Asthma Mortality in California, 1960–1989

Demographic Patterns and Occupational Associations

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We analyzed asthma mortality rates in California during the years 1960 to 1989. Sex- and race-specific rates were stratified by age group (0 to 4, 5 to 34, 35 to 64, and 65+ yr) and for all ages directly standardized to the 1970 U.S. age distribution. Observed and expected asthma deaths were also calculated by occupation for the period 1979 to 1981 among persons aged 16 to 64 yr using data from the California Occupational Mortality Study. Asthma mortality rates were strongly associated with increasing age, but no consistent differences were observed between men and women. Mortality rates among blacks under age 65 yr were two to four times the corresponding rate among whites between 1960 and 1989, but this difference was not observed for those over age 65. Asthma mortality rates were calculated for Hispanics and Asians from 1985 to 1989. In this time period the asthma mortality rate ratios for Hispanics were 0.4 to 0.8 compared with the age-stratified rates among whites, 0.1 to 0.2 times the black rates in age categories under 65, and 0.5 times the rate for blacks ages 65 and above. Asthma mortality rates among Asians under 65 yr of age were similar to rates for whites, but for Asians 65 yr of age and over the rate ratios for males and females compared with whites were 1.8 and 1.1, respectively. A decrease of approximately 50% in asthma mortality occurred from 1960 to 1970, and a marked increase occurred between 1975 and 1989. The rate of increase since 1975 was greater in blacks than in whites and greater in females than in males. For asthma deaths in 1979 to 1981, significant increases in mortality were observed for carpenters (O/E = 3.6; 95% CI 1.6, 6.9) and police and guards (O/E = 2.9; 95% CI 1.3, 5.6). Several other occupations had increased rate ratios that did not achieve statistical significance. Further research is indicated on the association of occupational exposures and asthma mortality.

An increase in asthma mortality rates since the mid- to late 1970s has been reported in several countries around the world (1–7). Although asthma mortality is lower in the United States than in most other industrialized countries, a similar pattern of increase in asthma mortality has been observed in this country (2, 8, 9). In addition morbidity data have shown a concomitant increase in prevalence and hospitalization rates for asthma in the United States (10). The increase in U.S. asthma mortality rates has been observed for all ages, and mortality rates have been consistently higher among blacks than among whites (2, 8–11). However, mortality rates have not been reported among Hispanics, and this was possible in California's large Hispanic population.

Although a consistent epidemiologic picture of an increase in asthma mortality has been observed, there has been variability in the geographic patterns of asthma deaths. For example, asthma mortality rates for blacks aged 5 to 34 have been highest in the Northeast and North Central regions of the United States, but among whites higher rates have been observed in the West (12). Analysis by smaller geographic areas has suggested that excess rates may be occurring in some large urban metropolitan areas across the United States, but increases have also been observed in suburban and rural areas (13, 14).

Numerous explanations have been suggested for the increase in asthma mortality, including inappropriate or deficient care and excessive exposures, but there is as yet no consistent explanation for this worldwide phenomenon (8, 9, 15–17). Although occupational and environmental factors are a known cause of asthma, there has been little investigation of these factors in relation to the rise in asthma mortality (18).

California is the most populous state in the country, and the availability of cause-specific mortality data for California since 1960 permitted analysis of asthma mortality trends among whites and blacks over a 30-yr period. Asthma mortality among Hispanics and Asians was analyzed only between 1985 and 1989 because of changes in racial coding in the census. Access to the California Occupational Mortality Study (COMS) data (19) permitted analysis of occupational associations with asthma mortality between 1979 and 1981.

METHODS

The International Classification of Disease (ICD) codes were used to classify deaths due to asthma and to other respiratory causes of death (table 1). A National Institute of Occupational Safety and Health life table program was used for deriving comparable codes for ICD-7, ICD-8, and ICD-9 (20).

Sex-, age-, and race-specific asthma mortality rates were calculated for the state as a whole for the years 1960 through 1989 and for individual California counties for 1980 through 1989. Age-adjusted rates were also calculated and directly standardized to the 1970 U.S. standard population, with each rate age adjusted by 10-yr age groups. Rates were calcu-

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TABLE 1

CODES FOR ICD-7, -8, AND -9 USED FOR CAUSE-SPECIFIC MORTALITY ANALYSES

Cause of Death	ICD-7	ICD-8	ICD-9
Asthma	241	493	493
Lung cancer	162, 163	162	162
Chronic and unspecified bronchitis	501–502	490–491	490–491
Acute respiratory infection	470–475, 500	460–466	460–466
Emphysema	527.1	492	492
Pneumoconiosis and other respiratory disease*	510–527.0 527.2	500–519	470–478 494–519

* In ICD-9, this group included "chronic obstructive pulmonary disease" (ICD-9 = 496).

lated for individual calendar years and for 5-yr averages. For most analyses, the 5-yr average annual mortality rates were used because of larger numbers and greater statistical stability.

Asthma Deaths

The numerators for all rates were derived from all asthma deaths reported on death certificates in the state during the years 1960 to 1989. The data on causes of death were extracted from the merged death tapes of the California Department of Health Services, Health Data and Statistics Branch. Underlying causes of death as coded by state nosologists were used for all analyses. The possibility of diagnostic labeling bias or a shift from other respiratory diagnoses to asthma was evaluated by comparing age-adjusted mortality rates from other respiratory diagnoses with those for asthma in the "white/other" population (table 1). Death registration in California is considered almost 100% complete, but underregistration may occur for deaths of children under 1 yr of age. Quality control procedures are applied to California death certificates that ensure coding error rates of less than 1% (21).

Population Estimates

Denominators for the death rates were the annual average number of people in each county, sex, race/ethnicity, and age group from 1960 to 1989. These were extracted from computerized census data tapes provided by the California Department of Finance, State Census Data Center. A straight line was used to calculate the midpoint population estimates for 5-yr periods between 1960 and 1990.

Analyses by Race

Categorization of race on death certificates has been modified over the years. From 1960 through 1977 race was categorized as white, black, Alaskan/American Indian, Chinese, Japanese, Filipino, all other, and unknown or not stated. This was modified in 1978 by the use of two fields on the certificate: a race field that was similar to the old one and a new ethnicity field that added four additional groups: Mexican-American, Hawaiian, Vietnamese, and other Spanish Hispanics. This was again modified in 1985 by adding a more detailed list of Asians and Pacific Islanders in the ethnicity field and by further breakdown of the Spanish and Hispanic category.

Race definitions for the 1960, 1970, and 1980 censuses of population have also changed over the years, particularly for Hispanics. In 1970, 93% of persons of Spanish origin in California were classified as white and only 1% as other. In 1980 only 56% of persons of Spanish origin were classified as white and approximately 40% as other (22). Consequently, 1980 population totals for white and other are not comparable with the corresponding 1970 figures. Thus, it was not possible to consider separately trends in asthma mortality since 1960 among Hispanics. To make asthma mortality figures comparable for the analysis of deaths since 1960, we grouped whites and all other races into one category and analyzed blacks as a separate category. Asthma mortality for Hispanics was calculated for 1985 to 1989 only using death certificate classification of ethnicity and an interpolated estimate of Hispanic population from the 1980 and 1990 censuses.

Asthma mortality rates for Asian were calculated by the grouping of five Asiatic populations (Chinese, Japanese, Korean, Filipino, and Vietnamese) and three Pacific Island groups (Hawaiian, Guamanian, and Samoan) in the numerators and denominators. In 1990 about 5% of Asians were of Hispanic origin, and this group was included in the Asian denominator.

Age-specific and Age-adjusted Rates

The age-specific rates were calculated by grouping the cases (numerators) and populations (denominators) into four clinically relevant age groups: 0 to 4, 5 to 34, 35 to 64, and 65+ yr of age. These groupings were also selected for comparability to other reports in the literature (1, 2, 5, 7, 12–14). Age-adjusted rates were directly standardized to the 1970 U.S. age distribution.

Seasonal comparisons of asthma mortality by race for 1960 to 1989 were made by accumulating deaths per month and grouping the appropriate months into seasons. Only total deaths per month and per season summed for all years are presented.

Occupational Mortality Analysis

For the analysis of asthma mortality by occupation, we used data from the California Occupational Mortality Study, a statewide study of rates based on 180,000 California deaths from 1979 to 1981 among persons aged 16 to 64, and U.S. Census estimates of occupations in California (19). Occupations listed on death certificates reflect "usual" occupation, and they were coded using the methods of the 1980 U.S. Census. Occupations were grouped into the 68 standard occupational categories used in the COMS, and only occupational categories with five or more deaths were analyzed. All deaths were included for which the underlying cause was coded as asthma under the Eighth Revision of the International Classification of Diseases (ICD = 493).

Asthma mortality rates in each occupation were compared with the rates for all occupations combined using the standardized mortality ratio (SMR), which is the ratio of the observed to expected numbers of deaths. Expected numbers of deaths were calculated by multiplying the race-, sex-, and age-specific asthma rates for all occupations combined times the 1980 California census population estimates for each occupation. Results were divided by 3 to produce average annual rates. Mortality ratios were adjusted for race, sex, and age using a computer program designed for analysis of census-based occupational mortality data (23). The categories for age adjustment were 16 to 44, 45 to 54, and 55 to 64. Confidence intervals and probabilities were calculated for the mortality rates with exact Poisson procedures when the observed numbers of deaths were six or fewer and with Byar approximations to the exact test when the observed deaths were greater than six (24).

RESULTS

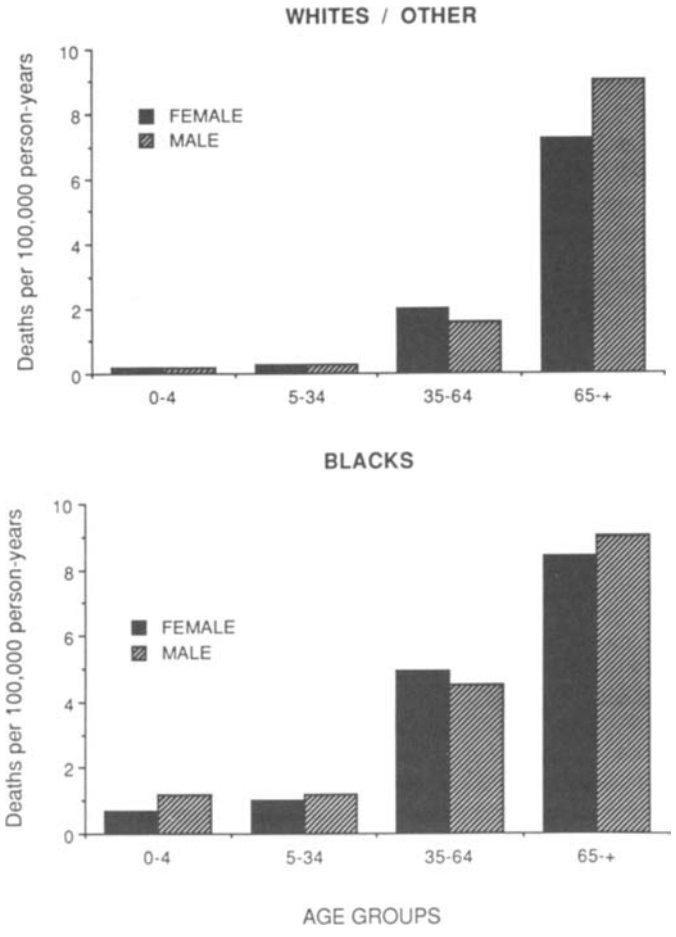
Between 1960 and 1989 there were 10,526 recorded deaths due to asthma in California, or approximately 350 deaths per year. For the years 1985 to 1989, the annual number of deaths was 528, of which 69% were among whites (mean = 363.2/yr), 14% among blacks (mean = 74.0/yr), 8% among Hispanics (mean = 42.0/yr), 7% among Asians (mean = 39.2/yr), and 2% among other races or ethnic groups (mean = 9.6/yr).

Age

Asthma mortality rates were strongly associated with increasing age (figure 1). For deaths under 35 yr of age, the mortality rate was generally less than 1 per 10^5 person-years. In the 35- to 64-yr-old age range, overall asthma mortality rates averaged 2 to 4 per 10^5 person-year, and in the age group 65 yr and older the average mortality rate for asthma was 7 to 9 per 10^5 person-year.

Gender

Small differences in mortality rates by sex were observed, but they did not show a consistent pattern among age groups (figure 1). For deaths occurring under 5 yr of age, mortality rates were slightly



greater among males than among females for most years since 1960 (data not shown). Among whites, there was little difference by sex in this age group, but among blacks, rates for males under 5 yr of age were approximately twice the rate for females. Only small differences in asthma mortality rates by sex were present between 5 and 64 yr of age. Among blacks over 65 yr of age, asthma mortality rates were greater among males than among females for most time periods from 1960 to 1989. However, a different pattern was observed among whites when gender was examined by year (figure 2). Asthma mortality rates for white males between 1960 and 1969 were approximately twice the rates for white females, but from 1970 through 1989 rates were similar for males and females.

Temporal Trends

A marked decrease in asthma mortality occurred in California from 1960 to 1970 (figures 2 and 3). The decrease represented a steady decline over the decade, not a precipitous decrease in any single year (figure 3). For all asthma deaths, the average annual age-adjusted mortality rates decreased approximately 50% over the 10-yr period. This decrease was observed in all age categories, but the absolute and percentage decreases were greatest for the older age groups. Mortality rates for 1970 to 1974 in the 65+ age category were one-fourth to one-half the rates for the same age group in 1960 to 1964.

Asthma mortality rates increased in California after 1975 (figure 2). Similar to the decline in the 1960s, this increase was a

Figure 1. Age-stratified asthma mortality rates for whites/others and blacks, California, 1960 to 1989.

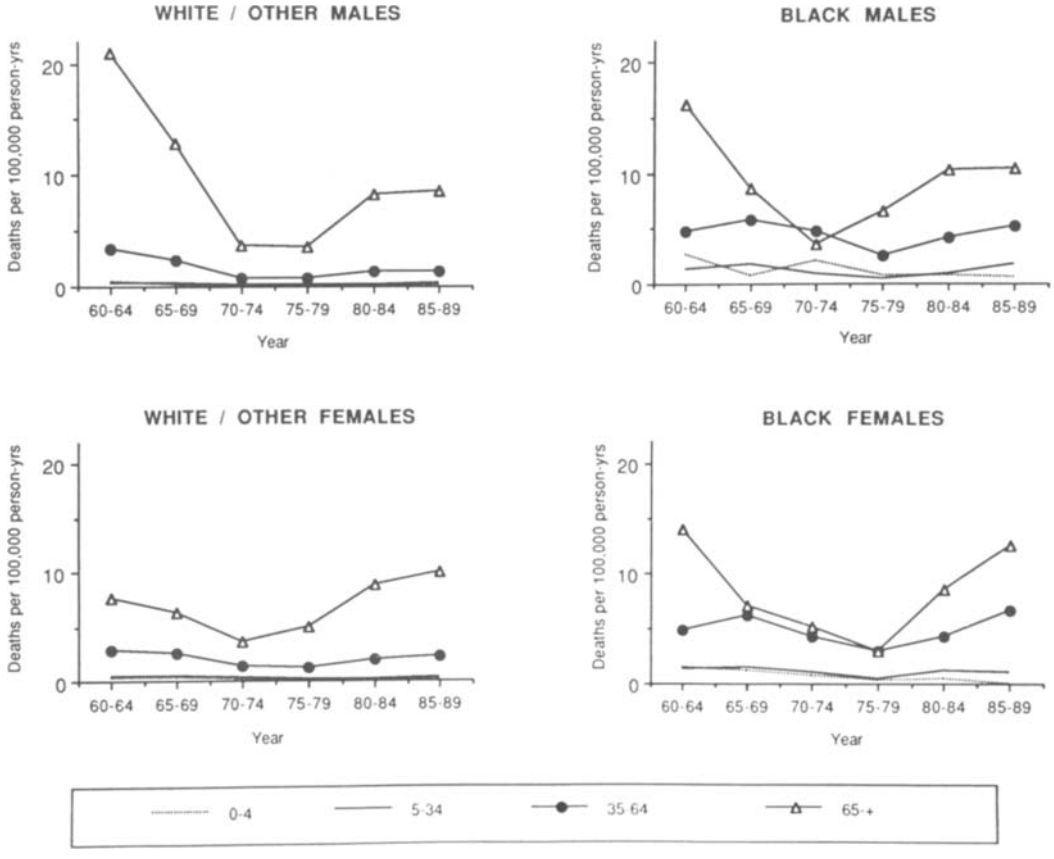


Figure 2. Mortality rates for whites/others and blacks by gender for 5-yr intervals, California, 1960 to 1989.

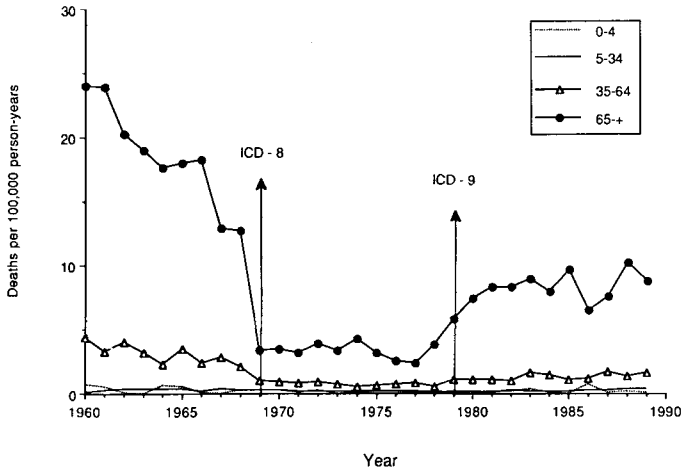


Figure 3. Annual age-specific asthma mortality rates per 100,000 person-years for white/other males, California, 1960 to 1989.

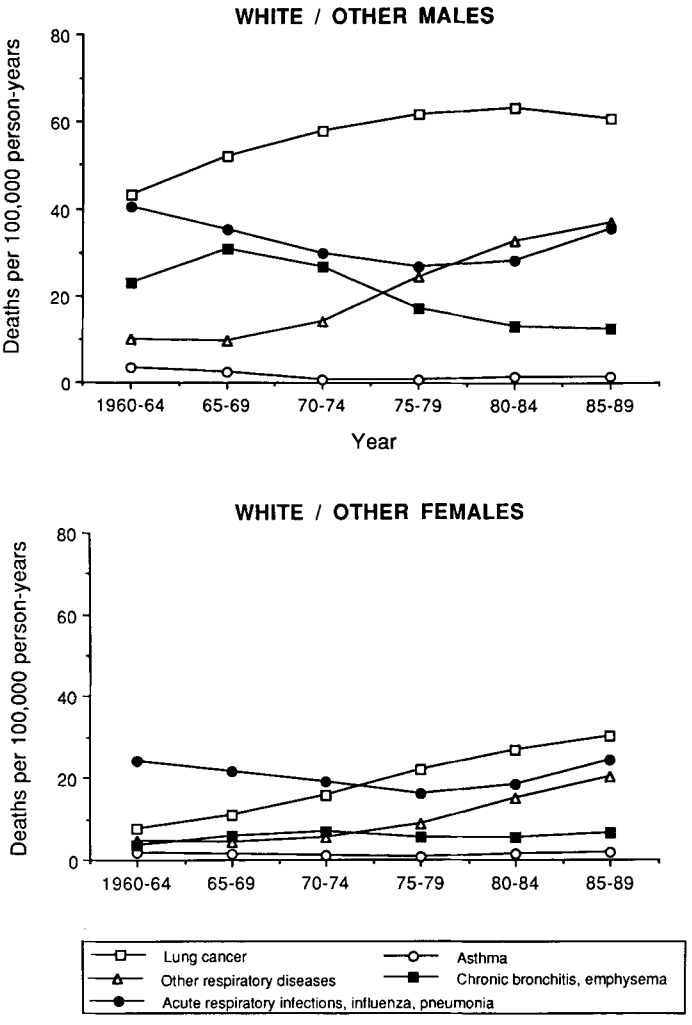


Figure 4. Age-adjusted mortality rates per 100,000 person-years for white/other males and females for asthma and other respiratory causes of death, California, 1960 to 1989.

steady rise, with the greatest increases seen in the older age groups, but increases were observed for all age categories. The percentage increase from the period 1975 to 1979 to 1980 to 1984 was slightly greater among blacks than whites and ranged from a 1.5 to 2.0 times increase in the sex- and race-specific groups (figure 2). From the period 1980 to 1984 to 1985 to 1989, the steep rate of increase in asthma mortality continued among blacks, with rates in 1985 to 1989 becoming similar to those in 1960 to 1964. Among whites, the rate of increase decreased from 1980 to 1984 to 1985 to 1989, with only small increases in mortality occurring over this time interval (figure 2). In the period 1985 to 1989, rates among white females were similar to rates in 1960 to 1964, but the rates for white males were less than half the corresponding rates in 1960 to 1964.

Other Respiratory Disease Mortality

Lung cancer mortality rates increased for men between 1960 and 1984 and for women increased between 1960 and 1989, consistent with national trends (figure 4). Between 1975 and 1979 and 1985 to 1989, deaths due to acute respiratory infections, influenza, and pneumonia also increased for men and women. Deaths coded as chronic bronchitis or emphysema for the underlying cause of death declined slightly for males since the period 1965 to 1969 but showed no change for females. Deaths from other respiratory diseases, including chronic obstructive pulmonary disease (COPD) in ICD-9, have shown a steady increase among men and women since the early 1970s. The apparent absence of much change in the asthma mortality rate in figure 4 results from asthma mortality being plotted on the same scale as other causes of respiratory disease mortality that have much higher rates.

Race

Since 1960, age-adjusted asthma mortality rates in California have been consistently higher among blacks than among whites (figure 5). For the period 1960 to 1964, mortality rates were 1.2 and 1.9 times higher for black males and females than for white males and females, respectively. Between 1985 and 1989, age-adjusted mortality rates for blacks were over twice the rates for whites, which represented the greatest disparity in rates between blacks and whites over the entire 30 yr of this study. The relative difference between blacks and whites was greatest in the younger ages and decreased with increasing age. From 1960 to 1989, ratios of asthma mortality rates for black males and females age 5 to 34 compared with white males and females were 4.0 and 3.3, respectively, and the rate ratios were similarly increased for the 0- to 4-yr age group (data not shown). Blacks also had higher rates than whites in the 35- to 64-yr age group, although the rate ratios were slightly smaller than for the younger age groups (rate ratios = 2.8 and 2.5 for males and females, respectively). However, much smaller and less consistent differences were seen between blacks and whites above 65 yr of age (rate ratios = 1.0 and 1.2 for males and females, respectively).

Asthma mortality rates for Hispanics in 1985 to 1989 were lower than the rates for whites, Asians, or blacks (figure 6). Mortality rates among Hispanics were 0.4 to 0.8 times the comparable age-stratified rates among whites. The difference between Hispanics and blacks was substantially greater, with Hispanic rates 0.1 to 0.2 times the black rate in age categories under 65 and 0.5 times the rate for blacks aged 65 and above.

Among Asians, asthma mortality rates were very similar to rates among whites for females and for males under 65 yr of age (figure 6). Over 65 yr of age, the asthma mortality rate was substantially greater among Asian males than among white males (rate ratio = 1.8, 75.1 versus 41.0 deaths per 10^5 person-year), but among females the rate was only slightly greater among Asians than

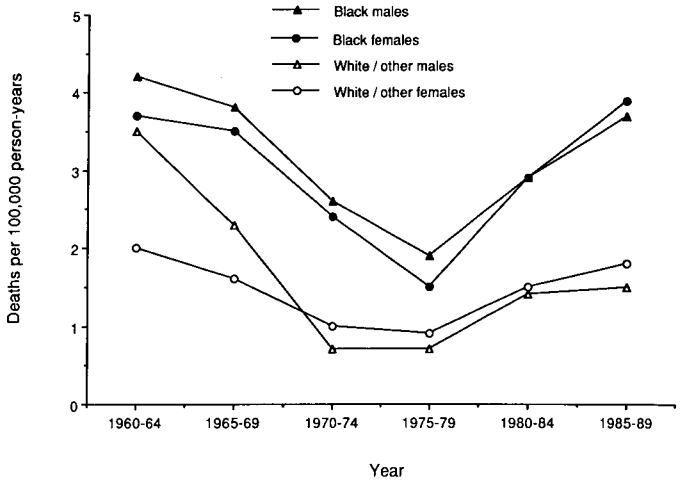


Figure 5. Age-adjusted asthma mortality rates for whites/others and blacks, California, 1960 to 1989.

whites (rate ratio = 1.1, 59.8 versus 52.6 deaths per 10^5 person-year, respectively).

Seasonality

A small seasonal association was observed for asthma deaths in California among cases over 34 yr of age (data not shown). Among whites aged 65 and older, approximately 25% more asthma deaths occurred in the winter and spring than in the summer and fall, and deaths were higher in winter for whites aged 35 to 64. No seasonal variation in asthma deaths was observed for whites or blacks under age 35. Among blacks aged 65 and older, deaths were also highest in the winter and spring.

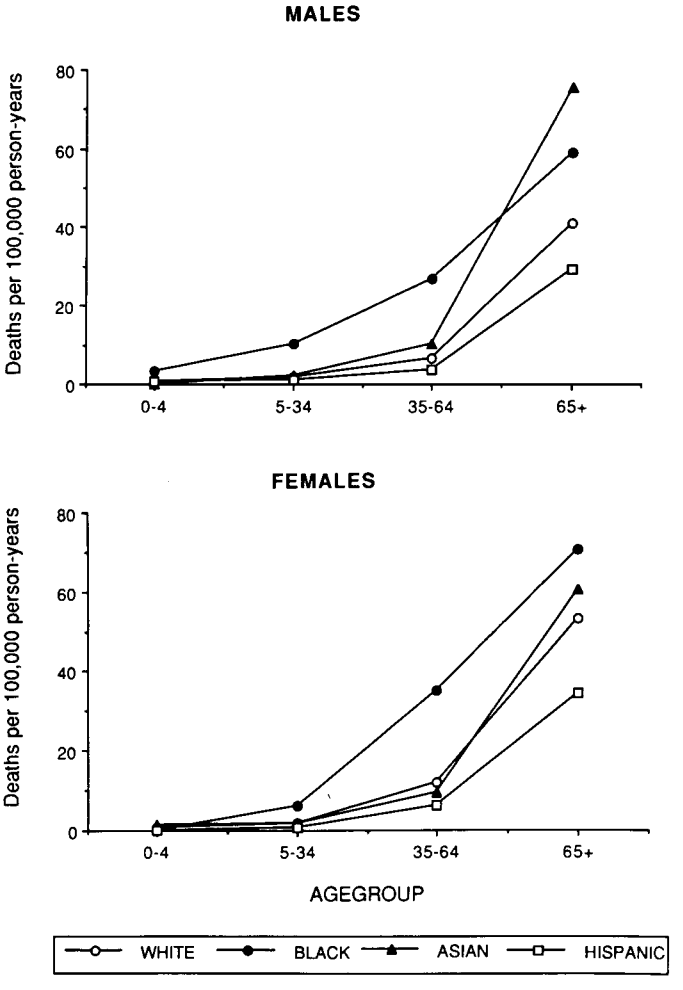


Figure 6. Age- and race-specific mortality rates per 100,000 person-years for Asians, blacks, Hispanics, and whites by gender, California, 1985 to 1989.

Occupation and Industry

The 21 occupations had five or more asthma deaths, and 2 of those had statistically significant excess mortality from asthma: carpenters and police and guards (table 2). The SMR for carpenters was 3.6 (95% confidence interval CI 1.5, 6.9) and for police and guards was 2.9 (95% CI 1.3, 5.6). Asthma mortality was elevated (but differences were not statistically significant) for some other occupational categories, including health aides, other health professionals, and textile workers. Deaths in these latter categories were generally based on small numbers.

DISCUSSION

California is the most populous site in the United States and provides a substantial, multicultural population in which to analyze trends in asthma mortality in a single state over several years. During the 30-yr time period covered by this analysis, there were over 4 million deaths from all causes in California. In addition to the state's ethnic diversity, variety in state geography and industry is associated with diverse home and workplace exposures among the population. Thus, we could compare asthma mortality among a wide range of demographic and occupational factors. However, despite the large population in the state, analyses by subgroups were often limited by small numbers. The analyses were also limited by changes in U.S. Census Bureau and California vital statistics coding of ethnic status over the 30-yr study in-

TABLE 2

ASTHMA DEATHS AND RATE RATIOS FOR SELECTED OCCUPATIONS IN THE CALIFORNIA OCCUPATIONAL MORTALITY STUDY, 1979 TO 1981*

Occupation*	Asthma Deaths	O/E†	95% CI Lower	95% CI Upper
Managers	161	0.6	0.3	1.0
Management-related jobs	8	1.0	0.4	1.9
Architects and engineers	5	0.8	0.2	1.8
Other health professionals	10	1.6	0.8	2.9
Health aides	6	1.5	0.5	3.1
Teachers	11	1.1	0.5	2.0
Other professional specialties	10	1.6	0.7	2.8
Technicians	6	1.3	0.5	2.7
Business salesworkers	6	0.6	0.2	1.2
Retail salesworkers	12	0.9	0.5	1.7
Clerical workers	44	0.9	0.7	1.3
Police and guards	9	2.9‡	1.3	5.6
Cooks	5	1.6	0.5	3.8
Other food service workers	6	1.1	0.4	2.4
Janitors	9	0.8	0.4	1.6
Carpenters	9	3.6‡	1.6	6.9
Metal workers	5	1.3	0.4	2.9
Textile workers	6	2.2	0.8	4.7
Miscellaneous production workers	14	1.4	0.8	2.4
Helpers and laborers	5	1.2	0.4	2.7

* The occupations are those in which there were five or more deaths or the rate ratio was greater than 2.0. Expected rates were based upon rates for all occupations combined, adjusted for age, sex, and race.

† Ratio of observed to expected asthma deaths.

‡ $p < 0.05$.

terval. Death certificate data do not include information on cigarette smoking or socioeconomic factors, which may explain some of the observed associations. Finally, asthma mortality provides only one aspect of asthma epidemiology, and difference inferences may be derived from morbidity data. We do not believe that these limitations significantly alter the findings of this study.

Asthma mortality has significantly increased in California from the mid- to late 1970s through 1989, as it has increased in the United States as a whole (2) and in several other countries around the world (1, 4, 6, 7). The rate has increased more rapidly among blacks than whites since 1975 to 1979, and the most recent rates reflect the largest difference in ratios of rates between blacks and whites. Deaths from 1960 to 1970 demonstrated a decline in asthma mortality similar to declines in asthma mortality observed in England and Wales and New Zealand during that decade (5).

Asthma mortality was highest over age 65 in the winter months, which is similar to data for the U.S. population (25) but unlike Canada, where asthma mortality is highest in the fall (26). This seasonal association in California was observed for deaths among whites and blacks over 65 yr of age but not for deaths in the younger ages. The absence of this association in the younger aged asthma deaths raises questions about the specificity of this finding with asthma mortality.

The possibility that the recent increase in asthma mortality was caused by changes in ICD coding was considered by other investigators, who concluded that there were inadequate data to support this explanation for the entire observed increase (8, 9, 11, 15). In California, the decline in asthma mortality rates in the 1960s occurred before the implementation of ICD-8, and the increase in the 1970s began before ICD-9 was implemented (figure 3). Thus, changes in the ICD coding systems are unlikely to fully explain the changes in asthma mortality in California.

We did not analyze medical records or other independent medical data and thus cannot comment directly on the accuracy of death certificates for deaths due to asthma in California. However, other investigators have found that inaccuracies in death certification cannot explain the increase in asthma mortality, particularly in young people, in whom asthma death coding is very accurate (15, 27). Between the periods 1975 to 1979 and 1985 to 1980, the increase in asthma mortality among blacks and whites below age 65 yr was broadly observed. This increase in asthma mortality in the ages for which death coding is most accurate provides strong support for a true increase in asthma mortality in California over this 10-yr period.

In a limited analysis, we did not find evidence of a compensatory coding bias to explain the increase in asthma mortality rates (figure 4). The increased mortality from other respiratory diseases including COPD since 1975 to 1979 in part reflects the plateau or decline in death certificate coding of chronic bronchitis or emphysema, but the magnitude of the increase does not provide support for a compensatory increase in coding of asthma deaths since the mid-1970s. Similarly, increases were seen in mortality from acute respiratory infections since the mid-1970s, which is also evidence against the increase in asthma mortality reflecting a decrease in these diagnoses.

Racial Associations

Blacks had a consistently greater mortality rate from asthma in California than whites, with the overall asthma mortality rates among blacks approximately double the rate among whites. Interestingly, this difference persisted during the decline in asthma mortality in the 1960s, and the difference increased in the 1970s. A similar difference in asthma mortality between blacks and whites has been observed for U.S. mortality data (2). This racial difference in asthma mortality is similar to racial differences in other indicators of asthma prevalence and severity. For example, analysis of the Second National Health and Nutritional Examination Survey found that black children had an adjusted relative odds of having asthma of 1.7 compared to white children (7). Hospitalization rates for asthma among blacks in the United States are 50% higher in adults and 150% greater in children (10), and in some urban areas this difference is even greater (14).

Asthma mortality among Hispanics in California was modestly lower than among whites and substantially lower than among blacks. This may in part reflect lower smoking prevalences or dose among Hispanics, but the magnitude of this difference and its uniformity at all ages suggests a true difference in asthma mortality. Furthermore, because the census undercounts minorities more than whites, it is likely that the observed differences between Hispanics and whites are a minimum, since an increase in the census bureau count of the Hispanic population would result in a further decrease in the observed rate (28). It is estimated that the census undercount of blacks is similar to the undercount of Hispanics, and thus this does not explain the sharp difference in asthma mortality rates between these two groups.

Asthma mortality rates were in general similar among Asians and whites. The exclusion from the Asian population estimate of approximately 5% of Asians who are of Hispanic origin would increase the rate among Asians by about 5%, but this would not change the overall similarity in rates between Asians and whites. The one exception to this similarity was higher asthma mortality rate among older Asian males, which may reflect greater rates of smoking in this group than among white males (29). As with the Hispanic population, this analysis greatly simplifies the many different ethnic groups that make up California's Asian population, and additional analyses will require more accurate and specific race or ethnicity information.

Occupational Associations

Death certificate-based occupational data have limitations that have been well described by other investigators (30–33). Our finding of significant excess mortality among carpenters (9 observed deaths and 2.5 expected) must be examined in the context of greater cigarette smoking among carpenters in general. At the time of the National Health Interview Survey in 1978 to 1980, 48% of carpenters were current smokers as opposed to 37% of all men (33). Greater smoking among carpenters could partially explain the observed increase in asthma mortality. However, the excess in asthma mortality is greater than the difference in smoking prevalence, and analysis of deaths occurring under age 65 reduces the effect of misclassification on these results.

Wood dust is a known cause of occupational asthma (34). In a recent Swedish asthma mortality study, carpenters had decreased smoking-adjusted asthma mortality, but increased asthma mortality was present for woodworking machine operators and woodworkers not otherwise classified (16). Asthma mortality has also been observed to be increased among paper mill workers (35), who may be exposed to high concentration of irritant gases, such as sulfur dioxide and chlorine.

Although other occupational associations for asthma mortality were based on small numbers, it is provocative that some of these occupations have exposures associated with acute and chronic respiratory disease and asthma. For example, health care workers are exposed to a variety of respiratory irritants and sensitizers, some of which have been associated with acute asthma (36), and textile workers may be exposed to cotton dust and endotoxin.

This type of analysis cannot address the possibility that asth-

matic individuals will avoid or change employment because of workplace reactions. However, clinical experience plus reported mortality from asthma in a sensitized subject following workplace exposure (37) suggest that continued working occurs despite sensitization. Even if changes in employment occur, they would tend to decrease the sensitivity of this type of analysis. Despite these limitations, our findings indicate that further analysis of the association of occupational exposures and asthma mortality is indicated. Occupational exposures are a well-described cause of acute asthma, and fatal occupational asthma has been described (37). Cigarette smoking should also be considered a possible contributing or interacting factor, an analysis that was not possible with these data.

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