.028 (0.981–1.078)	18.9	8
Los Angeles	17,340	1.000	1.000	1.000	28.2	9
Kern	790	0.944 (0.872–1.023)	0.950 (0.824–1.096)	0.941 (0.854–1.036)	30.9	10
Riverside	1575	0.959 (0.906–1.015)	1.022 (0.928–1.064)	0.926 (0.863–0.993)	42.0	11
Total	35,789				23.4	
Chi-square test of homogeneity (10 degrees of freedom)		$\chi^2 = 12.65\ p = .244$	$\chi^2 = 14.27\ p = .161$	$\chi^2 = 16.35\ p = .090$		
Two lowest $PM_{2.5}$ counties (Contra Costa and Santa Barbara)		0.991 (0.942–1.043)	0.948 (0.863–1.041)	1.010 (0.951–1.073)	13.1	
Next lowest $PM_{2.5}$ counties (Alameda, Butte, San Francisco)		0.965 (0.935–0.996)	0.955 (0.903–1.010)	0.969 (0.933–1.006)	15.1	
Next highest $PM_{2.5}$ counties (Fresno, San Diego, Santa Clara)		0.971 (0.942–1.002)	0.926 (0.875–0.980)	0.991 (0.955–1.029)	18.5	
Reference county (Los Angeles)		1.000	1.000	1.000	28.2	
Two highest $PM_{2.5}$ counties (Kern and Riverside)		0.954 (0.910–1.001)	1.000 (0.921–1.087)	0.931 (0.878–0.986)	36.1	
Chi-square test of homogeneity (4 degrees of freedom)		$\chi^2 = 8.48\ p = .075$	$\chi^2 = 8.72\ p = .069$	$\chi^2 = 8.02\ p = .091$		

females and their minimum age was 43 yr. The mean age of the subjects alive as of January 1, 1983, was 73.8 yr for males and 72.9 yr for females, and their minimum age was 53 yr.

The 1979–1983 $PM_{2.5}$ data from the IPN are shown in Appendix Table 1 for 11 California counties, with details for the 15 monitoring sites at which measurements were made.

The 1999 follow-up questionnaire provided important information about the confounding variables for survivors 40 yr after they originally enrolled in the study. Although these survivors were the younger members of the cohort, with a mean age of about 57 yr as of January 1, 1973, they provide a good indication of the risk factor changes that have occurred. A comparison of their 1959 and 1999 responses in Tables 1 and 2 shows that the variables of race, education level, exercise, body mass index, and fruit/fruit juice intake changed very little and were similar in the high and low $PM_{2.5}$ counties. The percentage of married subjects declined substantially in all counties because of the large fraction of spouses who died. The percentage of current cigarette smokers declined dramatically and uniformly in all counties, reflecting the large degree of smoking cessation that has already been documented in this cohort (Enstrom & Heath, 1999). Health status, used as an additional variable in a sensitivity analysis, also declined substantially among subjects in all counties, because the aging survivors had a much higher prevalence of cancer and other diseases in 1999 than they did in 1959.

Relative Risks by County of Residence

Table 3 shows the 1973–2002, 1973–1982, and 1983–2002 mortality risks relative to Los Angeles county, adjusted for age, sex, and eight confounding variables, for the 25 counties with the most CA CPS I subjects, including the 11 counties with 1979–1983 $PM_{2.5}$ data. Overall, the RRs were quite consistent with each other and most had a 95% CI that included 1.0. None of the RRs were greatly different from 1.0. Wald chi-square tests conducted on these RRs did not reject the hypothesis of homogeneity during any of the three follow-up periods. Also, Table 3 shows that, based on their counties of residence and death from 1972 to 1999, about 66% of the subjects remained in the same county during this period, indicating relative stability of residence. In particular, the stability of residence was similar in the two highest $PM_{2.5}$ counties (66%), the two lowest $PM_{2.5}$ counties (62%), and in Los Angeles county (64%).

Table 4 shows the mortality risks relative to Los Angeles county for 11 counties ranked in order by their 1979–1983 $PM_{2.5}$ value. During 1973–2002, the two counties (Kern and Riverside) with highest $PM_{2.5}$ levels (mean of 36.1 $\mu g/m^3$) had an RR of 0.954 (0.910–1.001), whereas the two counties (Contra Costa and Santa Barbara) with the lowest $PM_{2.5}$ levels (mean of 13.1 $\mu g/m^3$) had a slightly higher RR of 0.991 (0.942–1.043). During 1983–2002 there was a larger difference, with corresponding RRs of 0.931 (0.878–0.986) and 1.010 (0.951–1.073). During 1973–1982 there was a reverse pattern, with corresponding RRs of 1.000 (0.921–1.087) and 0.948 (0.863–1.041). Two groups of the six counties with medium $PM_{2.5}$ levels had inter-

mediate RRs that were consistent with the RRs for the high and low $PM_{2.5}$ counties. Although there is some variation, Wald chi-square tests conducted on these RRs did not reject the hypothesis of homogeneity during any of the three follow-up periods for the individual counties or for the groups of counties. These findings are consistent with those in Table 3.

Relative Risks by 1979–1983 $PM_{2.5}$ Level

Table 5 shows the relationship of 1973–2002 mortality to 1979–1983 $PM_{2.5}$ level, by decade of follow-up, based on assigning each subject the $PM_{2.5}$ level of the county in which they resided as of late 1972. Both the age- and sex-adjusted and fully adjusted 1973–2002 RRs are shown. Also shown are the 1973–2002 RRs for selected subgroups defined by sex, age (year of birth), education level, cigarette smoking status, and health status. These RRs were calculated based on a unit increase in $PM_{2.5}$ of 10 $\mu g/m^3$. The age- and sex-adjusted RRs and the fully adjusted RRs were slightly elevated ($\sim$1.04) during the first decade, 1973–1982, but were essentially 1.0 during the next two decades. Among the subgroups, the fully adjusted 1973–2002 RRs were slightly elevated (1.03) for females and younger subjects (those born during 1908–1929) and consistent with 1.0 for the others.

Table 6 shows the relationship of 1973–1982 mortality to 1979–1983 $PM_{2.5}$ levels for all subjects and for the same selected subgroups. The fully adjusted RRs were significantly elevated above 1.0 for all subjects (1.04), for females (1.05), for younger subjects (1.06), for the least educated (1.07), for former smokers (1.06), and for the healthy (1.05). Table 7 shows the relationship of 1983–2002 mortality to 1979–1983 $PM_{2.5}$ levels for all subjects and for the subgroups. Results for the entire 20 years are shown because they are virtually the same as the separate results for 1983–1992 and 1993–2002. The fully adjusted RRs were not elevated above 1.0 for any subgroup during 1983–2002. Taken as a whole, these results suggest there was a weak relationship between fine particulate pollution and mortality during 1973–1982, but none during 1983–2002. However, because of statistical fluctuation, effects of up to a 2% increase in mortality per 10 $\mu g/m^3$ of $PM_{2.5}$ cannot be ruled out during 1983–2002.

Sensitivity Analysis of Relative Risks

Table 8 presents a sensitivity analysis to determine the extent to which the RRs in Tables 5–7 were influenced by the confounding variables that were used. It shows the RRs during 1973–2002, 1973–1982, and 1983–2002 based on sequential proportional hazards regression models, beginning with 1979–1983 $PM_{2.5}$ as the only independent variable and then adding age, sex, and nine confounding variables, one at a time. The results were not particularly sensitive to the addition of any of the variables except age and cigarette smoking status. It is unknown how much the RRs would be changed if $PM_{2.5}$ data were available for years before and after 1979–1983. None of the RRs during 1973–2002 and 1983–2002 were significantly elevated above 1.0 after adjustment for age, but the RRs have

TABLE 5

Relative risk of death from all causes (RR and 95% CI) during 1/1/1973–12/31/2002 associated with change of 10 $\mu g/m^3$ in 1979–1983 PM$_{2.5}$, with subgroups defined by decade of follow-up, sex, year of birth, education level, cigarette smoking status as of 10/1/1972, and health status as of 10/1/1959

| | | Model based on 1979–1983 PM$_{2.5}$ | |
| | | Age-sex-adjusted | Fully adjusted |
Subgroups	Deaths/subjects	RR (95% CI)	RR (95% CI)
All subjects during each decade of full follow-up period (1/1/1973–12/31/2002)			
1/1/1973–12/31/1982	8795/35,783	1.032 (1.003–1.062)	1.039 (1.010–1.069)
1/1/1983–12/31/1992	10,821/26,988	0.989 (0.964–1.015)	0.996 (0.970–1.022)
1/1/1993–12/31/2002	8825/16,167	0.997 (0.969–1.026)	0.999 (0.970–1.028)
Subjects during full follow-up period (1/1/1973–12/31/2002)			
All subjects	28,441/35,783	1.005 (0.989–1.021)	1.010 (0.994–1.026)
All males	13,532/15,573	0.996 (0.973–1.020)	0.993 (0.970–1.016)
All females	14,909/20,210	1.013 (0.991–1.035)	1.027 (1.005–1.050)
Born 1908–1929 (1973 age 43–64)	13,354/20,086	1.022 (0.998–1.046)	1.027 (1.003–1.052)
Born 1873–1907 (1973 age 65–99)	15,082/15,697	0.991 (0.970–1.013)	0.996 (0.975–1.018)
<12 yr education	8025/9079	1.016 (0.987–1.047)	1.018 (0.989–1.049)
12 yr education	6346/8557	1.002 (0.969–1.037)	1.005 (0.972–1.040)
>12 yr education	14,070/18,147	0.998 (0.976–1.021)	1.007 (0.984–1.030)
Never smoker	11,528/15,181	1.020 (0.995–1.045)	1.019 (0.994–1.044)
Former smoker	10,074/12,400	1.005 (0.978–1.032)	1.005 (0.978–1.032)
Current smoker	6839/8202	1.003 (0.971–1.036)	0.999 (0.967–1.032)
Healthy	22,234/28,461	1.006 (0.988–1.024)	1.010 (0.992–1.028)
Unhealthy	5456/6439	0.981 (0.945–1.018)	0.993 (0.957–1.030)

TABLE 6

Relative risk of death from all causes (RR and 95% CI) during 1/1/1973–12/31/1982 associated with change of 10 $\mu g/m^3$ in 1979–1983 PM$_{2.5}$, with subgroups defined by sex, year of birth, education level, cigarette smoking status as of 10/1/1972, and health status as of 10/1/1959

| | | Model based on 1979–1983 PM$_{2.5}$ | |
| | | Age-sex-adjusted | Fully adjusted |
Subgroups	Deaths/subjects	RR (95% CI)	RR (95% CI)
Subjects during initial decade of follow-up (1/1/1973–12/31/1982)			
All subjects	8795/35,783	1.032 (1.003–1.062)	1.039 (1.010–1.069)
All males	4701/15,573	1.027 (0.988–1.067)	1.029 (0.990–1.069)
All females	4094/20,210	1.039 (0.996–1.083)	1.052 (1.009–1.096)
Born 1908–1929 (1973 age 43–64)	2637/20,086	1.062 (1.006–1.120)	1.064 (1.008–1.122)
Born 1873–1907 (1973 age 65–99)	6158/15,697	1.021 (0.988–1.056)	1.031 (0.997–1.066)
<12 yr education	3123/9079	1.064 (1.015–1.115)	1.072 (1.023–1.124)
12 yr education	1686/8557	1.045 (0.980–1.115)	1.046 (0.981–1.116)
>12 yr education	3986/18,147	1.001 (0.960–1.045)	1.011 (0.969–1.055)
Never smoker	3425/15,181	1.038 (0.993–1.086)	1.038 (0.992–1.085)
Former smoker	3264/12,400	1.059 (1.011–1.110)	1.058 (1.010–1.109)
Current smoker	2106/8202	1.014 (0.957–1.075)	1.009 (0.952–1.069)
Healthy	6432/28,461	1.043 (1.009–1.078)	1.050 (1.016–1.085)
Unhealthy	2104/6439	0.981 (0.925–1.040)	0.991 (0.935–1.051)

TABLE 7

Relative risk of death from all causes (RR and 95% CI) during 1/1/1983–12/31/2002 associated with change of 10 μg/m^3 in 1979–1983 PM$_{2.5}$, with subgroups defined by sex, year of birth, education level, cigarette smoking status as of 10/1/1972, and health status as of 10/1/1959

Subgroups	Deaths/subjects	Model based on 1979–1983 PM$_{2.5}$	
		Age-sex-adjusted RR (95% CI)	Fully adjusted RR (95% CI)
Subjects during last two decades of follow-up (1/1/1983–12/31/2002)			
All subjects	19,646/26,988	0.992 (0.973–1.011)	0.997 (0.978–1.016)
All males	8831/10,872	0.979 (0.951–1.008)	0.974 (0.947–1.003)
All females	10,815/16,116	1.003 (0.978–1.029)	1.018 (0.992–1.044)
Born 1908–1929 (1983 age 53–74)	10,717/17,449	1.012 (0.986–1.040)	1.018 (0.992–1.046)
Born 1873–1907 (1983 age 75–99)	8929/9539	0.972 (0.945–0.999)	0.975 (0.948–1.002)
<12 yr education	4902/5956	0.987 (0.950–1.025)	0.986 (0.949–1.024)
12 yr education	4660/6871	0.985 (0.947–1.026)	0.990 (0.951–1.030)
>12 yr education	10,084/14,161	0.997 (0.970–1.024)	1.005 (0.978–1.032)
Never smoker	8103/11,756	1.011 (0.982–1.042)	1.011 (0.981–1.041)
Former smoker	6810/9136	0.979 (0.947–1.012)	0.980 (0.949–1.013)
Current smoker	4733/6096	0.999 (0.961–1.039)	0.996 (0.958–1.036)
Healthy	15802/22,029	0.990 (0.969–1.012)	0.994 (0.973–1.015)
Unhealthy	3352/4335	0.980 (0.935–1.028)	0.995 (0.949–1.043)

upper confidence intervals as high as 1.028. All of the RRs during 1973–1982 were significantly elevated about 1.0, with upper confidence intervals as high as 1.071. Based on their large χ^2 values, the variables of age, sex, and cigarette smoking status were by far the most important variables in the model. After inclusion of age, sex, and cigarette smoking status, the addition of the next 7 independent variables changed the RRs by only about 0.1%. When initial health status was entered as an additional

TABLE 8

Relative risk of death from all causes (RR and 95% CI) during 1/1/1973–12/31/2002, 1/1/1973–12/31/1982, and 1/1/1983–12/31/2002 associated with change of 10 μg/m^3 in 1979–1983 PM$_{2.5}$, by individual confounding variables defined as of 1959, except for 1972 cigarette smoking; Age, sex, and nine confounding variables are added to the proportional hazards regression model one variable at a time

Cumulative PHREG model based on adding one variable at a time	1973–2002 Chi-square	1973–2002 RR (95% CI)	1973–1982 RR (95% CI)	1983–2002 RR (95% CI)
1979–1983 PM$_{2.5}$	0.68	1.029 (1.012–1.045)	1.058 (1.028–1.089)	1.016 (0.996–1.035)
+Age	14,445.92	1.003 (0.987–1.019)	1.029 (1.000–1.059)	0.991 (0.972–1.010)
+Sex	464.16	1.005 (0.989–1.021)[a]	1.032 (1.003–1.062)[a]	0.992 (0.973–1.011)[a]
+Cigarette smoking	1,610.59	1.011 (0.995–1.028)	1.041 (1.012–1.071)	0.998 (0.979–1.017)
+Race	0.93	1.011 (0.995–1.027)	1.041 (1.012–1.071)	0.997 (0.978–1.017)
+Education	53.67	1.011 (0.995–1.027)	1.041 (1.012–1.071)	0.997 (0.978–1.016)
+Martial status	26.16	1.011 (0.995–1.027)	1.041 (1.012–1.071)	0.997 (0.978–1.016)
+Body mass index	91.87	1.010 (0.994–1.026)	1.040 (1.011–1.070)	0.996 (0.977–1.016)
+Occupational exposure	3.28	1.010 (0.994–1.026)	1.040 (1.011–1.070)	0.996 (0.977–1.016)
+Exercise	0.02	1.010 (0.994–1.026)	1.039 (1.010–1.069)	0.997 (0.978–1.016)
+Fruit/fruit juice intake	42.54	1.010 (0.994–1.026)[b]	1.039 (1.010–1.069)[b]	0.997 (0.978–1.016)[b]
+Health status	156.15	1.007 (0.991–1.023)	1.036 (1.006–1.066)	0.994 (0.975–1.013)

[a]Age-sex-adjusted RR.

[b]Eight-variable fully adjusted RR.

TABLE 9
Fully-adjusted relative risk of death from all causes (RR and 95% CI) by cigarette smoking status as of 10/1/1972, during 1973–2002, 1973–1982, and 1983–2002 for both sexes, for the California CPS subjects in 11 counties with 1979–1983 PM$_{2.5}$ measurements, which were used as one of the confounding variables

Cigarette smoking status as of 10/1/1972	Fully adjusted 1973–2002 RR (95% CI)	Fully adjusted 1973–1982 RR (95% CI)	Fully adjusted 1983–2002 RR (95% CI)
Deaths/subjects	28,447/35,789	8801/35,789	19,646/26,988
Never (as of 1959 and 1972)	1.000	1.000	1.000
Former (as of 1959 and 1972)	1.054 (1.014–1.096)	1.061 (0.987–1.140)	1.049 (1.001–1.100)
Former (as of 1972 only)	1.253 (1.212–1.295)	1.312 (1.236–1.392)	1.224 (1.176–1.273)
Current: 1–9 cpd (as of 1972)	1.239 (1.150–1.336)	1.227 (1.065–1.414)	1.243 (1.138–1.357)
Current: 10–19 cpd (as of 1972)	1.597 (1.510–1.688)	1.667 (1.508–1.842)	1.566 (1.465–1.675)
Current: 20 cpd (as of 1972)	1.871 (1.791–1.953)	1.829 (1.689–1.980)	1.887 (1.792–1.987)
Current: 21–39 cpd (as of 1972)	2.068 (1.936–2.210)	1.889 (1.666–2.140)	2.145 (1.984–2.320)
Current: 40+ cpd (as of 1972)	2.543 (2.375–2.723)	2.460 (2.189–2.765)	2.587 (2.378–2.814)
Chi-square test of homogeneity (7 degrees of freedom)	$\chi^2 = 1701.75$ $p < .0001$	$\chi^2 = 478.14$ $p < .0001$	$\chi^2 = 1232.17$ $p < .0001$

Note. cpd, cigarettes per day.

independent variable, the RRs decreased by 0.3%. However, initial health status was not one of the eight confounding variables used in calculating the fully adjusted RRs in the other tables, because it may have been influenced by exposure to air pollution before entry into the study.

Relative Risks by 1972 Cigarette Smoking Level

Table 9 shows the fully adjusted RRs for eight levels of 1972 cigarette smoking, the strongest confounding variable in this study. Note there was a strong and clear dose-response relationship during 1973–2002. The dose-response relationship remained as strong during 1983–2002 as it was during 1973–1982, in spite of the large degree of smoking cessation that occurred from 1972 to 1999, as documented in Tables 1 and 2. This comparison supports the findings of an earlier paper, which examined smoking cessation and mortality trends in this cohort during 1960–1997 (Enstrom & Heath, 1999). The Wald chi-square test of homogeneity for each of the three follow-up periods, where $\chi^2 > 478$ for 7 degrees of freedom, clearly rejects the hypothesis that the RRs are equal (homogeneous). The large RRs related to increasing cigarette smoking level are shown here in order to put the RRs related to increasing PM$_{2.5}$ level in Table 4 in perspective.

DISCUSSION

Strengths and Uncertainties of This Study

This study has several important strengths: a large, diverse cohort of males and females distributed throughout California, a large number of deaths, extensive baseline and follow-up data on demographic and lifestyle characteristics, long-term follow-up of a high percentage of subjects, relative stability of sub-

jects based on their residential address history, and availability of PM$_{2.5}$ measurements for over 70% of the subjects. In addition, there is a wide range of PM$_{2.5}$ levels (10.6 to 42.0 μg/m^3) available for subjects in 11 counties. Although the CA CPS I cohort is not a random sample of the California population, previous examination has shown that mortality ratios based on cigarette smoking status are similar in this cohort (Enstrom & Heath, 1999) and in a cohort representative of the US population (Enstrom, 1999).

The results of this study, as in all epidemiology studies, are dependent upon the underlying data and the analytical methods that were used. Major uncertainties include the extent to which the available air quality data represent actual exposures, the validity of the proportional hazards regression calculations of the RRs, and the potentially important confounders that may have been omitted from the analysis.

The PM$_{2.5}$ air quality data are limited to 11 California counties and 8 of these counties had only one outdoor monitoring station each. The period of monitoring was from July 1979 to December 1983 and most counties had data for just a two to three year period. These sample data are assumed to represent long-term personal exposures of each subject based on their county of residence in late 1972. The validity of this assumption has not heen confirmed, but these same limited data have been used in other major cohort studies (Pope et al., 1995, 2002; Lipfert et al., 2000, 2003).

The assumption that individual exposures are the same as county-wide averages, as measured by a few centrally-located monitors, can result in the "ecological fallacy," where results based on group averages differ from those based on individual exposures (Piantadosi et al., 1988). However, it is impractical to monitor individual exposures for a large cohort, especially

TABLE 10

Relative risk (RR) and 95% confidence interval (CI) for long-term all-cause mortality per 10-μg/m^3 increase in PM$_{2.5}$ for U.S. cohort studies based on PM$_{2.5}$ data, circa 1980

Study (author, year)	PM$_{2.5}$ Data period	PM$_{2.5}$ Mean (range) (μg/m^3)	Study characteristics Cohort geographic definition	Follow-up period	Mean entry age for period	Number entered in cohort	Deaths in follow-up period	RR (95% CI)
Males								
Dockery et al., 1993	1979–1985	19 (11–30)	6 U.S. cities	1975–1989	~50	3671[a]	830[a]	1.15 (1.02–1.30)[b]
Pope et al., 1995	1979–1981	18 (9–34)	50 U.S. SMSAs	1982–1989	57	130,310[a]	~12,400[a]	1.07 (1.03–1.11)[b]
McDonnell et al., 2000	1973–1977	32 (17–45)	9 CA airsheds	1976–1992	58	≤1347	≤375	1.09 (0.98–1.21)[b]
Lipfert et al., 2000	1979–1981	24 (6–42)	42 U.S. counties	1975–1981	51	26,067	~4600[c]	0.95 (0.89–1.01)[c]
	1982–1984	22 (8–41)		1982–1988	57	~21,467	~6100[c]	0.94 (0.90–0.98)[c]
	1982–1984	22 (8–41)		1989–1996	63	~15,367	~5765[c]	0.89 (0.85–0.95)[c]
Pope et al., 2002	1979–1983	21 (10–30)	61 U.S. SMSAs	1982–1998	57	~159,000[a]	~36,000[a]	1.05 (1.01–1.10)
Enstrom, 2005	1979–1983	24 (11–42)	11 CA counties	1973–1982	66	15,573	4701	1.03 (0.99–1.07)
	1979–1983	24 (11–42)		1983–2002	74	10,872	8831	0.97 (0.95–1.00)
Females								
Dockery et al., 1993	1979–1985	19 (11–30)	6 U.S. cities	1975–1989	~50	4440[a]	599[a]	1.12 (0.96–1.30)[b]
Pope et al., 1995	1979–1981	18 (9–34)	50 U.S. SMSAs	1982–1989	57	164,913[a]	~8365[a]	1.06 (1.01–1.12)[b]
McDonnell et al., 2000	1973–1977	32 (17–45)	9 CA airsheds	1976–1992	58	≤2422	≤568	~1.00 (assumed)
Pope et al., 2002	1979–1983	21 (10–30)	61 U.S. SMSAs	1982–1998	57	~200,000[a]	~24,000[a]	1.02 (0.98–1.06)
Enstrom, 2005	1979–1983	24 (11–42)	11 CA counties	1973–1982	65	20,210	4094	1.05 (1.01–1.10)
	1979–1983	24 (11–42)		1983–2002	73	16,116	10,815	1.02 (0.99–1.04)
Both Sexes								
Dockery et al., 1993	1979–1985	19 (11–30)	6 U.S. cities	1975–1989	~50	8111	1430	1.13 (1.04–1.23)[b]
Pope et al., 1995	1979–1981	18 (9–34)	50 U.S. SMSAs	1982–1989	57	295,223	20,765	1.07 (1.04–1.10)[b]
Pope et al., 2002	1979–1983	21 (10–30)	61 U.S. SMSAs	1982–1998	57	~359,000	~60,000	1.04 (1.01–1.08)
Enstrom, 2005	1979–1983	24 (11–42)	11 CA counties	1973–1982	65	35,783	8795	1.04 (1.01–1.07)
	1979–1983	24 (11–42)		1983–2002	73	26,988	19,646	1.00 (0.98–1.02)

[a]Obtained from supplementary data (Krewski et al., 2000).

[b]Recalculated from published data (US EPA, 2004).

[c]Obtained from the author.

over the long-term. This analysis used the smallest practical geographic unit (counties), given typical mobility of the subjects, in hopes of minimizing exposure errors.

The relative risk results are all based on Cox proportional hazards regression (PHREG), which has been used in numerous cohort survival analyses. This statistical methodology depends on the assumption of proportionality (SAS, 2004). The validity of this assumption with respect to the $PM_{2.5}$ variable has heen confirmed for most RRs in Tables 3–9 by the Kolmogorov-type supremum test of functional form (SAS, 2004). Also, previous findings on cigarette smoking and mortality in this cohort showed that relative risks based on proportional hazards regression were similar to relative risks based on life table survival analysis (Enstrom & Heath, 1999).

With respect to the impact of additional potential confounding variables, ecological variables at the county level, such as climate, were explored and found to be uncritical. The analyses based on the eight-variable model found that after age and sex adjustment only one confounding variable, cigarette smoking status, had much impact on the RRs. Indeed, each fully-adjusted RR was within 1.5% of the corresponding age-sex-adjusted RR.

Comparisons with Other Cohort Studies

In Table 10 the major findings in this study are compared with those of the other U.S. cohort studies based on $PM_{2.5}$ data, circa 1980. The basic characteristics and relative risks for all-cause mortality are given for all six studies, where each relative risk (RR and 95% CI) is based on a 10 $\mu g/m^3$ increase in $PM_{2.5}$. The RRs were standardized to the extent possible by using the same conversion of published results that was used by the EPA in their latest criteria document on particulate matter (US EPA, 2004). For instance, the RR of 1.07 (1.04–1.10) during 1982–1989 for both sexes in the ACS CPS II study (Pope et al., 1995) is based on a mortality difference of 17% between the highest and lowest $PM_{2.5}$ areas and a $PM_{2.5}$ difference of 25 $\mu g/m^3$. By comparison, the RR of 1.00 (0.98–1.02) during 1983–2002 among both sexes in the current CA CPS I study is based on a $PM_{2.5}$ variation up to 31 $\mu g/m^3$ among 11 counties.

The RRs in Table 10 range from 0.89 to 1.15 and each corresponding 95% CI either includes 1.0 or is within 0.05 of including 1.0. Thus, the relationship between $PM_{2.5}$ and mortality is very weak and near the limit of detectability by epidemiologic methods. In order to define this relationship as accurately as possible, it is important to understand the differences that exist between the RRs. These differences could be due to the epidemiologic methodology used or they could be due to the characteristics of the study cohorts, such as their geographic location, follow-up period, demographics, and size. For instance, the RR of 1.07 in the ACS CPS II study is the average relationship between $PM_{2.5}$ level and mortality in 50 areas of the U.S. However, detailed reanalysis of this study reveals substantial geographic variation in the relationship (Krewski et al., 2000). In particular, a map of $PM_{2.5}$ levels and relative risk of mortality throughout the U.S. (Figure 21) shows that most areas of Califor-

nia had medium mortality risk and no areas had high mortality risk. This pattern suggests that the relationship between $PM_{2.5}$ and mortality among the California subjects in the CPS II cohort was weaker than the RR of 1.07 and consistent with the RR of 1.00 found in the CA CPS I cohort.

It is clear from Table 10 that no single result can adequately describe the relationship between $PM_{2.5}$ and mortality for the entire country. The complete body of epidemiologic evidence should be used to assess this relationship as accurately as possible within the limitations of epidemiologic methodology. A full comparative examination of the available cohort studies is warranted. Ideally, a standardized method of analysis should be applied to the underlying data in each cohort and the results should be presented in a standardized way. Such an analysis would make a substantial contribution to the research priorities for particulate matter (National Research Council, 2004).

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APPENDIX TABLE 1

1979–1983 PM$_{2.5}$ ("FINE15") data in California from the EPA Inhalable Particulate Network by county and monitoring site (Hinton et al., 1984, pages 108–113; Hinton et al., 1986, pages 53–55; Sune, 1999).

| County | City (Street) | SAROAD site | Monitoring period | Samples | Site PM$_{2.5}$ ($\mu g/m^3$) | | County PM$_{2.5}$ ($\mu g/m^3$) |
					Mean	SD	Mean
Santa Barbara	Lompoc	054080002A07	03-29-81 to 12-31-82	91	10.631	4.649	10.627
			01-06-83 to 03-01-83	8	10.586	4.062	
Contra Costa	Richmond	056300003A07	09-24-79 to 10-14-82	167	13.920	11.333	13.920
Alameda	Livermore (Railroad Ave)	054020002A07	09-24-79 to 12-17-80	58	17.398	15.547	14.389
	Livermore (Old First St)	054020003A07	03-29-81 to 08-21-82	82	12.260	8.654	
Butte	Chico	051260002A07	03-24-82 to 08-15-82	25	9.992	4.073	15.453
			01-24-83 to 12-26-83	50	18.183	10.793	
San Francisco	San Francisco East	056860003A07	11-22-79 to 09-14-82	115	16.352	12.676	16.352
Santa Clara	San Jose	056980004A07	09-30-79 to 10-14-82	174	17.788	16.487	17.788
Fresno	Fresno (East Olive)	052800005A07	09-14-82 to 09-20-82	2	10.315	0.728	18.373
	Five Points	052820002A07	09-30-79 to 10-20-82	153	18.478	17.535	
San Diego	El Cajon	052220003A07	09-25-81 to 12-31-82	66	19.873	13.929	18.919
			01-06-83 to 08-04-83	29	16.747	11.992	
Los Angeles	Azusa (Loren Ave)	050500002A07	10-18-79 to 11-07-82	92	28.765	19.200	28.224
	West Los Angeles	054180103A07	07-08-79 to 10-14-82	147	26.752	18.667	
	Pasadena	057760004A07	10-18-79 to 12-12-81	28	34.174	16.857	
Kern	Bakersfield (Chester Ave)	050520004A07	11-17-80 to 12-01-82	53	30.803	29.190	30.863
			01-18-83 to 01-30-83	3	31.920	30.178	
Riverside	Rubidoux (Mission Blvd)	056535001A07	08-19-79 to 12-31-82	127	43.337	28.669	42.012
			01-06-83 to 06-05-83	15	30.791	33.864	