APPENDIX AVAILABLE ON REQUEST

Special Report

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

Part II: Sensitivity Analyses

Appendix E. Selection of Ecologic Covariates for the ACS Study

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UNIVERSITY OF OTTAWA

Faculty of Medicine **Faculty of Health Sciences**

Re-analysis of the Harvard Six-Cities Study and the American Cancer Society Study of Air Pollution and Mortality, Phase II: Sensitivity Analysis

Appendix A, B, C, D, E, F, G, H, and I

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APPENDIX E: SELECTION OF ECOLOGIC COVARIATES FOR THE ACS STUDY

INTRODUCTION

The ACS Study can be considered as a hybrid design in that detailed individual information was collected but the primary exposure variable (fine particles and sulfate) were based on measurements taken on the city level. Thus, although the study provided data on the joint distribution of many covariates across the study population, exposure was assessed on an ecologic level. This may not be a serious difficulty, depending on the extent to which city-level ambient air pollution, as estimated from regularly collected data at the beginning of the study period, represents the relevant exposure metric for individuals. On the other hand, if these exposure metrics also represent certain characteristics inherent to the city, and these are correlated with other city-level characteristics, then it is possible that there could be residual confounding by these other city-level characteristics.

Our purpose for obtaining and adjusting for "ecologic covariates" was to assess the potential bias that could result if the latter situation pertained. We attempted to select variables that could be construed as measuring characteristics of cities; the contextual ecologic covariates that measure a social or other construct at the group level. Although many of the variables that we selected were aggregated from census data (eg, mean family income), in this case they estimate a social construct, the type of social milieu that subjects lived in, with the presumption that ones surroundings can significantly affect ones health, after accounting on the individual level for personal, familial, or genetic risk factors. Thus, it is not merely the biology and behavior of individuals that affects their health, but both the physical and social environment that individuals find themselves in (Evans and Stoddart 1990). It is also assumed that these factors act on the local or community level; for example, if one lives in a disadvantaged neighborhood then, despite ones own personal risk factors, the influence of the community through direct (eg, local sources of air or water pollution) or indirect means (eg, income disparity) may adversely affect ones health (for a review of these issues see Wilkinson 1996).

In fact, the inclusion of ecologic variables is the only way of studying group-level risk factors or "contextual effects" (Morgenstern 1998). Susser differentiates two types of variables that represent characteristics of groups: integral and contextual variables (1994). Variables such as the occurrence of a natural disaster, a law, latitude or barometric pressure that affect virtually everyone within a group are integral variables. A contextual variable, although describing a group-level characteristic, can be obtained from measurements at the level of the individuals making up that group. Contextual variables derived from measurements at the individual level may represent a different construct than the individual-level variable from which it is derived or to which it initially appears to correspond (Schwartz 1994). For example, although the Gini Coefficient is calculated from each individual's income in a city, the construct it measures is the distribution of income amongst city residents.

In interpreting the use of these variables in the context of the ACS Study, it should be recalled that the ACS Study was designed to enlist a highly selected cohort, whose members are not necessarily representative of the general population of the city from which they were selected. Moreover, these individuals likely live in diverse areas of the city for which city-level data may not be representative. Thus,

one potentially serious limitation of adjusting for city-level ecologic variables is that these data do not represent study subjects, and this will lead to misclassification. In addition, if air pollution also follows a similar geographic pattern as the ecologic covariates, then it is possible that effects from air pollution could not be distinguished from other effects measured at the same city level.

Misclassification could well be differential, in that smaller cities may be more homogeneous for these factors than larger cities. In any event, it has been shown that nondifferential misclassification in ecologic studies will always lead to an overestimation of effects in ecologic studies as compared to those derived from individual-level studies, even if there are no other sources of bias (Brenner et al 1992). Whether such effects would occur in the ACS Study is not known, but is plausible. Consider the following argument: after adjusting for individual level covariates, one is left with residuals that are regressed on the ecologic covariates. As one no longer can estimate the joint distributions between ecologic covariates, the study could then be considered ecologic, so that cross-level biases could occur (Piantadosi et al 1988; Greenland and Morgenstern 1989; Brenner et al 1992). Other effects arising from ecologic analyses could also be at play, including nonlinear effects and not considering the entire distribution of the ecologic covariates (Greenland and Robbins 1994).

In this appendix, we describe the variables that we have included and provide a justification for their inclusion.

THE ECOLOGIC COVARIATES USED IN THE SENSITIVITY ANALYSES

Because of the hybrid nature of the ACS Study, we were able to control for many individual-level-variables. Therefore the Reanalysis Team decided to focus on contextual ecologic covariates for this part of the analysis. There is a great deal of literature on the determinants of population health which emphasizes the importance of contextual risk factors on individual health. For example, in their important paper on the subject, Evans and Stoddart (1990) outline three categories of contextual risk factors for health: the social environment, the physical environment and the health care system. These three categories guided our search for possible ecologic confounders. A Medline search was done to find evidence of links between specific contextual variables within these categories and mortality. For those variables for which the literature indicated a possible health risk, we sought data from United States government sources that had been collected in the early 1980s for metropolitan areas or counties. Needless to say, data were not available at this geographic resolution for all possible contextual variables.

DETERMINANTS OF HEALTH

Interest in the socioeconomic and environmental determinants of population health emerged in the 19th century with the work of public health pioneers such as Virchow, Villerme, Chadwick, and Shatluck. It took until the 20th century, however, for researchers to establish a body of knowledge on these broader determinants of health (Amick et al 1995). Many studies have documented the importance of socioeconomic determinants of health over the past 20 years, including variables such as income (Kitagawa and Hauser 1973; Silver 1973; Pappas 1993), income disparity (Wilkinson 1992a,b; Kaplan et al 1996), poverty levels (Hadley 1982; Menchik 1993), unemployment rates (Ferrie et al 1995), education

(Kitagawa and Hauser 1973; Silver 1973; Weiss, et al 1992; Kunst and Mackenbach 1994), occupational status and hierarchy (UK Department of Health and Social Security 1980), marital status, family size (Rogers 1992), social support (Hibbard and Pope 1992), and interactions among some of these variables (Smith and Waitzman 1994; Birch et al 1997). In turn, some of these socioeconomic determinants appear to be associated with lifestyle "choices" that affect health. For example, increased smoking has been linked to lower socioeconomic status and to many health outcomes (Nelson 1994), and some studies have linked higher levels of unemployment to increased alcohol consumption (Brenner 1987; Catalano et al 1993). Socioeconomic status, as measured by indicators of income and education, could also exert indirect effects that may influence individual choices about the proximity of housing to noxious facilities (Been 1994). As well, the existence of deprived neighborhoods may have resulted in decisions to site these facilities in these areas, thereby discriminating against the poor or racial minorities or both (Bullard 1990; Hamilton JT.1995). As well, people with lower "permanent" or lifetime average incomes have been observed to accept higher health risks from occupational and environmental exposures (Graham et al 1992).

Evans and Stoddart (1990) provide a convincing and comprehensive statement concerning the determinants of health. In their conceptualization, the determinants are organized into three interrelated categories: (1) genetic endowment, (2) socioeconomic environment, and (3) biophysical environment. These broad categories, in turn, condition an individual's behavioral and biological response to external stimuli. Although most health experts would agree that these three broad categories influence both individual and population health, considerable disagreement exists over the relative weights to assign to each category. Moreover, it is likely that there is considerable heterogeneity within each of these levels. This disagreement magnifies at the definitional and technical levels (Bennett 1991).

Link and Phelan (1996) explain why socioeconomic differences in health outcomes have persisted over time in the face of reductions to specific population risk factors, such as poor public sanitation. These fundamental causes may be measured in the form of, say, income and education levels, but they likely represent more basic factors such as power, knowledge, influence, and the ability to make choices in support of healthy lifestyles. This conceptualization does much to illuminate potential determinants of health; however, operationalizing predictor variables that represent these can be difficult.

Wilkinson (1996) asserts the most important determinant is inequality, as measured by income and by other associated resources. His work suggests that societies with high levels of inequality are more likely to have unhealthy populations, so that relative levels of disparity exert a larger influence on health than absolute deprivation. His work and the now famous Whitehall studies (Marmot et al 1995) have heightened interest in inequality as a determinant of health.

Others have emphasized economic insecurity as a key determinant of health (Catalano 1991). This insecurity is usually operationalized by statistically exploring the relation between anticipated unemployment or actual unemployment and some form of health status or behavior known to affect health status (eg, alcohol consumption). Although some equivocal results have appeared, the majority of this research suggests that both anticipation of unemployment and actual unemployment show significant associations with risky behavior and with negative health outcomes (Catalano et al 1993; Ferrie et al 1995).

Taken together, these empirical findings and conceptualizations highlight the importance of considering social, economic, and behavioral factors. Lack of control for such variables may confound the results and falsely attribute the mortality effects to air pollution instead of correctly to some other variable such as community-level poverty or unemployment. Care must also be taken to avoid controlling for community-level attributes which are on the causal pathway between air pollution and mortality. Perhaps more interesting is the potential for effect modification when air pollution combines on a nonmultiplicative scale with other determinants of health.

Following Evans and Stoddardt (1990), the Reanalysis Team considered two broad categories of ecologic variables: attributes of the physical environment, and attributes of human communities (including access to health services) or the social environment.

The Physical Environment

Many aspects of the physical environment have been shown to be associated with mortality. These include climate variables, such as daily maximum temperature, daily minimum relative humidity, daily average barometric pressure; and the geographic variables latitude, longitude and altitude.

Weather Ambient temperature is an attribute of a place that affects almost all residents. Both extreme heat and extreme cold are associated with increased mortality (Greenberg et al 1983; Mannino and Washburn 1989; Larsen 1990; Kinney et al 1991; Smoyer 1998), primarily from myocardial infarction, stroke and pneumonia (Bull and Morton 1978; Danet et al 1999). Daily maximum temperature values were obtained for all the cities in the ACS Study that had weather stations that report to the National Oceans and Atmospheric Administration. Two variables were derived from this data: average daily maximum temperature and average monthly variation in maximum temperature. The latter measure likely provides an indication of the extremeness of a climate.

Barometric pressure is a contextual variable that affects everyone within a region and at least one study has found that barometric pressure is related to coronary and myocardial infarction deaths (Danet et al 1999). In time-series studies in Canada, we have found that changes in daily barometric pressure has a strong effect on daily mortality. The Reanalysis Team was only able to obtain data on station pressure. Station pressure is specific to the place at which it is measured and must be indexed to altitude in order to be comparable to measurements taken in other places. As the Reanalysis Team had no data on the altitude of the weather stations, we could not calculate barometric pressure at this time.

Relative humidity is another contextual variable for which there is evidence of an impact on death rates (Tselepidaki et al 1995; Salib 1997). In a study conducted in Greece, humidity was found to have a synergistic effect between air pollution on mortality (Katsouyanni et al 1993). However, this study applied to very hot conditions which are not relevant to many parts of the United States. Nevertheless, the minimum daily relative humidity was obtained from the US National Oceans and Atmospheric Administration (NOAA), monthly averages were derived and an average of those means was calculated. Again to provide an indication of the extremeness of relative humidity, average monthly variation was also calculated.

Air Conditioning There is some evidence that air conditioning has a protective effect against heat-related mortality (Marmor 1975; Ramlow and Kuller 1990; Rogot et al 1992-1995; Seretakis et al 1997); however, at least one study found no effect of air conditioning (Smoyer 1998). Although the Census Bureau does have data on air conditioning use at the state level, this data is not available at the metropolitan level. As well, although ambient temperature does impact upon everyone within a city, the air conditioning rate does not necessarily represent a useful group-level variable as only those with air conditioning are affected by it. Thus, we decided not to include this variable in the analysis.

Altitude Altitude, or altitude, appears to have a complicated relation with mortality. Although several studies have found positive associations between altitude and death rates from emphysema (Moore et al 1982), insignificant increases were found with altitude and asthma (Sly and O'Donnell 1989). Evidence of a link between altitude and chronic obstructive pulmonary disease is more controversial; whereas in one study a significant positive association (Cote et al 1993) was found, in another study a significant negative association (Coultas et al 1984) was observed. Negative associations between altitude and arteriosclerotic heart disease (Mortimer et al 1977) and cancers of the tongue, mouth, oesophagus, larynx, lung and melanoma (Amsel et al 1982) have also been found. Although altitude effects everyone who lives at that distance above sea level, there are problems involved with taking an average measure of altitude throughout a metropolitan area. For example, although there is little variation in altitude in some of the metropolitan areas in the midwest, within the metropolitan area of San Diego it varies by 1,600 m. Thus, metropolitan area may be an inappropriate scale of measurement for this variable.

Geographic position Latitude and longitude are two other contextual variables that were considered as potential confounding variables. In terms of biological mechanisms, however, melanotic skin cancer may be the only cause of death for which latitude can actually be considered to be causally related (Decarli and La Vecchia 1986; Lee and Scotto 1993). Latitude and longitude may serve as surrogates for other variables that, for cultural or geological reasons, vary along those geographic lines (Fabsitz and Feinleib 1980; Peter et al 1996). Because latitude and longitude are implicitly dealt with in the spatial analysis of ecologic variables discussed in Appendix H, these variables will not be considered further here.

Gaseous Copollutants were also considered as potential confounders at the ecologic level. Daily average concentrations of NO_2, sulfur dioxide, and carbon monoxide were obtained from 1980 to 1989, in addition to the daily one-hour maximum concentrations of ozone. City-specific annual averages of these gaseous copollutants (restricted to monitors with land use coded as residential, commercial, and mobile) for the year 1980 were used. In this analysis, monitors were restricted to those with land use coded as residential, commercial, or mobile, in order to avoid data from monitoring stations specifically located to monitor large point sources of pollution which may be not be reflective of general population exposures.

Other Airborne Toxic Substances The presence or absence of toxic substances in the environment can also be related to mortality. For example, exposure to benzo(a)pyrene from domestic and industrial coal burning, has been found to be associated with an increased risk of lung and stomach cancer (Lawther and Waller 1976; He et al 1991; Xu et al 1996; Nakanishi et al 1997). Although people are also exposed to benzo(a)pyrene from car exhaust (Lawther and Waller 1976), an American study concluded that the impact of such an exposure on lung cancer was most likely negligible compared to other more potent risk

factors such as smoking (Higgins 1977). Unfortunately, there is little consistent data on toxic substances such as benzo(a)pyrene available for metropolitan areas in the United States during the early 1980s, so it is not included herein.

Water Hardness The evidence as to whether the hardness of drinking water (as measured by the concentration of calcium carbonate, $CaCO_3$) is related to mortality is inconclusive. A source of discord arises from national-level studies for which association have been found and studies based on smaller regions showing no relations (Comstock 1979; Sharrett 1981). It is possible if not likely that ecologic bias is present in these investigations (Comstock 1979; Sharrett 1981). It has also been suggested that magnesium may have a protective effect against cardiovascular mortality (Neri and Johansen 1978; Comstock 1979 Sharrett 1981; Borgman 1985). Despite these misgivings, we have obtained US National Institute of Health data on water hardness from (Feinleib et al 1979; Lipfert et al 1988) and have included it in our analyses.

Radon Gas In analytic epidemiological studies, residential exposure to radon gas has been shown to be related to lung cancer mortality. At the county level, however, radon has a negative relation to county lung cancer mortality rates (Cohen 1995). This discrepancy is almost certainly due to ecologic confounding in the county level study (see Greenland and Robbins, 1994). Thus, we have decided not to include this variables in our analyses.

The Social Environment

With the emergence of the determinants of health model of population health (Evans and Stoddart 1990) has come a concurrent interest in the effect of social factors. In conducting the sensitivity analyses of the ACS Study, the Reanalysis Team considered a number of different social, economic and demographic factors.

Population Dynamics Increases in urban density appear to be associated with increased mortality from heart disease (Waddell 1983). Urban density itself is closely associated with the total size of the community or city as well as with traffic levels and hence with exposure to automobile-related air pollution. However, density varies greatly over a metropolitan area, from partly rural and suburban areas to congested inner cities. The average density of a metropolitan area is, therefore, not an appropriate measurement as it does not approximate exposures of the residents accurately. For this reason, density was not used in the reanalysis.

Population change, like unemployment rates, is an indicator of economic growth or decline. An area that is experiencing an economic boom will likely experience a concurrent growth in its population. Conversely, an area that is in an economic recession will shrink as people leave to seek employment elsewhere. We used population change as a crude indicator of what part of the boom and bust cycle the metropolitan area experienced in the early 1980s. It is also possible that those who are in better health are more likely to migrate between cities in search of work. Therefore, not only is population change a surrogate for a host of social, economic, behavioral and cultural attributes that are associated with recessions, it may also be the healthy people who are leaving the depressed regions and moving into the

developing ones.

Unemployment It is generally accepted that, at the individual level, unemployment is inversely related to health (Brenner and Mooney 1983; Sorlie and Rogot 1990). At the ecologic level, the unemployment rates of communities have also been associated with increased mortality (Colledge 1982; Guest et al 1998; Mansfield et al 1999). This ecologic effect may be due to an impact of the anticipation of unemployment on health and health related behavior (Catalano et al 1993; Ferrie et al 1995). Thus, we have included unemployment rate as a covariate in the reanalysis.

Social Inequality There is a growing literature linking social inequality to health outcomes (refer to Wilkinson 1996). One ecologic study showed that income disparity at the state level was related to overall mortality, even after controlling for poverty (Kennedy et al 1997). Although this study used the Robin Hood Index, we prefer the Gini coefficient which is a more widely used measure of income disparity and has also been related to increased all cause mortality (Kawachi and Kennedy 1997). The Gini coefficient is based on a Lorenz curve of the distribution of income in a population. When income is completely equitably distributed, each person has exactly the same income, the "curve" is a straight line (and the Gini coefficient would have a value of 0). As the distribution moves away from equality, the Gini coefficient moves toward 1. It has been hypothesized that both behavioral and psychosocial factors may be partly responsible for the association between income disparity and mortality (Wilkinson 1996). In our reanalysis, we used census data on income groups to calculate Gini coefficients for each metropolitan area.

Crime Rate Although crime detrimentally affects its victims, and living in an area of high crime may be stressful and injurious, there has been little research on the relation between crime rates and health outcomes at the community level. One recent study conducted at the state level provided an argument for the use of rates of various categories of crime as indicators for collective well being by showing that violent crime rates correlate with indicators of both relative deprivation (income disparity) and of low social capital (Kawachi et al 1999). In this study, social capital was operationalized as levels of interpersonal trust within a community (measured by a question on the General Social Survey) and as relative numbers of single-parent households. In the United States, the source for crime statistics is the FBI Uniform Crime Reporting Program which provides an index of serious crimes that includes: murder, non-negligent manslaughter, forcible rape, robbery, aggravated assault, burglary, larceny-theft, and motor vehicle theft (US Bureau of the Cesus1988). Unfortunately, crime statistics are not very reliable and the Census Bureau issues them with the warning that "data on serious crimes have not been adjusted for under-reporting; this may affect comparability among geographic areas or over time," (US Bureau of the Cesus1988). For this reason, crime was not used in the reanalysis.

Poverty Although poverty is generally thought of as an individual attribute, it is also relevant to think of communities as experiencing poverty. Although it has been shown repeatedly that poverty is related to mortality at the individual level (refer to Hahn et al 1996), less research has been done into the health effects of poverty on the community level. Nevertheless, the US Census Bureau has recently conducted important research on "poverty areas" (www.census.gov/socdemo/www/povarea.html). They found that poverty areas were significantly different from other areas in a number of essential ways, including racial composition, household composition, unemployment rates, average earnings, and levels of

education. Of particular relevance to our reanalysis is the finding that people who lived in poverty areas were more likely to have had a "health condition for at least the last six months which made it difficult for them to take care of personal needs (such as bathing or dressing) or go outside the home alone". A number of epidemiological studies have also found significant detrimental health effects of living in a poverty area, even after controlling for individual variables such as race, income, education, and smoking (Haan et al 1987; Carr et al 1992; Geronimus et al 1999; Polednak 1998; Waitzman and Smith 1998; Yen and Kaplan 1998, 1999). In our reanalysis, both poverty rates and per capita income variables were used to investigate the impact of the poverty on the findings.

Race Living in a poor neighborhood seems to have a more significant effect on African-Americans than on whites (Polednak 1993; Geronimus et al 1999). In the United States, race is clearly related to mortality at the individual level. Because the ACS cohort is predominantly (94%) white (Pope et al 1995), the impact of this relation on our analysis is not expected to be great. However, there are large differences between cities in terms of the proportion of African-Americans. As an ecologic variable, there is at least one study that examined proportion of African-Americans in a community as a contextual variable. This study found that living in a predominantly black, poor neighborhood had a significantly higher risk of mortality than living in a predominantly white poor neighborhood (Geronimus et al 1999). Studies of environmental justice have also shown that African-American communities are more likely to be burdened with toxic waste sites and industries that produce toxic pollution. As many of the pollutants from such sites are known to affect health, it seems reasonable to assume that the proportion of African-Americans in a community might impact mortality rates. Because other studies have shown that Hispanic and Native American communities are often also burdened in this way (Bullard 1993), the proportion of White Americans in a community will also be considered as an indirect measure of the proportion of minority group members residing in a city.

Education A great deal of research has shown differences in mortality according to education attainment (Feldman et al 1989; Christenson and Johnson 1995; Elo and Preston 1996). It is possible that these differential mortality patterns may be related to differences in health related behaviors. Studies have shown that most of the known risk factors for heart disease are more prevalent amongst less educated people (Garrison et al 1993). In another individual level study, Clay and collegues (1988) found that higher mortality rates among the undereducated were attributable to higher levels of smoking-related deaths. Although a cursory Medline search did not reveal any health articles which used education as a contextual ecologic variable, because education was found to be an important variable at the individual level, through the alternate models analysis, the Reanalysis Team decided to examine it as an ecologic variable as well. We calculated the percent of persons 25 years of age and over who had responded on the census that they had completed four years of secondary schooling or had completed some post-secondary education, and used this as a measure of the education levels of a city. We postulated that the education levels of a city might act as a surrogate measure of the type of economy of that city and of the predominance of certain health related behaviors in that city.

In light of these arguments, the predominance of health-related behaviors within a community might also be a relevant variable to study. Unfortunately, there is no reliable data available at the level of metropolitan areas regarding such things as diet, smoking, and exercise.

Serum Iron Levels Although there is inconsistent evidence that iron serum levels are a biomarker for elevated mortality risks (refer to Meyers 1996), such data are not available at the ecologic level. Although exposure to iron in air or water might be an appropriate variable to measure at the ecologic level, blood serum levels themselves do not represent a group exposure.

Health Care Services At the individual level, persons without health care insurance are at higher risk of mortality than those with insurance (Brown et al 1998). Medical insurance rates are available at the state level, but not at the metropolitan level. These state wide medical insurance rates have been shown to be associated with mortality rates (Kaplan et al 1996). This study also found that the prevalence of uninsured persons is highly correlated with income disparity, therefore by including income disparity we may control in part for health insurance prevalence.

Health services indicators that are readily available at the city level include the number of hospital beds and the number of physicians per capita. At least one study has found that the number of hospital beds is positively associated with hospitalization rates for respiratory disease, yet the number of physicians is negatively associated with this outcome (Morris and Munasinghe 1994). The cause-effect relation between health service provision and health outcomes is complex. Although access to health care can have a large impact upon the health of individuals within a community, health care services also tend to locate in areas which have greater health care needs.

Infant Mortality Rates Infant mortality rates (IMR) are often used as measures of development and especially of health care provision at the national level. Within the United States, IMR has been used as an outcome measure when examining racial differences in reproductive health (Geronimus 1986). IMR in the United States is highly correlated to both the percentage of African-Americans in a community and to the level of poverty within that community. Most of the influence of these two factors may be captured through some of the other ecologic covariates we used, such as poverty rates, mean income and percent African-American. Acute exposure to Pollution levels have been found to be may be related to IMR (Woodruff et al 1997; Loomis et al 1999), raising the possibility of over adjustment. For all of these reasons, the Reanalysis Team did not use IMR as an ecologic covariate.

Summary of Ecologic Covariates Included

Table E.1 shows those ecologic variables that were evaluated by the Reanalysis Team. This table lists the variable, key studies that provide evidence that the variable may or may not be linked to health outcomes, whether the Reanalysis Team analyzed the variable, the source of data for the variable and how the variable was derived.

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Table E.1. Ecologic Covariates Considered with Variable Description and Source of Data

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Demographic Data				
Change in population between 1980 and 1986	✔	Waddell 1983	The percent net change in number of residents between 1980 and 1986.	This figure is based on the US Bureau of the Census, *1986 Population Estimates by County with Components of Change*, cited in the County City Data Book, 1988.
Population density	✘	There is little evidence that the density of a metropolitan region contributes to health outcomes.		
Total population	✘	This variable was obtained to provide information about the relative size of cities. It was not used as an ecologic covariate as there is little evidence of a causal role for this variable	The population of the MSA for 1980.	from the 1980 Census of Population and Housing as of April 1, 1980, cited in the County City Data Book, 1988.
Racial Composition of Community				
Percent African American	✔	Geronimus et al 1999; Polednak 1993	The percent of persons residing in the MSA in 1980 who classify themselves as being of black race.	Geolytics software from 1980 Census of Population and Housing (April 1, 1980), STF3 data.
Percent White	✔	Geronimus et al 1999; Polednak 1993	The percent of persons residing in the MSA in 1980 who classify themselves as being of Caucasian race.	From the US Bureau of the Census County Population Estimates (experimental) By Age, Sex, and Race: 1980-1984, cited in the County City Data Book, 1988.
Health Services Data				

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Physicians per 100,000 residents	✔	Morris and Munasinghe 1994	The number of professionally active, non-Federal physicians with known addresses per 100,000 resident population as of July 1, 1985.	American Medical Association, Chicago, IL, Physician Characteristics and Distribution in the US, 1986 edition cited in the County City Data Book, 1988
Hospital beds per 100,000 residents	✔	Morris and Munasinghe 1994	The number of hospital beds per 100,000 resident population as of July 1, 1985. From a survey (September 30, 1985) of all hospitals (registered and un-registered), excluding old-age homes, convalescent homes and sanatoriums.	Source: American Hospital Association, Chicago, IL, Hospital Statistics, 1986, cited in the County City Data Book, 1988
Percentage with medical insurance	✘	Brown et al 1998 and Kaplan et al 1996	Data on health insurance rates is only available at the state level.	
Access to medical care by age, sex, race and level of education	✘		No suitable data available at the ecologic level.	
Infant mortality rate	✘	IMR is correlated with both poverty level and percentage of African Americans. IMR may also be correlated with air pollution, raising the possibility of overadjustment (Woodruff et al 1997; Loomis et al 1999).		
Iron serum levels	✘	Meyers 1996 finds inconclusive evidence of a link between iron intake and mortality	No suitable ecologic level data is available.	
Socio-economic Aspects of the Environment				

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Mean annual income in 1979	✔	Silver 1973; Kitagawa and Hauser 1973; Pappas et al. 1993	Per capita income for 1979.	Geolytics software from 1980 Census of Population and Housing (April 1, 1980), data. Geolytics
Unemployment rate	✔	Brenner and Mooney 1983; Colledge 1982; Catalano et al. 1993; Ferrie et al. 1995	Percent of total civilian labour force who were unemployed in 1986.	US Bureau of Labor Statistics, Employment and Unemployment in States and Local Areas, annual, cited in the County City Data Book, 1988
Individual poverty rate	✔	Geronimus et al 1999; Haan et al 1987; Kaplan 1996; Polednak 1998; Polednak 1993; Menchick 1993; Hadley 1982	The percent of individuals in 1979 who were classified as living below the poverty level specific to their family size, age, and number of dependents	US Bureau of the Census, Current Population Reports, Series P-26, Nos. 86-NE-SC, 86-S-SC, 86-ENC-SC, 86_WNC-SC, and 86-W-SC; and 1980 Census of Population and Housing, Summary Tape File 3C, cited in the County City Data Book, 1988
Percent with high school education	✔	Christenson 1995; Clay et al 1988; Elo and Preston 1996; Feldman et al 1989; Garrison et al 1993	The number of persons 25 years of age or older who indicated that they had completed 4 years of high school or some years of college divided by the total number of persons 25 years and over	Geolytics software from 1980 Census of Population and Housing, (April 1, 1980), STF3, data.
Gini coefficient	✔	Wilkinson 1996; Kawachi and Kennedy 1997	Calculated from income group data for 1979 as outlined in Shryock et al. 1976.	Geolytics software from 1980 Census of Population and Housing (April 1, 1980), STF3 data.

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Crime rate	✘	While at least one study has shown the potential relevance of crime rates to health outcomes (Kawachi, Kennedy and Wilkinson 1999). The problems with the data available made it impossible to use crime data in the Re-analysis.	The reported incidences of the following crimes in 1985: murder, nonnegligent manslaughter, forcible rape, robbery, aggravated assault, burglary, larceny-theft and motor vehicle theft. The total numbers were divided by the population for 1986. These numbers are not adjusted for underreporting which may make it difficult to compare across geographical areas	The FBI Uniform Crime Reporting Program which is compiled from the voluntary contribution of information from local law enforcement agencies. Cited in the County City Data Book, 1988.
Sedentary lifestyle	✘		No reliable data available at the ecologic level; however individual level data is available for the ACS cohort	
Diet	✘		No suitable data available at the ecologic level	
Climate Data				
Mean maximum daily temperature	✔	Bull and Morton 1978; Danet et al 1999; Gorjanc et al 1999; Greenberg et al 1983; Larsen 1989; Rogot and Padgett 1976	Maximum daily temperature in Fahrenheit for the years 1980 to 1989 inclusive was averaged by month. The average of all monthly averages was used as the ecologic covariate.	The data was provided to us by the US National Climatic Data Center of the National Oceanic and Atmospheric Administration.
Mean monthly variation in maximum temperature	✔		The monthly variation in maximum daily temperature in Fahrenheit for the years 1980 to 1989 inclusive was obtained. The average of this monthly variation was used as the ecologic covariate	The data was provided to us by the US National Climatic Data Center of the National Oceanic and Atmospheric Administration.

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Mean daily minimum relative humidity	✔	Katsouyanni et al 1993; Dalib 1997; Tselepidaki et al 1995	The minimum daily relative humidity in whole percent for the years 1984 to 1989 inclusive was averaged by month. The average of all monthly averages was used as the ecologic covariate.	The data was provided to us by the US National Climatic Data Center of the National Oceanic and Atmospheric Administration.
Mean monthly variation in minimum relative humidity	✔		The monthly variation in minimum daily relative humidity in whole percent for the years 1984 to 1989 inclusive was obtained. The average of this monthly variation was used as the ecologic covariate	The data was provided to us by the US National Climatic Data Center of the National Oceanic and Atmospheric Administration.
Mean and variation of barometric pressure	✘	While there is some evidence that barometric pressure may affect health (Danet et al 1999) We were unable to obtain reliable barometric pressure data.	Because no reliable measure of altitude could be derived for metropolitan areas we were unable to calculate an appropriate value for barometric pressure out of the daily station pressure data available from the NOAA	US National Climatic Data Center of the National Oceanic and Atmospheric Administration.
Residential use of air conditioning	✘	Seretakis et al 1997; Rogot et al 1994; Ramlow and Kuller 1990 and Marmor 1975	Data on air-conditioning use is only available at the state level	
Physical Environment Data				

Potential Covariates		Studies Showing Link With Mortality	Derivation of Variable	Source of Data
Altitude	✔	Amsel et al 1982; Cote et al 1993; Coultas et al 1984; Moore et al 1982; Mortimer et al 1977	It is measured in metres above sea-level. Only one measure of elevation was provided for each city. We do not have a measure of the variation of elevation within all cities, however, we know that in at least one metropolitan area used in the ACS study, the elevation varies by as much as 1600m.. Therefore usefulness of a single measure of elevation may be limited	Environmental Systems Research Institute US Places (24000+) file provided with their ArcView GIS software. Nassau was derived from monitor location data using spatial interpolation. Data for El Paso, TX was obtained from their official website
Latitude and longitude	✔	Peter et al 1996; Fabisitz and Feinleib 1980	Implicitly controlled for in the spatial analysis, see appendix **	
Water hardness	✔	Borgman 1985; Comstock 1979; Neri and Johansen 1978; Sharrett 1981	Data on concentration of CaCo3 (ppm) in drinking water, measured ca. 1970.	National Institute of Health data cited in Feinleib et al. 1979.
Radon	✘	Ecological studies contradict analytical studies		
Benzo(a)pyrene	✘	Higgins 1977	No comprehensive data base was located for the US	
Gaseous Co-pollutants				
Sulfur Dioxide	✔		All gaseous co-pollutants were measured as annual average of daily one-hour maximum concentrations for 1980 from residential, commercial or mobile monitors.	All data on gaseous co-pollutants came was compiled by Center for Air Pollution Impact and Trend Analysis (CAPITA) from the EPA AIRS database.
Carbon Monoxide	✔			
Nitrogen Dioxide	✔			
Ozone	✔			