THE ALLEGHENY COUNTY SHORT-TERM AIR POLLUTION EFFECTS (SHAPE) STUDY ON THE ELDERLY

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A few studies have assessed the effects of the current levels of air quality in relation to stationary and indoor emission sources, monitoring sites and susceptible populations. To address this issue, first, an ecological evaluation of admissions of the elderly aged ≥65 years and the PM_{10} for the period 1995-2000 was carried out to assess vulnerability of this population. Secondly, a longitudinal study was conducted during the period of May 2003 to May 2004 among adults aged 50 to 79 years who had a cardiopulmonary diagnosis and resided in Allegheny County. Each participant maintained a diary of symptoms, peak expiratory flow rates and daily activities for up to two months.

The ecological data showed high rates of admissions among the elderly. Individuals admitted multiple times often had a diagnosis related to acute conditions compared to the chronic diagnoses among those admitted only one-time. The admission category of whether an individual was admitted multiple times or one-time appeared to be significantly related to the PM_{10}. The longitudinal study included a total of 32 participants, mean age 66. The average 24-hr PM_{10} level was 24.36 $\mu g/m^3$. The results showed an association between PM_{10} and the cardiopulmonary symptoms suggesting a possible effect of air pollution. Additionally, the results of the continuous monitoring sites were highly correlated during both study periods. This finding proposes a review of the current federal and county air pollution monitoring strategies. Efforts should

be re-directed at appropriate apportionment of individuals' exposure levels and examining possible sources of emissions that impact the living environments. This can be achieved through personal monitoring in conjunction with physiological assessments for improved exposure-outcome extrapolation.

The public health significance of this study is that the less severe incidences reported by participants do not often require urgent medical support, but can eventually burden the body's physiological mechanism leading to hospitalization or death. The implication of the results is that the current ambient air quality standards do not appear to be entirely protective of all different population groups. The elderly who have underlying health conditions appear to be susceptible to the current exposure levels.

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1.0 INTRODUCTION

1.1 Statement of the Problem

Exposure to low levels of ambient air pollution is a concern that has emerged in recent research reports. While strides have been made to ascertain air pollution cause-effect in different populations, very few studies have examined the effect of the current levels on elderly populations. Even fewer studies have assessed the effect of polluting sources in relation to where people live.

Prior to 1995, research studies reported on levels of exposure generally around 100 $\mu g/m^3$ and showed effects of mortality and morbidity in different populations (Brunekreef 1995). Earlier research that drew the public and health professionals' attention to the effects of air pollution were due to exposure levels that were even higher than 100 μg/m3. The major air pollution incidents included the Meuse River Valley, Belgium in 1930 in which high concentrations of air pollution resulted in an atmospheric inversion that accounted for 60 deaths of mostly the elderly with previous heart and lung problems (Kaj Rohom 1937; Bell and Davis 2001). In addition, there is the Pennsylvania; Donora episode of 1948 where an atmospheric inversion occurred and resulted in 20 deaths and several hospitalizations (Bell and Davis 2001). And lastly, the London fog of 1952 claimed up to 4000 lives mainly the elderly and seriously ill patients (Greenbaum et al., 1999; Folinsbee 1993; Bell and Davis 2001). It is estimated that particulate matter exposures during the time of the London fog were as high as 270 $\mu g/m^3$, which is typically 5-19 times higher than the current standards (Bell and Davis 2001).

Other episodes occurred but with less degree of severity due in part to efforts of enactment of Clean Air Acts, and reduction and re-location of polluting industries. Over the years, air quality has improved but recent studies suggest a link of both chronic and acute respiratory, and cardiovascular system responses in all age groups at lower levels of exposures (Brunekreef, Dockery & Krzyzanowski, 1995; Schwartz et al., 1993; Shepard et al., 1999; Lawrence Folisnbee 1993; Bernard et al., 2001, Greenbaum, Bachmann, Krewski, Samet et al., 2001; Bryson, 1998; Zemp et al., 1999; Vedal et al., 2003; Bateson and Schwartz 2004).

The toxicological and physiological experiments in both animals and humans have dispelled doubts on air pollution cause and effect relationship. The studies have demonstrated that effect of air pollution on the respiratory and cardiovascular system effect is not a misnomer (Batalha, Saldiva, Clarke et al., 2002; Peters, et al., 2001; Watkinson et al., 2001; Schwartz, 1999; Arden Pope III 2000; Donaldson et al., 2001). Details of the physiological mechanisms are in chapter 2.

Numerous epidemiological research studies on air pollution have reported the effects of exposure to high concentrations of pollution that include cardiovascular diseases (Dockery et al., 2001; Mann et al., 2002; Checkoway et al., 1999; Peters et al., 2000; Goldberg et al., 2003; Zannobetti et al., 2003), respiratory diseases (Braga et al., 2000; Crater et al., 2001; Brunekreef & Holgate 2002; Desqueyroux et al., 2002), hospital admissions (Schwartz 2000; Atkinson et al., 1999; Morris, 2001), and diabetes (Zanobette & Schwartz 2002). Some studies have established the debilitating effects of air pollution in vulnerable age groups such as children (Keeler et al., 2002; Delfino et al., 2002) and the elderly (Samet 2002; Desqueyroux et al., 2002; Penttinen et al., 2001; Liao et al., 1999; Schwartz 1993). A few longitudinal studies reported on short-term effects of air pollution (Delfino et al., 2002 &2003; Penttinen et al., 2001; Osunsanya et al.,

2001; Yu et al., 2000). Penttinen et al., (2001) examined asthmatic adults for a correlation between deviations of peak expiratory flow rate (PEFR) volume and reported that the PM_{10}, $PM_{2.5\text{-}10}$ and $PM_{2.5}$ were positively associated with PEFR deviations.

Still, fewer studies have examined the acute effects of environmental exposures in relation to proximity to central air monitoring sites and neighborhood polluting stationary sources (Levy et al., 2002; Delfino et al., 2002 &2003; Osunsanya et al., 2001, Leaderer et al., 1999). To assess the background exposure to individuals, proper assignment of ambient exposures should take into account the distance of the participants from air pollution monitoring sites and major pollution sites, in conjunction to other contributing exposures such as indoor sources. Semi-individual studies have been proposed (Kunzil and Tager 1997), where assessment of individual health outcome is carried out but the independent variable of ambient air exposure and meteorological covariates remain ecological. Additionally, the effect of air pollution exposures can be improved by restricting the distance of exposure assignment within an arbitrarily assigned proximity to pollution sources and the monitoring sites.

1.2 Objectives of the Study

The goal of the Allegheny County short-term air pollution effects (SHAPE) study was to determine if there is an association between low levels of ambient air exposures and the incidence of cardiopulmonary symptoms and anti-inflammatory medication use in the study population. The area of health effects of PM_{10} and related compounds among the elderly adults in Allegheny County was approached in two ways:

1. An ecological framework, (i) to consider men and women aged 65years and older, in Allegheny County admitted to the hospitals during the years 1995–2000 for the purpose of describing the admitting and the discharge diagnosis, and rates of admission of individuals who were admitted only one time and those who were admitted more than one time, and (ii) an analysis of the relationship between air pollution and the hospital admission during the same time period.

2. A study of the short-term effects of ambient exposures through assessment of pulmonary function, respiratory and cardiac disease symptoms and anti-inflammatory medication uses in adults aged 50-79 years who have pre-existing cardiopulmonary diagnosis and who live in Allegheny County. This study was proposed to determine if daily changes in air pollution measured at the Allegheny County Health Department (ACHD) monitoring sites correlate with acute responses of symptoms, use of anti-inflammatory medication and pulmonary function changes. The SHAPE study considered also a relationship between individual residence and major air emission facilities identified from the EPA Toxic Registry Inventory (TRI) by recruiting people who lived within 15 km of the identified facility.

1.3 Significance of the Study

The SHAPE study is a follow up study to a retrospective ecological evaluation of the relationship between air pollution emissions and hospital admission rates for the period January, l995-December, 2000 in Allegheny County among adults ≥65 years old. Data from the PA Hospital Cost Containment Council (PACCC) which contains all in-patient hospital admissions of Allegheny County residents was used in the analysis. The admissions included International Classification of Disease (ICD)-9 codes 390 through 459 (cardiovascular and circulatory) and

460 through 519 (respiratory system). The data showed a total of 252,612 hospital admissions for cardiopulmonary diseases among the elderly (≥65 years old) with a mean age of 77.5 years and a mean length of hospital stay of 6.73 days. The admissions included 56,391 individuals admitted multiple times, mean age 76.77, and 58,373 individuals of mean age 77.54 admitted only one-time during the study period.

Ambient air levels of the criteria pollutants for all Allegheny County monitoring sites for January 1995 through December 2000 were obtained from the ACHD. In general air pollutant levels have decreased during the study period, though Lincoln and Liberty Borough showed consistently higher PM_{10} concentration levels compared to other sites.

In an earlier study of Allegheny County residents, Mazumdar and Sussman (1983), showed a significant risk estimate of 2.15 for total mortality and 3.14 for heart disease for all ages, for the same day particulates as measured by coefficient of haze (COH) values ranging from 0-3.5 units from the Hazelwood monitoring site data. When the authors analyzed the data of the age group ≥60 years, they yielded similar risk estimates. In terms of morbidity effects, Mazumdar and Sussman (1983) reported consistently significant associations between COH and total morbidity for the data of all the air pollution-monitoring sites (Hazelwood, Bellleuve, Logans Ferry) and for all ages.

The SHAPE follow-up study evaluated the effects of low-level ambient air pollution on adult individuals with pre-existing cardiopulmonary diseases because of the described patho-physiological mechanisms, the gaps in previous epidemiological-ecological studies and a need to strengthen and advance the science of environmental epidemiology through the proposed approach. Because this longitudinal short-term exposure study was a semi-individual design, this reduces the ecological fallacy that occurs with group associations. Allegheny County is also

ideal for this type of study because of the topography of very irregular deep river valleys and steep hills of 300-500 ft above valleys (Mazumdar and Sussman 1983) and makes for entrapment of ambient pollutants during a temperature inversion. These topographic characteristics make it uncertain to extrapolate other regional air pollution study results to the local population.

This study investigated the relationship between the average 24-hr PM_{10} increments and cardiopulmonary symptoms including pulmonary function as measured by a decrement in peak expiratory flow rate (PEFR). The results from this study will contribute to knowledge that can guide collaborative communication to inform the public of the impact of air pollution and influence a review of the strategies to air quality monitoring by the county, state and federal agencies. A survey study by Greenberg (2004) reported a decline of the public support for the antipollution regulations especially among the less affluent. Hence sharing of information from research of local and regional studies may be beneficial in education and empowerment of the general public about air quality in their communities and the effects to such exposures.

2.0 LITERATURE REVIEW

The link between air pollution and health has been a topic of much debate and investigation over the last several decades. Many studies have in particular examined the effects particulate matter (PM) because of the complex composition of the PM_{10} particles (Pope et al., 1997; Dockery 2001; Schwartz 1983; Delfino 2003). PM is the general term used for a mixture of solid particles and liquid droplets found in the air. The chemical composition of particles depends on location, time of year, and weather. PM can result from primary emissions such as dust from roads or elemental carbon (soot) from wood combustion, and other industrial processes and primary gaseous emissions. These include sulfate, formed from sulfur dioxide (SO_2), power plants and industrial facilities; and nitrates, formed from Nitrogen Oxides (NO_x), automobiles and other types of combustion sources.

PM_{10} is one of the seven criteria air pollutants that the US Environmental Protection Agency (USEPA) regulates under the National Ambient Air Quality Standards (NAAQS). PM_{10} is defined as PM with a mass median aerodynamic diameter less than 10 micrometer. The current USEPA standard for the PM_{10} is composed of both an acute (24-hr allowable average) and chronic component (annual allowable average). The standard is a 24-hr average not to exceed 150 micrograms per cubic meter of air ($\mu g/m^3$) more than three times in three years and an annual arithmetic average not to exceed a 50 $\mu g/m^3$ (EPA National Ambient Air Quality Standards, 1997).

2.1 History of Air pollution

Major episodes of air pollution in which excess morbidity and mortality were reported have influenced policy and research at a global level. These major episodes include the Meuse River Valley, Belgium in 1930 in which high concentrations of air pollution resulted in an atmospheric inversion which accounted for 60 deaths of mostly the elderly with previous heart and lung problems (Kaj Rohom 1937; Bell and Davis 2001); the Pennsylvania, Donora episode of 1948 where an atmospheric inversion resulted in 20 deaths and several hospitalizations (Bell and Davis 2001; Helfand et al., 2001); and the London fog of 1952 which claimed by far the highest number of lives of up to 4000 deaths mainly the elderly and seriously ill patients (Greenbaum, Bachmann, Krewski, et al., 2001; Folinsbee (1993), Bell and Davis 2001). It is estimated that particulate matter exposures during the time of the London fog was as high as 270 ug/m^3 which is typically 5-19 times higher than the current standards (Bell and Davis 2001).

These episodes provided indisputable evidence of the cause and effect of air pollution and led to the promulgation of the Clean Air Act of 1970 and the establishment of the National Ambient Air Quality Standard (NAAQ) for regulating criteria pollutants (nitrogen dioxide, sulfur dioxides, carbon monoxide, particulate matter (PM_{10}, $PM_{2.5}$), ozone, benzene.) Current research has been influenced by some of these major incidents.

Recent epidemiological studies on environmental exposures to air pollution have assessed a variety of pollutants and disease outcomes (von Klot et al., 2002, Yu et al., 2000; Penttinen et al., 2001; Brunekreef & Hoek 1993; Brunekreef et al., 1995; Desqueyroux et al., 2002) and have shown the need to continue to address the topic. Researchers continue to report on both acute and chronic disease outcomes due to air pollution exposures (Keeler et al., 2002; Delfino 2002). Other studies have reported on the patho-physiology mechanisms of air pollution (Batallha,

Salvida, and Clarke et al., (2002). Still others investigated the industrial and non-industrial stationary source pollutants and their contribution to air quality and conversely adverse health outcomes (Levy et al., 2002). Of concern is the disinterest and lack of support of the public of the antipollution regulations particularly among the less educated and also observed in the minority ethnic groups (Greenberg 2004). This lack of support may be due to problems in the public access to information and lack of knowledge on environmental concerns and to different competing economic challenges that the public experience.

2.2 Patho- Physiological Mechanisms of Air Pollution

2.2.1 Animal Studies

Animal studies have shown possible mechanisms of air particulate exposure consequences on the cardiovascular and pulmonary systems. Batalha, Saldiva, Clarke et al., (2002) showed results that indicated short-term effects of particulate matter on the cardiovascular system. The study showed that short-term vasoconstriction of small pulmonary arteries can occur in normal male rats exposed to concentrated ambient particles at levels ranging from 73 – 733 $\mu g/m^3$.

Watkinson, Mathew, Campen et al., (2001) showed that when rats are exposed to particulate matter consistent with acute exposure, they exhibit deficits in heart rate with a decrease of 50-100 beats per minute (bpm), changes in metabolism, minute ventilation, blood pressure, cardiac output, adverse changes in cardiac waveforms, and cardiac rhythm, frequently resulting in fatal outcome in apparently healthy rats. The authors reported further that in their study, the rats that were cardiopulmonary compromised demonstrated exaggerated bradycardia and hypothermic responses.

Goldeski et al., (2000) reported that in a controlled exposure experiment of ambient particles, dogs that had compromised coronary artery function started to show changes in ECG within hours of onset of exposure, an indication of accelerated development of ischemic heart disease. Costa and Dreher (1997) also showed ECG changes and lung inflammation in rats treated experimentally with soluble ash metals, an indication of acute inflammatory responses to particulate matter.

2.2.2 Human Studies

Human experimental studies have also reported on mechanism of pollutant-induced damage to the cardiovascular and pulmonary systems. Yeates and Manderly (2001) summarized studies on mechanisms of air pollution on cardiovascular and systematic responses and how non-respiratory organ health outcomes can occur following air pollution deposition in the respiratory.

Peters et al., (2001) reported that healthy adults exposed to episodes of high particulate air pollution through inhalation of air particles can show outcomes of pulmonary inflammation that in turn trigger systemic hyper-coagulability, with increases in the viscosity of blood and C-reactive protein (CPR). Similarly, Pope III (2001) reported on studies that showed alveolar inflammation resulting in the release of potentially harmful cytokines and increased blood coagulants, with autonomic nervous system-activated changes in blood viscosity, heart rate and heart rate variability (HRV) increasing the likelihood of cardiac death. Peters et al., (1997) reported that exposure to ambient pollution can result in increased plasma viscosity that can lead to cardiovascular illness. Donaldson et al., (2001) suggested a mechanism by which ultrafine particles can be deposited in the lungs of the elderly individual and cause a significant CPR increase. According to Donaldson et al., (2001), ultrafine PM can trigger oxidative stress and

inflammation in the lungs that can lead to a variety of pathologic endpoints such as atheromatous plaque, endothelial erosion and coagulation factors.

Nemmar et al., (2001) assessed the mechanisms of passage of inhaled particles into the blood circulation of humans by measuring the distribution of radioactivity of the particles in five healthy volunteers. Radioactivity was detected in the blood already at 1 minute and reached maximum at 1-20 minutes and remained at higher levels up to 60-minutes. The experiment showed how particles translocate from lungs to cardiac circulation, causing circulatory system damage. According to Verrier et al., (2002) ambient air particulate matter consists of a mixture of combustive by-products and re-suspended crystal material as well as biological materials such as pollen, endotoxins, bacteria and viruses. The authors reported that these inhaled particles could be detected within minutes of exposure in systemic circulation where they persist for hours, providing a route of entry to other organs.

Dockery (2001) described investigations on mechanisms by which particulates deposited in the lungs might produce an immediate fatal cardiac event. In a study of hypoxemia and cardiac physiology Dockery (2001) reported significant relevant clinical marker of an increase of heart rate of more than 5 beats per minute (bpm) and 10 bpm (increased 29% and 95% respectively) for an increase in 100 ug/m^3 exposure to PM_{10} on the previous day. Other studies have monitored dogs and shown morphologic changes on EKG output due to air particulate exposures (Godleski et al., 2000).

In a short-term longitudinal study, Liao et al., (1999) monitored daily changes in particulate matter and cardiac autonomic activity and showed that at levels >15 μg/m^3 of $PM_{2.5}$ the risk of lower cardiac autonomic control was 3.08 (95% CI 1.43, 6.59) suggesting a possible link between air pollution and cardiovascular disease mortality. Gold et al., (2000) and Stone et

al., (1999) also reported on path-physiological mechanisms that are likely to cause ECG changes, HRV or mortality in subjects. Brook and Brook et al., (2002), reported that after exposure of healthy adults to short term 2-hour exposure of 150 ug/m^3 concentrated ambient fine particles plus 120 ppb ozone, they observed acute arterial vasoconstriction in the individuals. The authors reported that the air pollution experimental exposures in their study are consistent with air pollution observed in urban cities. Ghio et al., (2000) exposed young healthy adults to ambient air particles and after 18 hours the lung tissues showed higher concentrations of neutrophils, a pathological marker of inflammation. In another study Ghio et al., (2003), showed that exposure of healthy individuals to concentrated air particles can be associated with decreases of both white blood cell count and LDH and increased concentrations of fibrinogen in the blood.

Devlin et al., (2003) assessed HRV in healthy elderly adults between the ages of 60 and 80 who were exposed twice for 2 hours: once to clean air and once to concentrated ambient air pollution particles. Participant's responses were measured immediately before, immediately following, and again 24 hours after exposure. Elderly subjects experienced significant decreases in HRV in both time and frequency domains immediately following exposure compared to data of young healthy volunteers. Some of these changes persisted for at least 24 hours showing that the elderly individuals show decreased HRV to variable exposures levels.

2.3 Air Pollution and Mortality

Though many research studies continue to show mortality due to air pollution, Pope III et al., (1999) reported that more research is needed on specific pollutants, mixtures of pollutants and biological mechanisms. A previous study by Mazumdar and Sussman (1983) showed a relationship between same day particulate levels and mortality and morbidity outcomes of respiratory and cardiovascular disease in Allegheny County, PA. The study used the Hospital

Utilization Project and Presbyterian University Hospital data to examine morbidity outcomes due to particulate measured by the Coefficient of Haze (COH) and SO_2 pollutants exposures. Joel Schwartz (2000) examined 10 cities including Pittsburgh and reported an overall effect of 1.4% increase in deaths (95% CI= 1.15-1.68) for an increase in exposure of 10 ug/m^3 on a single day. Another regional study was by Schwartz and Dockery (1992) examined an 11-year period data 1974-1984 in Steubenville, Ohio and reported an association between daily 4% increase in mortality on a succeeding day for an increase in particulate matter of 100 μg/m³.

In other regions, Goldberg, Burnett, Valois et al., (2003) analyzed data using all residents of Montreal who died during the period 1984-1993 and reported an increase in daily mortality for persons 65 years and older with mean percent increase in the coefficient of haze (COH) across the interquartile range 4.32% (95% CI: 0.95-7.80). Pope, Burnett, Thun et al., (2002) reported increased risk of all-cause, cardiopulmonary and lung cancer of about 4%, 6% and 8% for each 10 μg/m³ increase of fine particulate.

International studies have reported comparable results. In a Seoul study, Lee and Schwartz (1999) reported that premature death can occur due to particulate matter exposures and reported a relative risk of death of 1.010 (95% CI, 0.988-1.032) per 100 μg/m³ total suspended particles (TSP) exposure. In the Netherlands, Hoek, Brunekreef, Goldbohm et al., (2002) showed that cardiopulmonary mortality was associated with living near major roads. Schwartz, Ballester, Saez et al., (2001) also reported on excess daily mortality from low levels of particles with a 10 μg/m³ resulting in 0.88% increase in deaths (95% CI, 0.56%- 1.20%) in eight Spanish cities.

In Dublin, Ireland, Clancy et al., (2002) carried out an intervention study of the ban of coal use showed that after 72 months, about 116 fewer respiratory deaths and 243 fewer

cardiovascular deaths were seen per year which accounted for 5.7% decrease in respiratory death (95% CI, 4-7, p<0.0001) and cardiovascular by 10.3% (95% CI, 8-13, p<. 0001). Generally, most studies on mortality appear to show effects at higher ambient air pollution levels than do morbidity studies.

Levy et al. 2002, found that the higher level, of particle concentration was found in areas closest to the power plant and that these exposures may have impacted mostly those with lower education attainment. The mortality relative risk for an annual mean increase of 10 μg/m³ $PM_{2.5}$ concentration was noted to be 1.085 ((95% CI, 1.031-1.142) for individuals with less than high school education and 1.003 (95% CI, 0.9671-1.040) for individuals with more than high school education.

2.4 Air Pollution and Morbidity

Several studies have examined a correlation between air pollution levels and hospital admissions for cardiac and pulmonary diseases (Checkoway, et al., 2000; Schwartz 1999; Morris 2001; Atkinson et al., 1999; Peters et al., 2000, and came up with variable results. Studies have shown that PM_{10} levels at which health outcomes can be observed vary from as low as 24-hr minimum levels of 6.8 μg/m³ to a 24-hr maximum of 998 μg/m³ maximum (Atkinson et al., (1999). Brunekreef, et al., (1995) reported on health outcomes due to exposures PM not exceeding a 24-hr average of 115 μg/m³. Zanobetti et al., (2000) reported on deleterious health outcomes at exposure levels of 33 μg/m³ PM_{10} levels. The studies show contrary results due to factors such as the type of pollutant under investigation, region of study, limitations of sample sizes and exposure misclassifications bias.

2.4.1 Respiratory Disease Outcomes

Several studies have included both children and adults to assess the effects of environmental exposures in individuals with pre-existing respiratory diseases such as asthma, COPD and other respiratory diseases to explain the etiology of some of the disease burden.

2.4.1.1 Asthma studies

According to the ALA (2000), an estimated 31 million Americans had asthma diagnosed by a health professional. Delfino et al., (2002) investigated an association of asthma symptoms, anti-inflammatory medication use and particulate air pollution in southern California. The study investigated 22 asthmatic children aged 9-19 years of age and followed them from March to April 1996. Asthma symptoms were recorded daily resulting in repeated measurements. The study showed a strong associations between an average of 7-32 $\mu g/m^3$ of PM_{10}, NO_2, O_3, and fungi and asthmatic kids not taking anti-inflammatory medicines (OR=2.80, 95% CI, 0.92-8.49), compared to those on anti-inflammatory (OR= 1.93, 95% CI, 1.01-3.71).

In another study, Delfino et al., (2003) examined asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants in 22 children aged 10-15years of age with asthma living in Los Angeles where there is high traffic density. The study participants completed diaries of PEFR for three months November 1999 to January 2000. The home and school addresses were within a 3 mile radius of the central air pollutant measuring site enhancing the relevance of ambient exposure to personal exposures. The results showed that traffic air pollutants toxic mixture and industrial sources may be associated with adverse health outcomes. There were no significant associations with PEFR, but the study found positive associations for

bothersome or more severe asthma symptoms from interquartile range increases in 37 $\mu g/m^3$ PM_{10}, 1.45 (95% CI, 1.11-1.90).

A study by Keeler et al., (2002) involved assessing the indoor air quality using personal samples, environmental air quality measurements from central station, twice daily PEFR, medication and asthma symptoms four times each year for a two-week duration each season in children aged 7-11 years who had moderate to severe asthma. Twenty children participated in this Community Action Against Asthma (CAAA) in Detroit Michigan. The results showed significance differences in community level exposures. The southwest Detroit, community showed increased levels of PM_{10} exposure compared to the east (PM_{10} 28.9 ±14.4 for southwest compared to PM_{10} 23.8 ±12.1 for the east side). The increased level in the southwest is thought to be due to heavy industrial sites in that area of Detroit.

Yu et al., (2000) observed 133 children aged 5-13 years of age in Seattle, Washington for 58 days in relation to ambient air pollution and daily self-reporting of asthma symptoms. The children were enrolled into the study during screening for Childhood Asthma Management Program (CAMP) study-a randomized clinical trial to evaluate long-term effects of daily anti-inflammatory medication. Results showed a total of 1,658 daily diary records collected over 580 days with each child completing a minimal of 28 days and an average of 58 days. The study reported an association between increases in PM_{10} average of 24.7 $\mu g/m^3$ and asthma symptoms in study participants. When the authors considered a lag of 1 day, the relative odds of symptoms, was 4.6 (95% CI, 3.6-5.9). However, the diagnosis for the children was not clinically validated by a physician.

In a study involving adults, Penttien et al., (2001) observed asthmatics subjects with a positive diagnosis of asthma in Finland who maintained 3 times daily PEFR, symptoms and

medication during a six months period. The study proposed to test a hypothesis that particulate ambient air might cause alveolar inflammation and subsequently resulting in exhalations problems in individuals with pre-existing cardiopulmonary diseases. The results showed that daily mean number of particles concentration ranging from PM_{10} averages of 3.8–73.7 μg/m³ was negatively associated with PEFR deviations.

Osunsanya et al., (2001) also explored a correlation of day-to-day PEFR deviation in an adult populations and air pollution exposure levels and reported a borderline significance association of a 19% increase in the rate of 10% decrements in daytime PEFR and PM_{10}. A change in PM_{10} from 10 to 20 $\mu g/m^3$ was significantly associated with a 14% increase in the rate of high scores of shortness of breath and increase use of medicines.

Desqueyroux et al., (2002) assessed the short-term effects of low-level air pollution on respiratory health of adults suffering from moderate to severe asthma. The physicians monitored for three months subjects who had a positive diagnosis of asthma, average age 55 years, a physician-diagnosed asthma, and on beta 2-agonist inhalation and living in Paris. This study showed significant associations between PM_{10} of winter 24-hr Average 28 ±14 $\mu g/m^3$ and summer 24-hr Average 23 ±9 $\mu g/m^3$ and asthma attacks in individuals with severe asthma even though they were on medication treatment (OR =1.20, 95% CI=1.03 -1.41).

2.4.1.2 Chronic Obstructive Pulmonary Disease (COPD)

Schwartz (1994) examined Medicare admission records for pneumonia and COPD for a period of 1986 -1989 among the elderly in Birmingham, Alabama for associations with daily monitoring of particles. Significant associations were found between PM_{10} and hospital admissions for pneumonia and COPD. The study found that particulate matter particles were a risk factor for admission for pneumonia (for an increase of 100μg/m³ daily relative risk, (RR = 1.19, 95% C.I, 1.08 - 1.50).

Harre et al., (1997) followed up a New Zealand cohort of 55 years and older individuals with COPD for 3 months to investigate the relationship between air pollution level and respiratory symptoms and PEFR. Only subjects residing within 5km radius of the air pollution-monitoring site were recruited. No associations were reported between PEFR and any pollution variables. However, a rise in PM_{10} concentration equivalent to the inter-quartile range of 35.04 $\mu g/m^3$ was associated with an increase in nighttime chest symptoms (RR = 1.38, 95% 1.07-1.78).

In the United Kingdom, Osunsanya et al., (2001) investigated whether the fractions of particulate matter of sizes 100 nm could be responsible for changes in health in patients with chronic flow obstruction with either asthma or COPD aged 50 years and older living within 5 miles of an air monitoring site. The study did not show evidence to support the hypothesis.

2.4.1.3 Upper and lower respiratory symptoms outcomes

Vichit-Vadakan et al., (2001) examined the responses of three different panels to particulate matter in Bangkok, Thailand. Nurses, school children and other adults were asked to report daily any upper and lower respiratory symptoms for 3 months. Adult participants lived within 2km of the air pollution-monitoring site, did not smoke, and did not have air conditioners at work or

home. The results showed high completion rates of diaries, 95% adults, 99% school children and 99.9% nurses and evidence of an association between upper and lower respiratory symptoms and PM_{10}. An inter-quartile increase of 45 ug/m^3 in PM_{10} was associated with about 50% increase in lower respiratory symptoms in highly exposed adults, OR= 1.49 (95% CI= 1.35-1.64).

In Taiwan, Hwang and Chan (2002) examined a one-year (1998) records of all age groups from 50 sites to estimate an association of criteria pollutants and daily numbers of clinic visits for lower respiratory tract illness. The study found that people over the age of 65years were the most susceptible population to air pollutants and that the air pollutants had greater effect on the lower respiratory symptoms for a PM_{10}, 10% increase at lag 0, (OR= .8%, 95% CI= 0.4 - 1.1). Brunekreef, Dockery and Krzyzanowski (1995) reported on studies that have shown health effects of lung function, acute respiratory symptoms and medication use at levels of PM_{10} exposure not exceeding a 24-hr average of 115 µg/m³.

2.4.2 Cardiovascular Disease Outcomes

Cardiovascular diseases (CVD) rank as the leading cause of death in both men and women and among all racial and ethnic groups in the nation (Fried et al., 1991) with more than 2600 deaths occurring each day (American Heart Association Statistics, 1999). Some studies have shown that individuals who have pre-existing conditions may report more adverse cardiac reactions with decrease in air quality. Mann et al., (2002) assessed the increased vulnerability among persons admitted with cardiac diseases and showed increases in hospital admissions with an increase in concentration of air pollutants for ischemic heart disease (IHD) ICD-9 410-414, myocardial infarction (MI) ICD-9 410) and other acute IHD for ICD-9 411. For a 24-hour mean PM_{10} (ug/m3) of 43.7 µg/m³ ±27.7 the percentage increase for IHD admissions was 0.19 (95% CI, -

0.57-0.95), for MI -0.10 (95% CI, -1.33-1.12) and for other acute IHD 0.36 (95% CI, -0.87-1.60). CO and NO_2 were consistently associated with the IHD, MI, CHF and other IHD in this study.

Peters et al., (1999) evaluated data of 2,681 men and women who were participants in the MONICA Augsburg cohort study for effects of air pollution on heart rate by measuring the participants' resting EKG during the years 1984-1985 and 1987-1988. The larger change in heart rate was seen during the air pollution episode of January 1985 that affected the larger part of Europe. The most significant change was from the effect of total suspended particulate (70 ug/m3) episode changes from 5^{th} to 95^{th} percentile on the same day exposure (mean heart rate change of 1.61 (95% CI=0.38-2.85). Additionally, on the determinants of Myocardial Onset Study of 722 patients Peters et al., (2001), reported that elevated concentration of fine particles in the air might transiently elevate the risk of MI onset within a few hours and 1 day after $PM_{2.5}$ exposure of 20 ug/m^3, OR=1.69 (95% CI, 1.09, 2.02).

In another study, Peters et al., (2000) tested the hypothesis that people with implanted cardiovetter defibrillators experienced potentially life-threatening arrhythmias after air pollution episodes. Implantable cardioverter Defibrillators (ICDs) are small electronic devices implanted to treat dangerously fast heartbeats that can lead to sudden cardiac arrest. ICDs are implanted under the skin of the chest, near the left collarbone, with wires running to the heart. Implantable cardioverter defibrillators monitor deliver electrical shocks to the heart as necessary to eliminate abnormal rhythms. For bradycardia, the ICD functions as a pacemaker and sends electric signals to the heart. For tachycardia, it sends defibrillation shocks to stop the abnormal rhythm. Among the study groups increased risk of cardiac arrhythmias was observed at concentrations of PM_{10} and $PM_{2.5}$ of maximum levels of 62.5 μg/m³ and 53.2 μg/m³, respectively. According to the

authors, patients with ten or more interventions of ICD use experienced increased arrhythmias in association with nitrogen dioxide, carbon monoxide, black carbon and fine particle mass, suggesting that elevated levels of air pollutants are associated with potentially life-threatening arrhythmia leading to therapeutic interventions by an ICD. Similarly Robert et al. (2002), in a study of healthy adults, showed significant brachial artery vasoconstriction of -0.09± 0.15mm in exposure to 150 μg/m³ of the fine particulate versus +0.01 ± 0.18 mm filtered air exposure. The authors reported that these exposures are comparable to urban fine particulate and ozone.

2.4.3 Susceptibility Groups and Air Pollution

Groups of individuals have been included in studies to ascertain which group of the population is most susceptible to PM pollution. According to Arden Pope III (2000) general studies seem to suggest that the elderly, young, children and persons with chronic and asthma are more likely to be susceptible. Additional studies need to be carried out to assess the relationship of these groups to air pollution exposures levels.

Levy et al., (2002) assessed the contribution five power plants emissions have on premature mortality on the subpopulation that includes the less educated, diabetics, and the African Americans living in a 50 km geographic radius of Washington DC. Using estimate models the authors concluded that 51% of the deaths from this study area are among individuals with less than high school education. The study also concluded that individuals with diabetes, and the African Americans had a disproportionate share of cardiovascular hospital admissions and asthma emergency respectively, per year. Such information can help in targeting future air pollution exposure assessment or epidemiological efforts to those identified to be more at risk.

Penttinen et al., (2001) examined an adult asthmatic cohort to assess whether the fine particles in ambient air might provoke alveolar inflammation in susceptible individuals with preexisting cardiopulmonary diseases. No association was observed between respiratory symptoms and medications and the daily mean particles. Roemer et al., (1998) followed asthmatic children in a multi-center PEACE in Europe for at least 2 months to assess the acute effects of pollution and asthma children using PEFR and symptom medication use diary. The study did not show any association between PEFR, respiratory symptoms or bronchodilator use and PM_{10}, SO_2 and NO_2. Conversely, in a study by Koenig et al., (1993) to investigate the relationship between fine particulate matter pulmonary function in young children, the study indicated that an increase in particulate matter was associated with declines in forced expiratory flow volume (FEV) and with forced vital capacity (FVC) by 34 ml and 37ml, respectively, for each increase of a corresponding $PM_{2.5}$ of 20 $\mu g/m^3$.

Lastly, von Klot et al., (2002) assessed a panel of 53 adults in Ergrut, Germany by comparing their daily health status and medication use and air pollution exposure to PM_{10}, $PM_{2.5}$, and NO_2 and SO_2 and found that increased inhaled asthma medication use and symptoms of asthma were associated with particulate air and gaseous pollution. A study by Delfino et al., (2002) examined the group that was not on anti-inflammatory and showed a risk of symptoms, OR 1.19 (95% CI) (0.75-1.88) for an 8 hr- PM_{10} exposure.

2.4.4 Summary of Literature Review

Particulate matter includes both fine and coarse particles. Exposure to coarse particles is primarily associated with the aggravation of respiratory conditions, such as asthma. Fine particles have been associated with increased hospital admissions and emergency room visits for heart and lung disease, increased respiratory disease and symptoms such as asthma, decreased lung function, and even premature death. Groups that are thought to be at greater risk to these effects include the elderly, children, individuals with cardiopulmonary disease such as asthma, and, the African American and the less educated.

Increased mortality and morbidity have been linked to periods of high outdoor PM concentrations. The PM non-specific chemical agent characteristics make identifying health effects associated with its environmental levels a significant issue. In general, PM_{10} particulates, are formed during burning processes and include fly ash from power plants (Levy et al., 2002; Aekplakorn et al., 2003), carbon black from automobiles and diesel engines (Jinsart et al., 2002), and soot from fireplaces and wood stoves. Jinsart et al., (2002), reported in their study of roadside monitoring data that automobile exhaust fumes were the main source of PM emission. Aekplakorn et al., (2003) reported that PM_{10} changes of a 10 $\mu g/m^3$ increment was associated with changes in pulmonary function of children who resided near a coal-fired power plant in Thailand. Exposure to particulate matter may lead to increased use of medication and more visits to the doctor or emergency room. Health effects may include coughing, wheezing, shortness of breath, aggravated asthma, lung damage, (including decreased lung function and lifelong respiratory disease), HRV and disease of the circulatory system.

Human and animal patho-physiological studies have shown a mechanism by which the body system can incur injury following exposure to air pollutants. Several epidemiology studies

have shown a positive correlation between air pollution levels and mortality and morbidity. Other acute responses have shown been to occur such as responses of pulmonary lung function. Reports, however, continue to show different results and outcomes possibly due to different pollutants under investigation, regional differences of pollutant mix.

In the study using data obtained from the PACCC admission database for Allegheny County, the results showed that nearly 50% of the adults are admitted for cardiopulmonary causes in Allegheny County. Additionally, other areas in Allegheny County show consistently high levels of air pollution although relatively lower than the USEPA standard. Other studies of Allegheny County residents have reported an association between air pollution and cardiopulmonary disease morbidity and mortality in Pittsburgh (Muzumdar and Sussman 1983; Schwartz 2000; Chock et al., 2000). The study results of the PACCC data and previous studies in the region were of interest to us as this established an antecedent to a longitudinal study targeting the elederly in Allegheny County.

Many of the ecological studies that have shown a correlation between air pollution and disease outcome have used exposure level from central stationary air monitoring sites. Very few studies have apportioned individual exposures. All these factors need further exploration to improve on air pollution exposure studies and to inform the local, state and regional entities with concrete evidence of such research outcomes.

Table 1: Summary of morbidity studies of low-level particulate matter: 1996-2004

Author (Country)	Level of Exposure	End Point	Risk Estimate
Devlin et al., (2003) (US)	$PM_{2.5}$: Individual 24-hr Average 21.2-80 μg/m^3	Decrease in heart rate variability in elderly 60-80yrs	35.7% Decrement in Heart Rate Variability
Ghio et al., (2000) (US)	$PM_{2.5}$: 24-hr Average 23-31μg/m^3	Lung inflammation and hypoxia in healthy adults ≥27yrs	8.44±1.99 in Bronchial Neutrophils and 4.2±1.69 Alveolar Fraction
Jedrychowski et al., (1999) (Poland)	Suspended PM: 24-hr Average 52.6 ± 53.98μg/m^3	Pulmonary function retardation in pre-adolescent 9yr-olds	OR 2.15 (1.25-3.69)
Zemp et al., (1999) (Switzerland)	PM_{10}: 24-hr Average 10.1-33.4 μg/m^3	Respiratory symptoms in non-smokers in Adults 18-60yrs	OR 1.48 (1.23-1.78) (Breathless in day) for an increase in 10μg/m^3
Pope et al., (2004) (US)	$PM_{2.5:}$ 24-hr Average 18.9 ± 13.4μg/m^3	CVD, HRV blood markers & inflammation in adults 54-89yrs	35 (SE=8) msec decline in SD of all normal R-R intervals HRV measured as SDNN for an increase in 100 μg/m^3
Boezen et al., (1998) (Netherlands)	PM_{10}: Urban 24-hr Average 41.55 (12.1-112.7). Rural 24-hr Average 44.1(7.9-242.2)	Upper respiratory symptoms (URS) Lower respiratory symptoms (LRS) in adults 48-73yrs	OR 0.77 (0.62-0.96) (URS) for ≤5% Peak expiratory flow rate decrease OR 1.10 (0.81-1.50) (LRS) for ≤5% Peak expiratory flow rate decrease
Koken et al., (2003) (US)	$PM_{10:}$ 24-hr Average 24.2± 6.25	CVD arrhythmias in adults ≥65yrs	¯17.6% (¯26.7- ¯7.5) 8.9 (¯0.34-18.93) % Change in Hospital admissions

Table 1 (Cont'd)

Author (Country)	Level of Exposure	End Point	Risk Estimate
Delfino (1998) (US)	PM_{10}: 24-hr Average 25 μg/m^3	Respiratory symptoms in children	OR 1.50 (0.8-2.8) 90th percentile
Hernandez- Cadena et al., (2000) (Mexico)	PM_{10}: 24-hr Average 34.46 μg/m^3	Respiratory diseases in children <15yrs	OR 4.97 (0.77-9.13) for an increase in 20μg/m^3
Hwang and Chan (2002) (Taiwan)	PM_{10}: 24-hr Average 58.9 ± 14 μg/m^3	Lower respiratory tract illness in adults ≥65yrs	RR 1.8 (1.4-2.2) for increase in 10%
Ibald-Mulli et al., (2004) (Germany)	$PM_{2.5}$: 24-hr Average 12.7-20 μg/m^3 (±39.8-118 μg/m^3 for 3 cities)	Blood Pressure increase heart in adults 40-84yrs	β -0.27 (-0.5-.03) for increase in 10 μg/m^3
Keeler et al., (2002) (US)	PM_{10}: 24-hr Average 28.9 ± 14.4 μg/m^3 (west Detroit) 23.8 ± 12.1 μg/m^3 (east Detroit) $PM_{2.5}$: 24-hr Average 17.0 ± 9.3 μg/m^3 (west) 15.5 ± 9.0 μg/m^3 (east)	Respiratory disease in children	N/A
Liao et al., (1999) US	$PM_{2.5}$: 24-hr Average ≥ 15 μg/ m^3	CVD, HRV in adults 65-84yrs	OR 3.08 (1.43-6.59)
Mc Connell et al., (1999) (US)	PM_{10}: 24-hr Average 34.8 μg/m^3	Respiratory symptoms bronchitis in children	OR 1.4 (1.1-1.4) for increase in 10 μg/m^3
Pentinen et al., (2001) (Finland)	PM_{10}: Median 13.5 μg/m^3 Range 3.8-73.7 μg/m^3 $PM_{2.5}$: Median 8.4 μg/m^3 Range 2.4-38.3 μg/m^3	Respiratory symptoms PEF and asthma in adults mean age 53yrs	At lag 0 Symptoms β 0.001 (SEM 0.04)
Peters et al., (2001) (US)	PM10: 24-hr Average 19.4 ± 9.4 μg/m^3	CVD in adults mean age 61.6 ± 13.4yrs	OR 1.69 (1.13-2.34) for increase in 20 μg/m^3

Table 1 (Cont'd)

Author (Country)	Level of Exposure	End Point	Risk Estimate
Slaughter et al., (2003) (US)	PM_{10}: 21.0 μg/m^3 (75th Percentile =29.3 μg/m^3)	Respiratory symptoms asthma attacks in children	OR 1.12 (1.04-1.22) for increase in 10 μg/m^3
von Klot et al., (2001) (Germany)	PM_{10}: 24-hr Average 45.4 μg/m^3 $PM_{2.5}$: 24-hr Average 10.3 μg/m^3	Respiratory symptoms in adults mean age 59yrs	OR 1.01 (.95-1.06) for increase in 1 IQR of 12
Yu et al., (2000) (US)	PM_{10}: 24-hr Average 24.7 μg/m^3	Respiratory symptoms asthma in children mean age 8.6 ± 2.1yrs	OR18% (5-33) for increase in 10 μg/m^3
Peters et al., (2000) (US)	PM_{10}: 24-hr Average 19.3 μg/m^3	CVD arrhythmias in adults mean age 62.2yrs	OR 0.95 (0.59-1.54) for Same day defibrillation discharge for 1 event
Desqueyroux et al., (2002) (France)	PM_{10} Winter 24-hr Average 28 ±14 μg/m^3 Summer 24-hr Average 23 ±9 μg/m^3	Respiratory symptoms asthma in adults mean age 55yrs	OR 1.41 (1.16-1.7) for increase in 10 μg/m^3
Delfino et al., (2002) (US)	PM_{10}: 24-hr Average 7-32 μg/m^3	Respiratory disease asthma in children	OR 1.35 (0.82-2.2) v/s OR 0.80 (0.24-2.69) for Lag 0 vs.90th percentile
de Hartog et al., (2003) (Amsterdam Finland Germany)	$PM_{2.5}$: Average 24-hr 12.8-23.4 μg/m^3 PM_{10}: Average 24-hr 19.6-36.5 μg/m^3	Cardio-respiratory symptoms in elderly	OR 1.12 (1.02-1.24) OR 1.09 (0.97-1.22) for increase in 10 μg/m^3

This project will test the following study hypothesis:

Hypothesis 1. Increased PM_{10} changes of 10 μg/m³ will be linked to cardiopulmonary symptoms in the most susceptible adult populations.

Hypothesis 2. The peak expiratory flow rates will decrease by 10% from the mean individual peak flow rate when PM_{10} levels increase by levels of 10 μg/m³ in individuals with pre-existing cardiopulmonary conditions

Hypothesis 3. Individuals with pre-existing cardiopulmonary conditions who are not on anti-inflammatory medication will experience increased cardiopulmonary symptoms when PM_{10} increase by levels of 10 μg/m³.

3.0 RESEARCH DESIGN AND METHODOLOGY

The goal of the Allegheny County short-term air pollution effects (SHAPE) study was to determine if there is an association between ambient air exposures and the incidence of short-term cardiopulmonary responses in susceptible adult individuals aged between 50–79 years old. Inhalable ambient particulate matter ≤10 um in aerodynamic diameter (PM_{10}) from a selected Allegheny County Health Department (ACHD) Division of Air Quality monitoring site was used in the analysis. The study was carried out in a portion of Allegheny County, PA, which is in the south west of Pennsylvania (Figure 1).

3.1 Rationale of Selection of the Study

The SHAPE study focused on effects of air pollution on residents in the southwest part of the county because of the major stationary polluting sources that are still operating in the area, including a major coal fired coke plant. The selection of the study area was additionally influenced by a concurrent evaluation of the PACCC admission data of Allegheny County, 1995-2000 which showed that the local health facility in the south west of the county, had the second largest number of admissions among the elderly aged ≥65 years old compared to other facilities. The facility also had the highest number of admissions from surrounding zip codes areas, an indication that the communities utilize mainly their local health facility for tertiary health care.

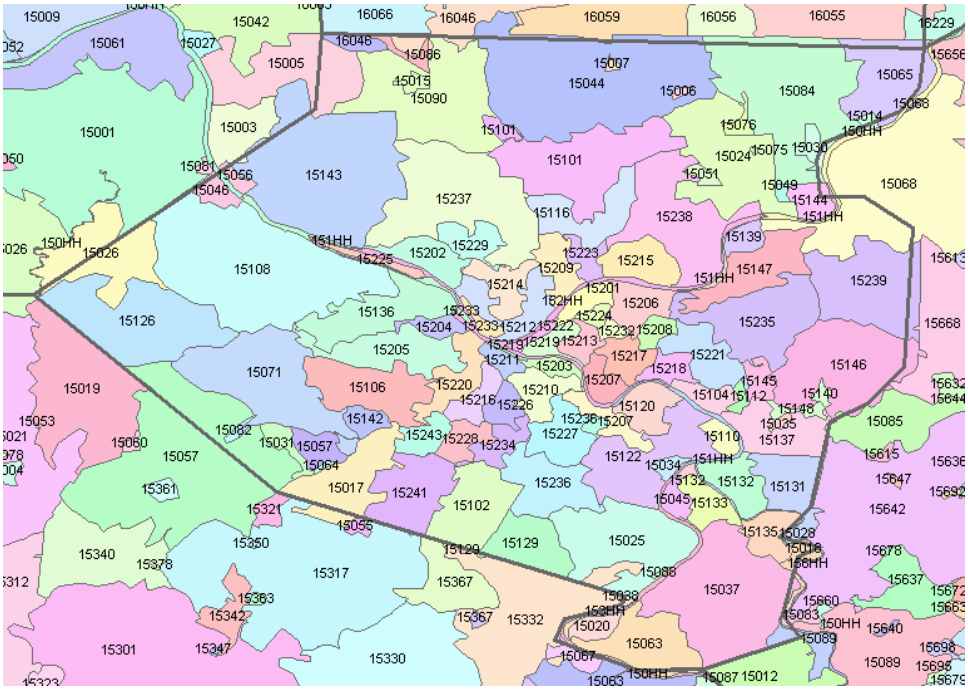


Figure 1: A Map of Allegheny County study area showing boundaries to other counties

Furthermore, the analysis of the PACCC admission data of years 1995-2000 showed that a total of 588,678 hospital admissions were of the elderly aged ≥65 years old admitted to the Allegheny County health facilities that exclude nursing homes, hospice and long-term facilities. Forty-three percent (252,612) of these admissions were due to cardiopulmonary primary conditions, ICD-9 codes 390-519. Over 60% of the elderly were aged less than 80 years. More females were admitted to the hospitals compared to the males (Table 2). The mean length of hospital stay was 7 days (STD±7.592). Perez-Hoyos et al., (2000) reported an average length of stay in the hospital emergency room of 5.21 hours for asthma and 6.32 hours for COPD and longer among study subjects. The authors caution air pollution studies that examine hospital admission data and the lag effects of air pollution. The date of admission can be erroneous for a subject who is admitted late at night to the ER and then later on admitted to the hospital in the

early hours of the following day. When the data was examined further for patterns of discharge diagnosis (primary diagnosis), among the 252,612 hospital admissions for the six-year study period the results showed that the majority of the discharge diagnoses were for cardiovascular diseases (72.7%) and 27.3% for respiratory disease causes (Table 3). Ischemic heart disease (IHD) conditions accounted for 21.81% of the admissions. These IHD include acute myocardial infarction, and angina pectoris and other forms of IHD. Twenty-five percent (25%) of the admissions were due to other forms of heart disease that included heart failure (15%), and cardiac arrhythmias (8%). Pneumonia and influenza accounted for the highest number of admissions among respiratory diseases conditions (10.50%), followed by COPD (9.28%).

Forty nine percent of the individuals were admitted multiple times during the 6–year study period 1995- 2000. The discharge diagnosis of each individual's first-ever admission to a health facility was evaluated for both the individuals admitted multiple times and those admitted only one. Tables 4 shows the rates of admissions by ICD Codes of the primary diagnosis. For those admitted more than one time we show the diagnoses obtained at their ever first admission during the study period. The results show that individuals admitted more than one time had frequently a diagnosis of acute conditions compared to those admitted only one time. For example the rate of admission for IHD was 6,335 /100,000 for the multiple admissions group compared to 5,285 among the group admitted only one time. The one-time admission group was frequently admitted for chronic causes such as disease of the veins and lymphatic circulation 1363/100,000 compared to 797/100,000 among the multiple admissions group; pneumoconiosis and other lung diseases 844/100,000 compared to 444/100,000 among those admitted multiple times. The rates were calculated using the 2000 U.S. Census Bureau population data for the Allegheny County age group ≥65 years.

Further, the PACCC data was examined for the admitting diagnosis of those admitted multiple times (an admitting diagnosis is a diagnosis assigned when an individual first arrives to a hospital). There were a total of 463 specific ICD-9 codes assigned to the cohort. The results showed that 16% of the admitting diagnoses were for heart failure (ICD code 428), 11% for unspecified respiratory symptoms (ICD code, 786), 8% for pneumonia and other unspecified organisms (ICD code, 486), 7% for cardiac dysrhythmias (ICD code, 427), 5% for acute myocardial infraction and other acute and subacute form of ischemic heart disease (ICD code, 411 and ICD code 410) respectively, 4% for chronic bronchitis (ICD code, 491).

The admission rates of this age group ≥65 years old remained relatively constant across the age groups. Higher rates for the age group ≥75 increased slightly each year. The rates of admissions were higher in females compared to males during the entire study (Table 5). The admission rates across ethnicity groups were consistent with the different population groups in Allegheny County where more whites than other races were admitted to the hospitals.

An analysis of the discharge status of the multiple admissions showed that more than half (55%) of this age group is discharged home for self-care following hospitalization (Table 6). These results also showed that this group of patients is discharged home mostly for independent living. The premise is that these individuals live actively in their communities and may endure environmental exposures equally as much as any other age group but their susceptibility to the environmental exposures may be higher (Goldberg et al., 2000; Zanobetti et al., 2000; Delfino et al., 1997; Pope et al., 1999; Liao et al., 1999; Gold et al., 2000; Stone et al., 1999). This requires regional longitudinal investigation.

Furthermore, during the PACCC data evaluation for the period (1995-2000) the local county air pollution showed a maximum 24-hr PM_{10} of 490 $\mu g/m^3$ and average 24-hour PM_{10} of

28 $\mu g/m^3$. In general, the pollution levels have declined with the average 24-hour PM_{10} of 31 $\mu g/m^3$ observed in year1995 to 27 $\mu g/m^3$ observed in year 2000 (Table 7). The PM_{10} averages for both the mean and the maximum showed high peak levels during the summer and fall months (Figure 2). The results also showed that the air pollution is improving over time. For example the 24-hr average PM_{10} was 30 $\mu g/m^3$ in 1995 and 25 $\mu g/m^3$ in year 2000 (Table 7, Figure 2). Additionally, the air pollution level showed that Lincoln and Liberty Borough exhibited high levels of particulate matter emissions compared to other continuous monitoring sites (Lincoln maximum 101 $\mu g/m^3$, average 40 $\mu g/m^3$; and Liberty maximum 74 $\mu g/m^3$, average 30 $\mu g/m^3$). These two sites were located to monitor compliance of the industrial plants in the southwest of Allegheny County.

For additional analysis, we stratified the data into admission category, that is, individuals who were admitted only one time and individuals who were admitted more than one time but only considering the first time an individual was ever admitted during the study period. A logistic regression using the SAS system was carried out to assess the effect of the 24-hr average PM_{10}, and confounding meteorological variables of dew point average, mean temperature, mean relative humidity, pressure, and also effects of seasonality, day of the week and age group. The results showed highly significant association between PM_{10} ($p<.0001$) and the type of admission of the elderly individuals and a very narrow margin of risk (OR =1.002, 95% CI= 1.002 – 1.003). However, seasonality, pressure and age group also had high significant effect ($p<.0001$) on type of admission.

Table 2: Comparison of Admission frequency by age group and gender: 1995-2000

* Age Group	Multiple Admissions			One-time Admission		
	Males	Females	Total	Males	Females	Total
65-69	5,733	5,001	10,734	5,435	5,232	10,667
% within Gender	22.7%	16.1%	19.0%	22.9%	15.0%	18.2%
70-74	6,409	6,292	12,701	5,746	6,529	12,275
% within Gender	25.4%	20.2%	22.5%	24.2%	18.7%	20.9%
75-79	5,925	7,124	13,049	5,255	7,333	12,588
% within Gender	23.4%	22.9%	23.1%	22.2%	21.0%	21.4%
80+	7,204	12,703	19,907	7,287	15,884	23,171
% within Gender	28.5%	40.8%	35.3%	30.7%	45.4%	39.5%
Total	25,271	31,120	56,391	23,723	34,978	58,701

* Mean age for multiple admissions is 76.77. Mean age for one time admission is 77.54

Table 3: Distribution of admission for the elderly by primary diagnosis: 1995-2000

Cause of Admission	ICD Code	N	%
DISEASE OF THE CIRCULATORY SYSTEM	390-459		
Acute and Chronic Rheumatic Heart Disease	**390-392**	**15**	**0.00**
Chronic Rheumatic Heart Disease	**393-398**	**2,012**	**0.80**
Disease of Mitral Valve	394	140	0.06
Disease of Aortic Valve	395	36	0.01
Disease of Mitral and Aortic Valve	396	586	0.23
Disease of other Endocardial Structure	397	18	0.00
Other Rheumatic Heart Disease	393, 398	1,232	0.50
Hypertensive Diseases	**401-405**	**5,072**	**2.01**
Essential Hypertension	401	1,255	0.50
Hypertensive Heart Disease	402	2,278	0.90
Hypertensive renal Disease	403	809	0.32
Hypertensive heart and renal Disease	404	692	0.27
Secondary Hypertension	405	38	0.02
Ischemic Heart Disease	**410-414**	**55,103**	**21.81**
Acute Myocardial Infarction	410	20,424	8.09
Other Acute and Subacute Form of Ischemic Heart Disease	411	3,394	1.34
Old Myocardial Infarction	412	3	0.00
Angina Pectoris	413	1,038	0.41
Other Forms of Ischemic Heart Disease	414	30,244	11.97
Disease of the Pulmonary Circulation	**415-417**	**2,164**	**0.85**
Acute pulmonary heart disease	415	1,858	0.73
Chronic pulmonary heart disease	416	303	0.12
Disease of other pulmonary circulation	417	3	0.00

Table 3 (Cont'd)

Cause of Admission	ICD Code	N	%
Other Forms of Heart Disease	**420-429**	**63,802**	**25.27**
Acute pericarditis and pericardium diseases	420, 423	470	0.19
Acute and subacute endocarditis	421	277	0.11
Other disease of endocardium	424	1,490	0.59
Cardiomyopathy	425	611	0.24
Conduction disorders	426	1,538	0.61
Cardiac dysrhythmias	427	20,501	8.12
Heart failure	428	38,740	15.34
Other and ill-defined heart disease	422,429	175	0.06
Cerebrovascular Diseases	**430-438**	**35,341**	**13.99**
Subarachnoid hemorrhage	430	398	0.16
Intracerebral hemorrhage	431	2,110	0.84
Other and unspecified intracranial hemorrhage	432	509	0.20
Occlusion and stenosis of precerebral arteries	433	6,526	2.58
Occlusion of cerebral arteries	434	12,607	4.99
Transient cerebral ischemia	435	8,261	3.27
Acute but ill-defined cerebrovascular disease	436	3,853	1.53
Other ill-defined cerebrovascular disease	437	901	0.36
Late effects of cerebrovascular disease	438	176	0.07
Disease of Arteries, Arterioles and Capillaries	**440-448**	**10,780**	**4.26**
Atherosclerosis	440	4,290	1.70
Aortic aneurysm	441	2,656	1.05
Other aneurysm	442	295	0.12
Other peripheral vascular disease	443	1,175	0.47
Arterial embolism and thrombosis	444	1,558	0.62
Polyarteritis nodosa and allied conditions	446	240	0.10
Other disorders of arteries and arterioles	447	545	0.22
Disease of capillaries	448	21	0.00

Table 3 (Cont'd)

Cause of Admission	ICD Code	N	%
Disease of Veins, Lymphatic and Others Diseases of Circulatory System	**451-459**	**9,060**	**3.59**
Phlebitis and thrombophlebitis	451	728	0.29
Other venous embolism and thrombosis	452-453	4,197	1.66
Varicose veins	454-456	1,179	0.47
Hypotension	458	2,278	0.90
Other disorders of circulatory system	457, 459	678	0.27
DISEASE OF THE RESPIRATORY SYSTEM	**460-519**		
Acute Respiratory Infection	**460-466**	**2,242**	**0.89**
Acute bronchitis and bronchiolitis	466	1,941	0.77
Other acute respiratory infections	460-465	301	0.12
Other Diseases of Upper Respiratory Tract	**470-478**	**240**	**0.10**
Pneumonia and Influenza	**480-487**	**26,521**	**10.50**
Viral pneumonia	480	188	0.07
Pneumococcal pneumonia	481	1,002	0.40
Other bacterial pneumonia	482	5,217	2.07
Bronchopneumonia, organism unspecified	485	290	0.11
Pneumonia, other, unspecified	483, 484, 486	19,598	7.76
Influenza	487	226	0.09
Chronic Obstructive Pulmonary Disease and Allied Conditions	**490- 496**	**23,449**	**9.28**
Bronchitis, not specified as acute or chronic	490	376	0.15
Chronic bronchitis	491	16,842	6.67
Emphysema	492	849	0.34
Asthma	493	3109	1.23
Bronchiectasis	494	192	0.08
Extrinsic allergic alveolitis and other chronic airways obstruction	495-496	2,081	0.82

Table 3 (Cont'd)

Cause of Admission	ICD Code	N	%
Pneumoconiosis and Other Lung Disease Due to External Agents	**500-508**	**7,529**	**2.98**
Coalworker's pneumoconiosis	500	23	0.01
Asbestosis and pneumoconiosis due to other silica or silicates	501-502	35	0.02
Pneumoconiosis, other and unspecified	503-505	5	0.00
Pneumonitis due to solids and liquids	507	7,395	2.93
Respiratory conditions due to other and unspecified external agents	506, 508	71	0.02
Other Disease of the Respiratory System	**510-519**	**9,282**	**3.67**
Emphysema	510	171	0.07
Pleurisy	511	1,541	0.61
Pneumothorax	512	590	0.23
Abscess of lung and mediastinum	513	123	0.05
Pulmonary congestion and hypostasis	514	147	0.06
Postinflammatory pulmonary fibrosis	515	428	0.17
Other alveolar and parietoalveolar pneumopathy	516	333	0.13
Other disease of the lung	517-518	5,751	2.28
Other disease of respiratory system	519	198	0.08
Total Admissions	**390-519**	**252,612**	**100**

Table 4: Rates of admission by discharge diagnosis among the elderly admitted multiple and one-time 1995-2000

Diagnosis and Diagnostic Codes		* First ever admission of multiple admissions			**One time admission		
Primary Diagnosis	**ICD Code**	**N**	**%**	**Rates*** **	**N**	**%**	**Rates*** **
DISEASES OF CIRCULATORY SYSTEM							
Acute and Chronic Rheumatic Heart Disease	390-392	1	0		2	0	
Chronic Rheumatic Heart Disease	**393-398**	**381**	**0.65**	**166.80**	**324**	**0.55**	**142.72**
Disease of Mitral Valve	394	30	0.05	13.13	31	0.05	13.57
Disease of Aortic Valve	395	7	0.01	3.06	11	0.02	4.82
Disease of Mitral and Aortic Valve	396	130	0.22	56.91	150	0.26	66.55
Disease of other Endocardial Structure	397	3	0	1.31	5	0.01	2.19
Other Rheumatic Heart Disease	393, 398	211	0.37	92.38	127	0.21	55.60
Hypertensive Diseases	**401-405**	**1,077**	**1.92**	**471.51**	**1,090**	**1.86**	**478.95**
Essential Hypertension	401	303	0.54	132.65	473	0.81	207.95
Hypertensive Heart Disease	402	496	0.88	217.15	393	0.67	172.49
Hypertensive renal Disease	403	167	0.3	73.11	136	0.23	59.98
Hypertensive heart and renal Disease	404	102	0.18	44.66	80	0.14	35.02
Secondary Hypertension	405	9	0.02	3.94	8	0.01	3.50
Ischemic Heart Disease	**410-414**	**14,472**	**25.64**	**6,335.81**	**12,014**	**20.56**	**5,285.09**
Acute Myocardial Infarction	410	6,012	10.64	2,632.04	4,756	8.16	2,098.36
Other Acute and Subacute Form of Ischemic Heart Disease	411	1,225	2.17	536.30	682	1.17	300.33
Old Myocardial Infarction	412	1	0	0.44	0	0	0.00
Angina Pectoris	413	332	0.59	145.35	314	0.54	138.34
Other Forms of Ischemic Heart Disease	414	6,902	12.24	3,021.68	6,262	10.69	2,748.06

*The first-ever admission shows the first diagnosis among individuals admitted multiple times during the six years of study. ** Total number of people admitted only one time during the six years of study. Percent is calculated from the total admissions. ***Rate per 100,000 Populations, US Census Bureau 2000

Table 4 (Cont'd)

Diagnosis and Diagnostic Codes		* First ever admission of multiple admissions			**One time admission		
Primary Diagnosis	**ICD Codes**	**N**	**%**	**Rates*** **	**N**	**%**	**Rates*** **
Disease of the Pulmonary Circulation	**415-417**	**416**	**.75**	**182.12**	**768**	**1.32**	**338.42**
Acute pulmonary heart disease	415	363	0.65	158.92	700	1.2	308.21
Chronic pulmonary heart disease	416	52	0.1	22.77	68	0.12	30.21
Disease of other pulmonary circulation	417	1	0	0.44	0	0	0.00
Other Forms of Heart Disease	**420-429**	**13,365**	**23.72**	**5,851.17**	**11,746**	**20.11**	**5,170.39**
Acute pericarditis and pericardium diseases	420, 423	101	0.18	44.22	161	0.27	70.92
Acute and subacute endocarditis	421	49	0.08	21.45	62	0.11	27.14
Other disease of endocardium	424	336	0.6	147.10	409	0.7	179.50
Cardiomyopathy	425	118	0.2	51.66	111	0.21	53.85
Conduction disorders	426	394	0.71	172.49	587	1	256.99
Cardiac dysrhythmias	427	4,877	8.66	2,135.14	5,270	9.01	2,315.95
Heart failure	428	7,463	13.24	3,267.28	5,105	8.76	2,252.03
Other and ill-defined heart disease	422,429	27	0.05	11.82	31	0.05	14.01
Cerebrovascular Diseases	**430-438**	**8,816**	**15.63**	**3,859.62**	**10,633**	**18.2**	**4,681.37**
Subarachnoid hemorrhage	430	75	0.13	32.83	169	0.29	75.74
Intracerebral hemorrhage	431	409	0.73	179.06	828	1.42	364.69
Other and unspecified intracranial hemorrhage	432	95	0.17	41.59	187	0.32	81.87
Occlusion and stenosis of precerebral arteries	433	1,979	3.5	866.40	1,722	2.94	756.08
Occlusion of cerebral arteries	434	3,278	5.82	1,435.10	3,846	6.6	1,697.34
Transient cerebral ischemia	435	2,072	3.68	907.12	2,602	4.44	1,141.34
Acute but ill-defined cerebrovascular disease	436	708	1.26	309.96	975	1.67	430.36

*The first-ever admission shows the first diagnosis among individuals admitted multiple times during the six years of study. ** Total number of people admitted only one time during the six years of study. Percent is calculated from the total admissions. ***Rate per 100,000 Populations, US Census Bureau 2000

Table 4 (Cont'd)

Diagnosis and Diagnostic Codes		* First ever admission of multiple admissions			**One time admission		
Primary Diagnosis	**ICD Codes**	**N**	**%**	**Rates*** **	**N**	**%**	**Rates*** **
Other ill-defined cerebrovascular disease	437	178	0.31	77.93	275	0.47	121.27
Late effects of cerebrovascular disease	438	22	0.03	9.63	29	0.05	12.70
Disease of Arteries, Arterioles and Capillaries	**440-448**	**2,434**	**4.27**	**1,065.60**	**2,681**	**4.59**	**1,178.11**
Atherosclerosis	440	965	1.72	422.47	795	1.36	349.36
Aortic aneurysm	441	537	0.95	235.10	1,059	1.81	464.94
Other aneurysm	442	67	0.12	29.33	63	0.11	28.02
Other peripheral vascular disease	443	269	0.47	117.77	190	0.32	83.18
Arterial embolism and thrombosis	444	393	0.71	172.05	377	0.65	166.36
Polyarteritis nodosa and allied conditions	446	63	0.11	27.58	74	0.13	32.40
Other disorders of arteries and arterioles	447	135	0.19	59.10	116	0.2	50.78
Disease of capillaries	448	5	0	2.19	7	0.01	3.06
Disease of Veins, Lymphatic and Others Diseases of Circulatory System	**451-459**	**1,817**	**3.2**	**795.48**	**3,104**	**5.3**	**1,363.30**
Phlebitis and thrombophlebitis	451	184	0.32	80.55	282	0.48	124.33
Other venous embolism and thrombosis	452-453	822	1.46	359.87	1,589	2.72	697.41
Varicose veins	454-456	256	0.45	112.08	420	0.71	184.31
Hypotension	458	427	0.75	186.94	620	1.06	272.75
Other disorders of circulatory system	457, 459	128	0.22	56.04	193	0.33	84.49
DISEASE OF THE RESPIRATORY SYSTEM							
Acute Respiratory Infection	**460-466**	**576**	**1.05**	**252.17**	**765**	**1.29**	**336.23**
Acute bronchitis and bronchiolitis	466	498	0.89	218.02	651	1.11	286.32
Other acute respiratory infections	460-465	78	0.16	34.15	114	0.18	49.91
Other Diseases of Upper Respiratory Tract	**470-478**	**48**	**0.07**	**21.01**	**97**	**<1**	**42.47**

*The first-ever admission shows the first diagnosis among individuals admitted multiple times during the six years of study. ** Total number of people admitted only one time during the six years of study. Percent is calculated from the total admissions. ***Rate per 100,000 Populations, US Census Bureau 2000

Table 4 (Cont'd)

Diagnosis and Diagnostic Codes		* First ever admission of multiple admissions			**One time admission		
Primary Diagnosis	**ICD Codes**	**N**	**%**	**Rates*** **	**n**	**%**	**Rates*** **
Pneumonia and influenza	**480-487**	**5,580**	**9.89**	**2,442.91**	**7,485**	**12.85**	**3,304.06**
Viral pneumonia	480	51	0.1	22.33	59	0.1	25.83
Pneumococcal pneumonia	481	256	0.45	112.08	316	0.54	138.78
Other bacterial pneumonia	482	1,121	1.98	490.77	1,302	2.25	577.46
Bronchopneumonia, organism unspecified	485	72	0.13	31.52	77	0.13	34.59
Pneumonia, other, unspecified	483,484, 486	4,041	7.16	1769.14	5,606	9.66	2,483.63
Influenza	487	39	0.07	17.07	100	0.17	43.78
Chronic Obstructive Pulmonary Disease and Allied Conditions	**490- 496**	**4,981**	**9.72**	**2,180.67**	**3,667**	**6.3**	**1,615.91**
Bronchitis, not specified as acute or chronic	490	108	0.19	47.28	111	0.19	48.60
Chronic bronchitis	491	3,277	5.81	1,434.66	2,356	4.04	1,037.14
Emphysema	492	231	0.41	101.13	121	0.21	53.41
Asthma	493	789	1.39	345.42	734	1.26	323.09
Bronchiectasis	494	41	0.97	17.95	28	0.05	12.26
Extrinsic allergic alveolitis and other chronic airways obstruction	495-496	535	0.95	234.22	317	0.55	141.41
Pneumoconiosis and Other Lung Disease Due to External Agents	**500-508**	**939**	**1.65**	**411.09**	**1,916**	**3.28**	**844.51**
Coalworker's pneumoconiosis	500	5	0.01	2.19	8	0.01	3.50
Asbestosis and pneumoconiosis due to other silica or silicates	501-502	12	0.02	5.25	6	0.01	2.63
Pneumoconiosis, other and unspecified	503-505	2	0	0.88	2	0	0.88
Pneumonitis due to solids and liquids	507	907	1.6	397.08	1,877	3.22	827.44

*The first-ever admission shows the first diagnosis among individuals admitted multiple times during the six years of study. ** Total number of people admitted only one time during the six years of study. Percent is calculated from the total admissions. ***Rate per 100,000 Populations, US Census Bureau 2000

Table 4 (Cont'd)

Diagnosis and Diagnostic Codes		* First ever admission of multiple admissions			**One time admission		
Primary Diagnosis	**ICD Codes**	**N**	**%**	**Rates*** **	**n**	**%**	**Rates*** **
Respiratory conditions due to other and unspecified external agents	506, 508	13	0.02	5.69	23	0.04	10.07
Other Disease of the Respiratory System	**510-519**	**1,487**	**2.58**	**651.01**	**2,081**	**3.58**	**919.81**
Emphysema	510	30	0.06	13.13	52	0.09	22.77
Pleurisy	511	221	0.39	96.75	375	0.64	165.05
Pneumothorax	512	159	0.28	69.61	166	0.28	73.11
Abscess of lung and mediastinum	513	18	0.03	7.88	25	0.04	10.94
Pulmonary congestion and hypostasis	514	38	0.07	16.64	24	0.04	10.51
Postinflammatory pulmonary fibrosis	515	80	0.14	35.02	103	0.18	45.09
Other alveolar and parietoalveolar pneumopathy	516	68	0.12	29.77	80	0.14	36.34
Other disease of the lung	517-518	837	1.49	366.44	1,217	2.1	538.93
Other disease of respiratory system	519	36		15.76	39	0.07	17.07
Total Admissions	**390-519**	**56,391**	**100**	**24,687.85**	**58,373**	**100**	**25,700.91**

*The first-ever admission shows the first diagnosis among individuals admitted multiple times during the six years of study. ** Total number of people admitted only one time during the six years of study. Percent is calculated from the total admissions. ***Rate per 100,000 Populations, US Census Bureau 2000

Table 5: Rates of admissions of elderly in Allegheny County for cardiopulmonary causes: 1995-2000

Year of Admission	*Rates of Admissions Persons 65-74 Years	*Rates of Admissions Persons ≥75 Years	*Rates of Admissions Male	*Rates of Admissions Female
	Rates (N)	Rates (N)	Rates (N)	Rates (N)
1995	50.18 (11,872)	72.33 (17,112)	52.79 (12,490)	69.71 (16,493)
1996	49.39 (11,633)	73.19 (17,238)	53.84 (12,682)	69.16 (16,289)
1997	47.63 (11,047)	75.04 (17,404)	52.61 (12,201)	70.06 (16,250)
1998	44.24 (10,188)	76.32 (17,574)	52.83 (12,165)	69.44 (15,989)
1999	45.16 (10,228)	81.66 (18,494)	54.68 (12,383)	72.14 (16,337)
2000	42.18 (9,635)	81.52 (18,620)	53.04 (12,114)	70.66 (16,141)

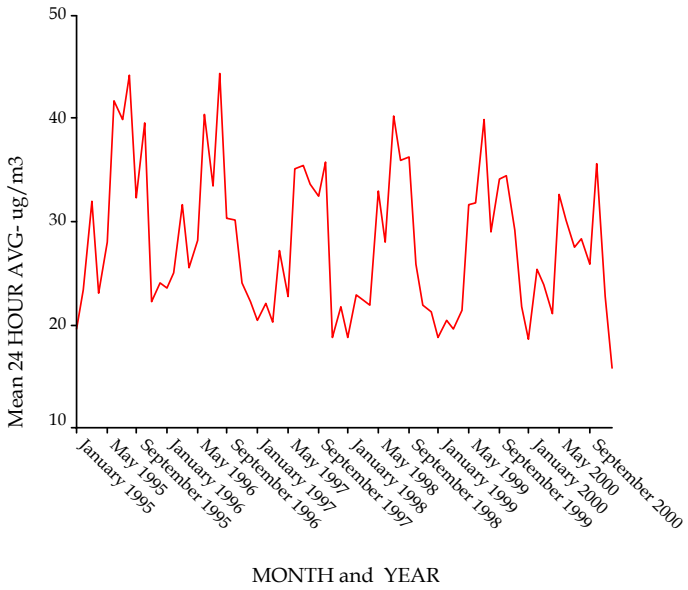
*Rates of admissions are expressed for population per 1,000. N= number of admissions. The denominator is from the Allegheny County Population Estimates for 1995-2000 and 2000 US Census Data for Allegheny County. The rates of hospital admissions among Persons 65-74 years group show a decline from 1995-2000, and an increase among Persons ≥75 Years.

Table 6: Discharge status of elderly admitted multiple times: 1995-2000

Discharge Status	Frequency	Percent
Discharged home-self care	105,817	54.57
Transferred to another General Hospital	9,935	5.12
Discharged to a skilled nursing facility	27,356	14.11
Discharged to an intermediate care facility	2,111	1.09
Discharged to another type of inpatient care	13,451	6.94
Discharged home under Home service care services	26,051	13.43
Expired	8,666	4.47
Other discharge status	520	0.27
Total	**193,907**	**100**

Table 7: Mean and maximum PM_{10} µg/m^3 averages for Allegheny County: 1995-2000

YEAR		24-hr Max-µg/m^3	24-hr Ave-µg/m^3
1995	Maximum	454.00	192.35
	Mean	69.95	30.84
	Std. Deviation	57.00	20.67
1996	Maximum	461.00	145.53
	Mean	70.00	29.97
	Std. Deviation	54.87	18.86
1997	Maximum	376.00	158.38
	Mean	62.92	27.18
	Std. Deviation	50.04	17.95
1998	Maximum	400.00	147.10
	Mean	60.10	27.32
	Std. Deviation	47.29	17.40
1999	Maximum	379.00	141.59
	Mean	66.16	27.21
	Std. Deviation	53.35	18.59
2000	Maximum	490.00	150.00
	Mean	56.57	25.57
	Std. Deviation	47.30	16.71



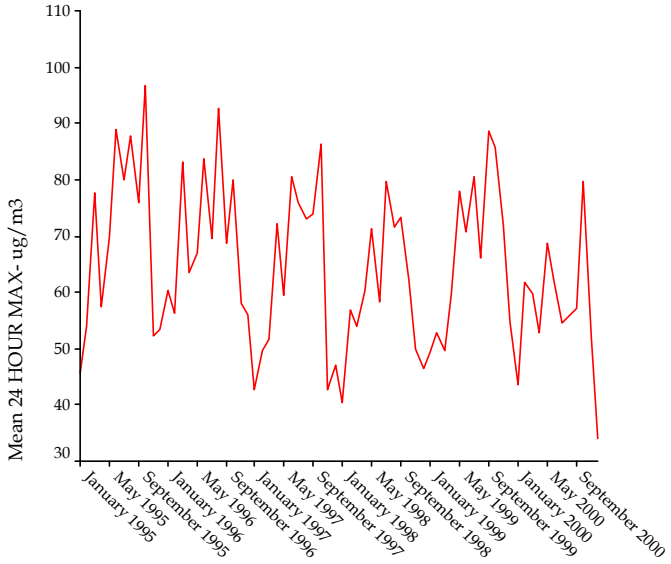


Figure 2: Mean and maximum PM_{10} µg/m^3 levels for Allegheny County, 1995-2000

A search of the USEPA Toxics Release Inventory (TRI) database identified industrial sites in this part of Allegheny County that reported high amounts total air emission of toxic chemicals through stack and fugitives in 2001 (Table 8). According to the USEPA, the TRI data reports toxic emissions and other waste management activities of chemicals with no inference to human health. However, the data serves as a good starting point in research of exposure and health outcomes. Allegheny County houses several chemical plants, including several coke plants, as well as other heavy manufacturing facilities. Most of these plants are strategically located along the main river valleys, which have topography of jagged hills, and valleys that can entrap pollution during a temperature inversion. An example of these sites is the Neville Island located on the Ohio River, whose toxic release inventory, account for 25% of the annual toxic chemical releases in Allegheny County. The USEPA declared portions of the Neville Island as a Superfund Waste Site in April 1990. Another plant, in the southwest of Allegheny County reported 1,175,414 lbs total air emissions in 2001, reporting the largest emission amounts that year. Allegheny County housed 6% of the TRI sites in the state of Pennsylvanian and contributed 7% to the total reported emissions in the state for year 2001. The aim of the SHAPE study was to consider all these factors of environmental concerns and to determine if susceptible populations are affected deleteriously during short-tem exposures to variable air pollution concentrations.

Table 8: Selected Allegheny County TRI sites showing quantity of emissions by facility: 2001

Name of Facility	Fugitive Air Emissions	Stack Air Emissions	Total Air Emissions	On /Off Site Emissions
Guardian Industries Corp Floreffe	0	84,919	84,919	84,945
Large Plant of TYK America INC.	500	1,000	1,500	1,500
Liberty Pultrusions	0	750	750	750
Safety-Kleen Systems (414502)	0	5	5	5
Tech MET INC	491	967	1,458	1,458
Whemco-Steel Castings INC	43	0	43	7,953
USS Clairton Works	879,785	295,729	1,175,510	1,616,860
USS Mon Valley Works Irvin Plant	9	21,982	21,982	65,937
***TOTAL ALL ALLEGHENY**	**1,238,280**	**5,396,079**	**6,634,360**	**15,639,800**

Sites are shown of Zip Codes area 15025, 15122, 15045, and 15120. *Total All Allegheny is emission totals in pounds (lbs) of all of the 94 self-reported sites in Allegheny County, 2001

3.2 Study Design

This is a longitudinal study that involved participation of individuals over a period of 60 days to assess whether there is an association between ambient air pollution exposure and cardiopulmonary illness. Participants monitored their peak expiratory flow rates, acute symptoms and medication use for a maximum of two months. The relationship between PM_{10} and cardiopulmonary responses of daily peak expiratory flow rate (PEFR), as well as anti-inflammatory medication use can be expressed in a hypothetical way where exposure can result in either respiratory or cardiovascular conditions or both (Figure 4). There is no direct relationship between exposure and medication. However, exposures to air pollution triggers the respiratory or cardiac physiological mechanisms resulting the need for an individual to regulate their medication use (Figure 4). Because of lack of individual exposure and utilizing ecological exposure, the assumption of this type of study is that all participants are exposed to the same levels of particulate matter in a given period. The effect on all participants will be relatively similar regardless of health condition.

All measurements were obtained from a population living within the same area and at varying periods of the year with each individual participating for a consecutive 60-day maximum period. The data acquired from the study participants were repeated measurements, which make it possible to establish, with some detail, the temporality of causal associations and to examine acute exposure-response relationships at the level of an individual subject. When a study is of repeated measure, subjects can act as their own control over time, analogous to a clinical crossover trial (Delfino et al., 2002; Checkoway et al., 2000; Mittleman et al., 1995). Longitudinal design with repeated measures can be an efficient way to maximize information derived from a small number of subjects (Stokes et al., 2001; Rochon J, 1998). According to

Delfino, (2002) power and precision in longitudinal studies can be enhanced because the repeated measures reduce the variability of the response variable without reducing the magnitude of the true exposure-response relationships. Thus data from each subject is expected to be correlated overtime.

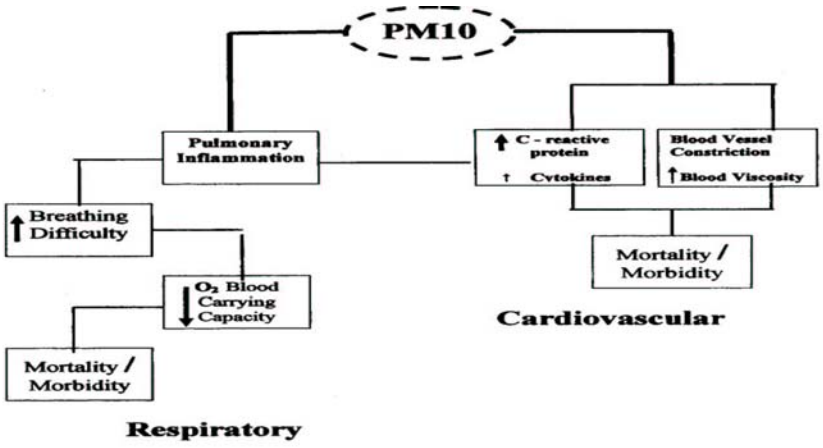


Figure 3: A hypothetical schematic of patho-physiological response to PM_{10} exposure

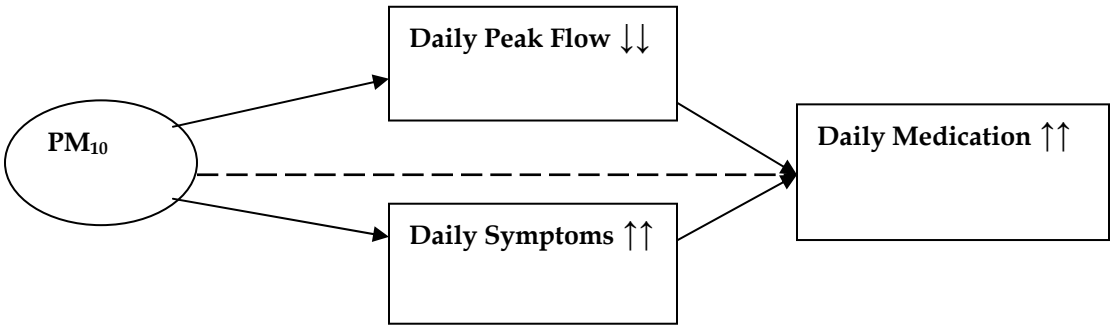


Figure 4: A hypothetical relationship of daily medication and PM_{10} exposure

3.3 Study Population

3.3.1 Sample size

Sample size is estimated with a desire to detect the smallest difference if one exists. Hoek et al. (1998) reported on a panel study and outcomes of respiratory symptoms increases of 1-3% associated with a 10 μg/m³ increase in PM_{10}, and 0.1% decrease of the peak expiratory flow rate (PEFR) at the same exposure and significant relative increase of 2.7% (95% CI 1.6-3.8) in prevalence of decrements greater than 10%. Koenig et al. (1993) reported similar results with a single case group 30 out of the 326 participants. Osunsnya et al., (2001) showed a 19% increase in PEFR decrements of 10% in a study population of 44, with 27 having complete data for PEFR analysis. Other studies have reported on borderline PEFR decrements (Penttinen, et al., 2001) with 57 participants.

Many air pollution studies have used peak flow meters to measure pulmonary function (Timonen and Pekkanen, 1997; Pettinen et al., 2001; Penttinen et al., 2002; Yu et al. 2000; Osunsanya et al., 2001). A peak flow meter is a small portable inexpensive device with a measuring gauge that ranges from 60 to 800 L/Min. A peak flow meter measures the force and speed that the air is blown out of the lungs giving a PEFR. The unit of the PEFR is L/Min. Daily PEFR is a valuable tool to detect early warning signs of airways responses that may indicate removal from a triggering exposure, adjustment of medication or adding new medication. The normal PEFR depend on age, sex and other factors but should be within 80% to 120% of personal best. The OMRON Peak Air flow meter (Model PF9940) was selected because

of its easy instructions, durability, portability and re-usable mouthpiece, good grip handle for the elderly and inexpensive cost.

In this study we were expecting a small change in PEFR. Our sample size is based on a small effect size. Sample size determination is calculated at alpha arbitrarily set at .05, power .80 and a small effect size of .22. According to Stevens, (1986), there are no real tables for repeated measures longitudinal study sample size calculation although it is assumed single sample case correlation for repeated measures can be used. Using the tables provided by Stevens, (1986) and assuming power of .80 and a small effect size of .22 at alpha =.05 and 7 repeated measures we would require a sample size of 47. The sample size requirement gets smaller with the number of repeated measures and selected effect size. Using this information and the upper level of the confidence interval with an alpha =. 05 (two tailed), beta 0.20 (power 80%) the sample size needed would be about 30 subjects.

Additionally, the statistical analysis of repeated measures using the generalized estimation equation (GEE) procedures are efficient even for small sample sizes (Rochon, 1998). Similar studies have recruited similar sample sizes (Delfino et al., 2002& 2003, twenty-two subjects; Osunsanya et al., 2001, twenty seven of the 44 subjects had complete data; Penttinen et al., 2001, fifty seven subjects; de Hartog et al., 2003, ranged from 37 to 47 for each city). We therefore decided on a sample size of 30 subjects because this would give us the power that we wanted to achieve and also constraints of financial and personnel for a quality control is achievable with this sample size.

3.3.2 Population

The SHAPE study was conducted in the southwestern part of Allegheny County. Participants who were regular patients of the Pulmonary and the Cardiac Outpatients Clinics were identified by the physicians from their database and invited to participate on the study. The University of Pittsburgh Institutional Review Board (IRB) approved the study protocol IRB #301014. Subjects who signed an informed written consent were allowed to participate on the study. Subjects received a monetary incentive for their participation on the study.

To be eligible for the study, the subject had to meet the following criteria: (a) A positive physician-diagnosed respiratory or circulatory disease identified by the International Classification of Disease, 9th edition, World Health Organization, Geneva (ICD-9) codes that include asthma (ICD-9 code 493), COPD (ICD-9 code 490-496, excluding 493), pneumonia (ICD-9 code 480-487), acute bronchitis (ICD-9 code 466), acute respiratory illness (ICD-9 code 460-466), and a circulatory disease such as CHF (ICD-9 code 428) <40% ejection fraction, Class II-III angina symptoms, myocardial infarction (ICD-9 code 410), conduction disorders (ICD-9 code 426), and dysrhythmias (ICD-9 code 427), (Zanobetti et al., 2000); (b) Age from 50 to 79 years; (c) A resident of a selected area of south west Allegheny County; (d) independent living.

A total of forty-nine (49) subjects agreed to participate on the study. The cohort represented subjects who were able to complete the study based on their willingness indicated by their return of a post card of invitation to the study. Additionally, the age and health restrictions implied that this would be the age group most likely to comply and perform daily PEFR, and complete the medication and the symptom components of the diary (Geyh et al., 2002).

Only subjects with a confirmed pulmonary disease or heart disease were admitted to the study. The medical group practice physicians identified and invited into the study subjects who

were adults aged 50-79 years old with a respiratory or circulatory disease identified by the International Classification of Disease, World Health Organization, Geneva (ICD-9) codes classification (Table 3.7).

3.3.3 Exclusion Criteria

Individuals were excluded from the study if they did not have respiratory and circulatory disease diagnosis criteria as defined in the inclusion criteria and individuals who were younger than 50 years. Individuals with severe forms of cardiopulmonary diseases such as lung cancer, or Class 1 or IV angina symptoms were also excluded from the study. Individuals who did not give a written consent were automatically excluded from participation.

3.3.4 Recruitment Procedures

The physicians mailed letters to potential subjects informing them of the study and inviting them to participate. The physician did not make available or pass on medical information of a potential subject to the investigators. The potential subjects received an envelope that included a postcard which they mailed back in a stamped addressed envelop to the physician with their response. If a potential subject indicated on the postcard that they want to be contacted by an investigator with further information about the study, an investigator contacted the potential subject by phone and made arrangements for a clinic visit that took place at their home or doctor's office. The visits lasted approximately 45 minutes.

At the initial visit the investigator informed the subject of the study and gave the potential subject a consent form to review and complete if interested in being enrolled in the study. If the subject met the study eligibility criteria, he/she was asked to complete a questionnaire on

environmental exposures. The investigator instructed the subject on the correct method of performing a peak flow test and demonstrated how to record the results in the daily symptoms diary. The subjects were contacted weekly by phone to reinforce the proper use of the peak flow meter and to ensure that the diary entries are completed appropriately.

3.3.5 Environmental Health Study Questionnaire

Participants were asked to complete an environmental health study questionnaire (EHSQ) (Appendix A.1) at the beginning of the study to ascertain the subjects' pre-existing health conditions, smoking history, assess socio-demographic status and indoor environmental exposures. Some of the questions used in EHSQ were adapted and modified from a previous asthma and risk of cardiac events study by Rosero, Zareba, et al., (1999); an indoor air pollution and asthma events study by Simoyi et al., (1995); and air pollution and respiratory symptoms by de Hartog, et al., (2003). The EHSQ addressed the demographic information, respiratory and cardiac symptoms, housing conditions, and possible sources of indoor air pollution such as household smoking, heating sources used, and home dampness. The data from the EHSQ questions were analyzed to describe the conditions of indoor air pollution, the perceptions of the study participants to air pollution in their community and to assess their previous cardiopulmonary health status.

3.3.6 Peak Expiratory Flow Rate (PEFR) Procedure

The study subjects were instructed to measure their PEFR every day in a sitting position immediately after getting up in the morning (6:00 am-8:00 am), and in the afternoon (2:00pm-6:00pm) before taking any medication. The PEFR maneuver was demonstrated. The test requires

that the subject take three readings at each time and records the best (highest reading) of the three PEFR maneuvers in the morning and in the afternoon. At the end of the study PEFR data was entered into the data base using the methods described by Osunsanya et al., (2001) and by Hoek et al., (1998) that provides a sound clinical comparison between peak flow and prevalence of acute lower respiratory symptoms. First, the actual values were entered in the database. Secondly, we calculated the individual's daily PEFR percentage decrement by subtracting the daily PEFR from the mean PEFR divided by mean PEFR. Thirdly, we calculated from the initial PEFR variable and the percentage decrement a binary variable that represented the presence or absence of a 10% decrement.

3.3.7 Daily Medication Use

Subjects were asked to record daily their medication and patterns of medication use. Subjects recorded medication as to whether there is no change in medication dose (record =0), whether medication dose is increased (record= 1) and whether medication decreased (record 2). At the end of the study records of medication were categorized into anti-inflammatory and non- anti-inflammatory using a binary "Yes" or "No" (Delfino et al., 2002 &2003) for analysis.

3.3.8 Daily Cardio-Pulmonary Symptoms

Participants reported the daily severity of symptoms using a scale that incorporates the impact of the severity of respiratory and cardiovascular symptoms on daily activities. Subjects rated the symptoms in terms of a 4-level ordinal scale. On each day the subjects ranked the symptoms with "0" if no symptoms are present, a "1" if mild symptoms are present but do not cause any discomfort, a "2", if moderate symptoms are present and cause discomfort but do not interfere

with daily activities or sleep and a "3" if severe symptoms are present and interfere with most activities and may cause the subject to stay in bed, return from work, call or visit a doctor or hospital. At the end of the study all symptoms were dichotomized for data entry in the database as binary variables of 0 and 1 (reported scale 0 represent no symptoms and scale 1-3 of mild, moderate, severe represents symptoms =1), (Delfino et al., 2002 & 2003, Yu et al., 2000, Pentitinen et al., 2001). If a subject reported any one of the symptoms, the subject was defined as having presence of symptoms.

Subjects also entered a "Yes" or a "No" to a question "did you have any of these symptoms today?" Questions on muscle aches, nose congestion, runny nose, fever or achy chills, and headache required the subject to answer a "Yes or a "No." These symptoms were entered in the database as =0 for no respiratory infection symptoms and =1 for respiratory infection symptoms if more than one of the symptoms are reported (Delfino et al., 2002).

A record of emergency room or unscheduled doctor's visits, exposure to tobacco, and time spent outdoors or away from home were also recorded daily in the diary.

3.3.9 Quality Control and Management of Data

The participants were followed-up weekly by phone to assess the compliance of PEFR monitoring and symptoms diary (APPENDIX B.1) maintenance and to identify any adverse events during peak flow tests. In addition the participants were given a 5 ½" by 8 ½" card with instructions on each component of the study that included Instructions for Recording Peak Flow, Instructions for Recording Your Medication, Instructions for Recording Symptoms, Instructions for Recording other Symptoms and Questions. The card included instruction on what to expect from the investigators each week, at the end of 1 month and at the end of the 2nd month. Contact

information was given at the end of the card for participants to contact the investigators with concerns. Participants were advised to keep the card on a refrigerator with a magnet or on a bedside table.

At the end of the first month (4 weeks), a clinic visit was arranged to collect the diaries and to give the subject another diary to continue the study during the second study period. This visit enabled the study staff to assess the data for compliance and errors.

3.3.10 Data Sources for Ambient PM_{10}

A database of air pollution PM_{10} levels monitored by the Allegheny County Health Department (ACHD) Air Quality Division was obtained for the eight continuous stationary monitors. The ACHD Air Quality Division measures criteria air pollutant PM_{10} using the USEPA reference methods. Air monitoring for ambient levels of criteria pollutants was promulgated through the Clean Air Act of 1970. The ACHD is the primary regulatory body for monitoring air emissions and ambient air quality for the county. There are various types of mechanical monitors that measure ambient criteria pollutant levels. The two types of samplers used for PM_{10} are a high volume (hi-vol) air sampler and a tapered element oscillating microbalance (TEOM). The TEOM air sampler is a USEPA equivalent monitor used for air quality index calculations. These monitoring samplers are operated continuously and the results reported electronically.

There are 21 air pollution-monitoring sites that have multiple ambient air samplers throughout the Allegheny County. These locations do not necessarily reflect a true ambient level concentration representative of the county. Since the start of the ACHD regulatory program, some of these facilities have either stopped operations or relocated. Of the 21 sampling locations,

8 sites had continuous monitors for PM_{10} levels using the TEOM methods with data logger, and telemetered to central computer by each hour.

Some of the ACHD monitoring sites, such as the Liberty Borough monitoring site, were initiated for compliance of air polluting sources from the major coke plant in the area. Such measurements provide the area background exposures similar to other studies (Penttinen et al., 2001; de Hartog et al., 2003; Osunsanya et al., 2001; Yu et al., 200; Delfino et al., 2002 &2003; Desqueyroux et al., 2002). Data on the hourly and 24-hourly PM_{10} concentration, 24-hourly maximum and minimum were obtained for the period of May 1, 2003 to May 31, 2004 from all of the 8 ACHD continuous monitoring sites.

A few studies on environmental epidemiology studies have correlated the standard USEPA monitoring data to the indoor and outdoor air of individual homes to ascertain whether indoor air correlates to ambient exposures (Leaderer et al., 1999). Leaderer et al., (1999) carried out an extensive air pollution study to assess the daily particulate exposures of inside and outside of 280 homes and central monitoring sites in Virginia and Connecticut during the period 1994- 1998. The authors reported that the PM_{10} concentration measured at the regional sites were not significantly different from those measured either outside or inside of homes, neither were PM_{10} concentrations measured outside homes different from those measured inside homes. The study sampled homes that were located as far as 175 km from the regional sampling site, yet no significant differences in mean concentrations of PM_{10} were reported. This is one of the most extensive studies to characterize apportionment of central sites measurement to residents in an area. Based on this assessment, our study used the data from the ACHD monitoring sites as an ecological independent variable and individual clinical assessments data as dependent variables.

Because the clinical data in this study was obtained at four different times during the entire study period, it was necessary to define four homogenous subgroups of participants. The periods were defined as June 2003, October 2003, November 2003, and April 2004. An average 24-hr PM_{10} was calculated for the entire study period to observe trend during the study period in general. This average 24-hr PM_{10} was matched to each day for that period to enable us to calculate the daily PM_{10} deviations which was calculated by subtracting the average PM_{10} of each day from the average 24-hr PM_{10} of that period. Scatter plots were analyzed to assess this deviation from the mean. We also calculated a 10 $\mu g/m^3$ increment variable from the average 24-hr PM_{10} to enable us to assess a dose-response relationship between symptoms and the air pollution. Additionally, we calculated a daily change in average 24-hr PM_{10} and a daily change in PEFR by subtracting the previous day level from the present day in order to assess a relationship between the two variables.

3.3.11 Meteorological Data

Weather variables can confound the effect of air pollution on health outcomes. The weather variables of interest were temperature, dew point average, pressure and relative humidity because of their interrelationship and their effect on health outcomes. Studies have shown that these weather variables can affect individuals in different ways including ischemic heart disease, higher blood pressure changes and death (Donaldson and Keating, 1997; Eldwood et al., 1993. The daily averages of temperature, dew point average, pressure and relative humidity were obtained from the National Weather Service, the National Oceanic and Ambient Air agency for the Pittsburgh International Airport weather station for the period May 1, 2003 to May 31, 2004.

3.3.12 Recruitment Area Boundaries Using GIS Mapping

Subjects were recruited from an area within 15km from the identified TRI sites associated with zip codes of interest. Different studies have used arbitrarily assigned boundaries for similar recruitments. Penttinen et al., (2001) restricted their entire study group to within 2 km of the air quality-monitoring site; Leaderer et al., (1999) up to 175 km; Vichit-Vadakan et al., (2001) 2km; Haree et al., (1997) 5 km; Delfino et al., (2003) 3 mile radius. Participants who resided in the selected 0-15 km zones drawn around identified eight toxic release inventory sites were eligible to participate on the SHAPE study.

Using the zip codes resolution, the physicians at the out-patients clinics identified participants to invite to the study. Zip codes boundaries do not always match the street or county boundaries. To ensure that we were recruiting participants in the intended area we used the geographic information system (GIS) in two stages. First, we geocoded the participants' address, that is, we transformed addresses into X and Y coordinates using MapInfo /ArcGIS (Bellander et al., 2001). The street addresses were matched to the nationwide US Census Bureau database of streets and enabled us to geocode all the participants' addresses resulting in this map (Figure 5). Secondly, we generated buffer zones around the identified 8 TRI plants for a distance of up to 15km. The process involved representing each TRI sites on the map as a point and resulted in the map below (Figure 6). Notice that a number of participants fall within 5km of the TRI plants with only one participant in the west lying beyond the 15km buffer zone.

We also considered the contribution of traffic emissions to air pollution in Allegheny County. We generated a map of the road networks in the area to visualize the possible influence of traffic emissions health. The map showed that the area of study has lesser road density in the south and begins to congest northwards (Figure 7). The wind direction in the Allegheny region is frequently NE direction. If the frequently observed wind direction is taken into consideration, the NW effect is probably not pronounced. This assessment was not pursed further in this study but was performed as a precursor to future air pollution study in the region.

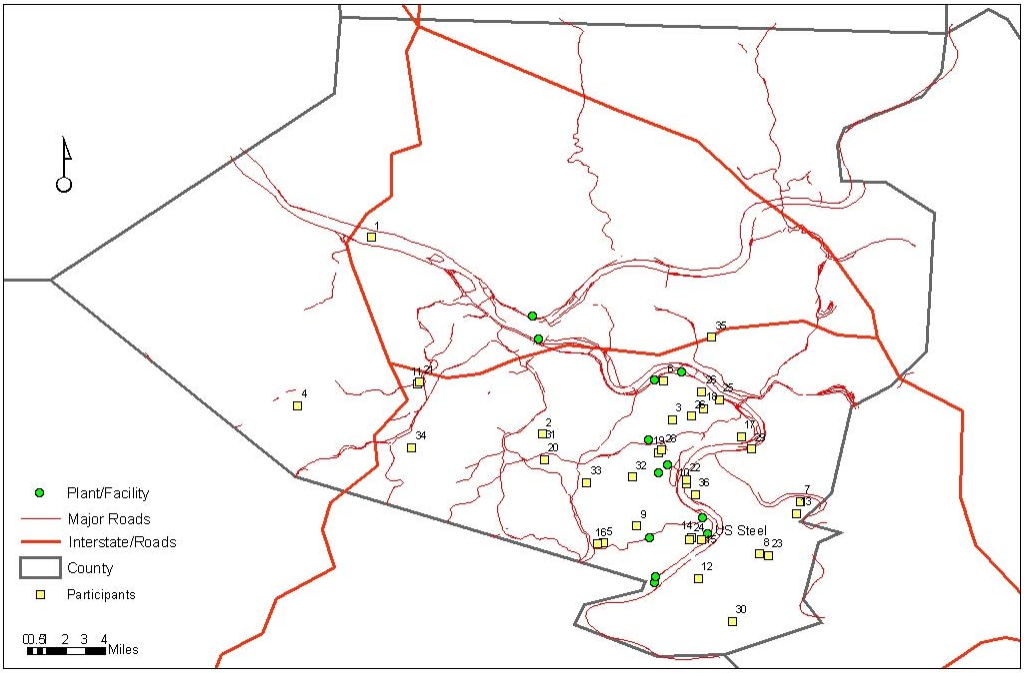


Figure 5: Address geocoding of TRI facilities in relationship to participants' residents

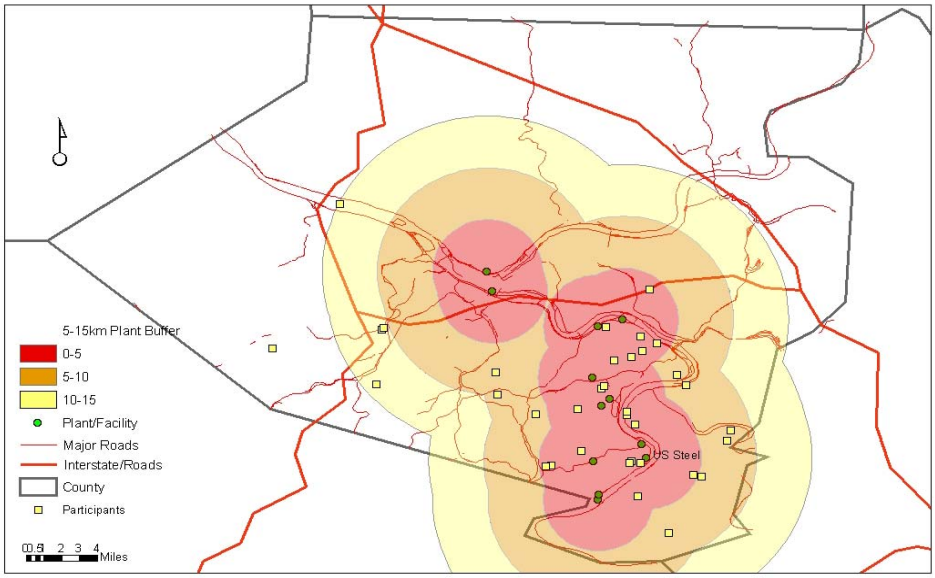


Figure 6: 5-15km buffer zones around TRI facilities and addresses of participants

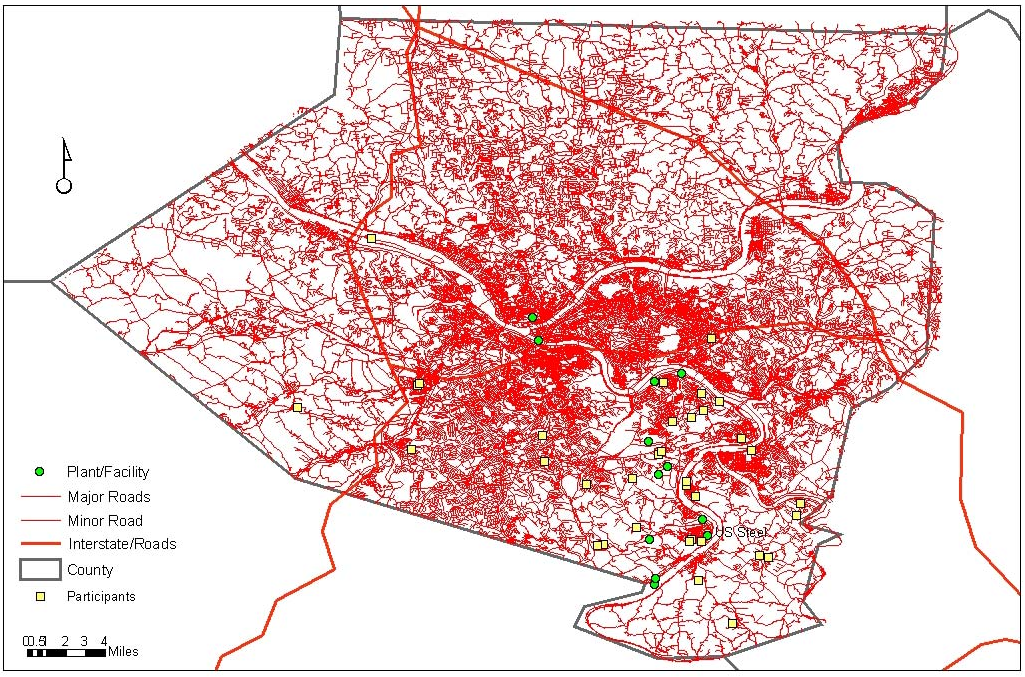


Figure 7: Geocoding of TRI sites and study participants showing road networks dispersion

3.3.13 Statistical Analysis of Data

The statistical analysis of this longitudinal data was carried out systematically addressing each hypothesis. Univariate analysis, bivariate correlations and logistic regressions models were used to explore and describe the relationships between the environmental exposures and the health outcomes and also to answer each hypothesis. The data was analyzed using statistical packages including SAS, JMP and SPSS statistical packages.

The data was summarized descriptively for the subjects' socio-demographics, and daily PEFR, symptoms and medication. The air pollution data was examined for temporal trends for the average 24-hr and maximum 24-hr PM_{10} concentrations. The meteorological variables were summarized descriptively as well. The association between air pollution and health outcomes was analyzed using chi-square (χ^2) analysis with dependent binary variables that have two levels

(yes/no) and coded into either 0 or 1. The tests were used to assess the probability of having symptoms or no symptoms in the presence of different levels of PM_{10} exposures. Because of the small numbers and inherent longitudinal studies missing values we also performed the generalized estimation equation model (GEE) proposed by Kung-Yee and Zeger, (1986) and discussed further by Desqueyroux et al., 2002; Yu et al., 2000; Osunsanya et al., 2001; Delfino et al., 1998, 2002 & 2003]. The GEE model is a practical method of analysis with ability to handle repeated measures of a longitudinal study where data may be missing. The GEE is an extension of the generalized linear model (GLM), with facilities in SAS/ GENMOD function (Stokes et al., 2001). According to Stokes et al., (2001), the GLM relates to mean response to a vector of explanatory variables as follows:

$$g\,[E\,(y_i)] = g\,(u_i) = X_i'\beta$$

where y_i is the response variable (i=1,…., n), ui= E (y_i), g is the link function, x_i is a vector of independent variables, and β is the vector of regression parameters to be estimated.

For an individual's data to be included in the analysis a total of 30 days of participation (50% of an expected individual participation) was required. The reason for this was that participants were given a 1-month diary to complete and return before starting on another diary for the other month. Because the participants entered the study at varying times, first we analyzed data of all eligible study participants. We then created four homogeneous subgroups from the entire study participants to remove an imbalance that may be created by participants who contributed more person days than others and by individuals entering the study at varying times an also to assess the effect of seasonality. The subgroups also identify which period of the

year participants reported more symptoms because each individual fell into a distinct subgroup with no overlap.

We estimated the air pollutants effect on the binary outcomes of the symptoms and the presence of 10% decrements of PEFR from the mean among the four groups. In addition, we stratified the air pollution data into six levels of PM_{10} concentrations in order to investigate dose-response effects on symptoms. Additionally, two medication groups (anti-inflammatory and non-anti-inflammatory) were created and examined separately to assess differences of symptoms outcomes in the two groups.

Odds ratio and confidence interval of the within subjects short-term effect of PM_{10} on health outcomes are reported. The other summary that was included was of data obtained from the EHSQ and included questions such as how long a subject had lived in Allegheny County; subjects' perceptions of the air quality; how long a subject has lived at their current residence; and other pre-existing health conditions and indoor environments.

Meteorological variables that included mean temperature, relative humidity, and pressure were considered as confounding variables in order to determine the unique role played by the PM_{10} concentrations in predicting the PEFR decrements and symptoms.

4.0 RESULTS

4.1 Response Rate

Forty-nine individuals agreed to participate on the study by mailing back a post card to the two medical center physicians. Thirty-five individuals signed consent forms, completed the environmental health study questionnaire and maintained symptoms diaries for a mean average of 54 days beginning May 21, 2003 to May 31, 2004. Three individuals were omitted from the initial analysis because the number of days of participation was less than 30 days of the required possible days. Of the 32 remaining eligible sample 34.4% of the individuals contributed more than 60 days each to the study. Four individuals (12.50%) contributed less than 40 days each to the study (Table 9).

Table 10 summarizes the characteristics of the subjects included in the initial analysis. Ten (31%) of the participants reported a current diagnosis of cardiovascular diseases and twenty-two (69%) of the participants reported a respiratory disease diagnosis. Twenty two percent of the participants had a history of asthma and 31% reported a history of other lung diseases. The participants reported their previous diagnosis that included heart diseases (22%), chronic obstructive airways disease (13%), and myocardial infarction (2%). Seventy percent of the participants had their current diagnosis before age 65.

Table 9: Frequency of individuals' participation by number of days contributed to study

Number of Participation Days	Frequency	Percent
≤ 39	4	12.500
40 - 44	2	6.250
45 - 49	4	12.500
50 - 54	2	6.250
55 - 59	5	15.625
≥ 60	15	46.875
1716	32	100.00

Thirty four percent of the participants reported that they had been hospitalized in the past year for their current cardiopulmonary condition. Forty one percent reported a past history of emergency room visit and 19 % reported ever being placed on a ventilator in the past. Eighty one percent of the participants reported that exposure to environmental factors such as cold air; humidity, exercise, dust and dander triggered their respiratory or heart problems or bring on an attack of cardiopulmonary condition. All the participants reported that they had lived in Allegheny County for more than 36 years. When asked about their perception of air pollution in Allegheny County, 84% of the participants believed that the air pollution has improved. Nine percent of the participants reported a past history of smoking and exposure to secondary tobacco

smoke and 3% reported being current cigarettes smokers. Thirty five percent of the participants reported that they live in houses that are less than 50 years old and 31% reported having damp rooms or basements in their homes. When asked about the type of heating source in the home, 82% reported that they use gas-heated forced air and 9% use steam and water radiators. The results showed that the participants spend 29% of the time more than 10 miles away from home during the study period. The results also showed that on average the participants spend 69% of their time indoors.

4.2 Particulate Measurements

The analysis of each of the eight fixed monitors in Allegheny County showed that Lincoln had the highest average PM_{10} levels (35 μg/m³) followed by Braddock (31 μg/m³) and Liberty (31 μg/m³) (Table 11) during the study period May 1, 2003 to May 31, 2004. The average 24-hr PM_{10} across the monitoring sites was 24.36 μg /m^3 with a standard deviation of ±13.65 μg/m³, and the maximum PM_{10} was 447 μg/m^3 (Table 12). The percentiles of the average PM_{10} were 13.63 μg/m3 (25%), 20.93 μg/m3 (50%) and 31.61 μg/m^3 (75%).

The data was also examined by month for the average 24-hr PM_{10} (Figure 8) and showed that the highest average levels were recorded in June 2003 and the lowest levels in January 2004. A linear regression was performed to model the relationship between PM_{10} and time of study in a model form:

Y = **a** + **bX**, where **X** is the explanatory variable and **Y** is the dependent variable, with slope of the line **b**, and **a,** the intercept. A linear regression line did not show a notable trend to indicate an association between the average 24-hr PM_{10} (p= 0. 7336) variables with date of observation.

The PM_{10} deviations from the average 24-hr PM_{10} were calculated by month and showed a clustering between -20 μg/m³ to 56 μg/m³ (Figure 9). The deviation from the mean was greatest during the month of June followed by December and October 2003. However, a linear regression line did not show a notable trend ($p=0.8465$) to indicate an association between the PM_{10} deviations from the average 24-hr PM_{10} and date of observations. In general, the PM_{10} correlation analysis of the data from the 8 monitoring sites showed that all the monitors were significantly correlated ($p< 0.01$) for the average 24-hr PM_{10} (Table 13). A strong positive correlation ranging from 0.629 to 0.905 was observed between all the monitors except for the Liberty site where the correlation ranged from 0.382 to 0.487.

4.3 Meteorological Measurements

The average mean temperature (MNTP) was 59° F, with the highest temperature recorded at 79°F. The data for the MNTP was examined by month and year and the results showed that the month of August 2003 had the highest recorded temperature (79°F) followed by July and June 2003. The months of January and February 2004 and December 2003 recorded the lowest temperatures. The mean relative humidity (MNRH) was 53.57 %, dew point average temperature (DPTP) 43.15 °F, and pressure (PRES) 28.75 inHg (Table 14).

Table 10: Summary characteristic of study population (N=32)

	Frequency	Percent
Race		
Black	1	3
White	31	97
Gender		
Male	16	50
Female	16	50
Have you ever been told by a physician that you have a lung or heart disease?		
Lung disease	10	31
Asthma	7	22
Heart disease	7	22
Chronic obstructive pulmonary disease	4	13
Myocardial infarction	2	6
Congestive heart failure	1	3
Emphysema	1	3
Have you ever been admitted to the emergency room for heart/lung problems?		
No	17	53
Yes	13	41
Unknown	2	6
Have you ever been admitted to a hospital for respiratory or heart problems in the past year?		
No	21	66
Yes	11	34
Have you ever been placed on a ventilator?		
No	26	81
Yes	6	19
Are you still being treated for lungs or heart problems?		
Respiratory	22	69
Cardiovascular	10	31
What factors aggravate your respiratory or heart problems or bring on an attack?		
Some triggers (cold, humidity, exercise, dust, other)	26	81
None	5	16
Don't know	1	3
What is the main source of heating in your home?		
Gas- heated forced air (vents)	26	82
Radiators (steam or water)	3	9
Electric- heated forced air (vents)	2	6
Gas stove/fireplace/wall furnace	1	3

Table 10 (Cont'd)

	Frequency	Percent
Are there rooms including basement in your house that are damp?		
No	20	63
Yes	10	31
Missing	2	6
Has the air pollution improved since you first lived in Allegheny County?		
Improved	27	84
No change	4	13
Don't know	1	3

Table 11: Descriptive statistics of average 24-hr and maximum PM_{10} by monitoring site: Allegheny County May 2003-May 2004

	N	Maximum	Mean	Std. Dev
Avalon	391	77	19.85	11.23
Braddock	397	104	31.40	20.28
Flag Plaza	397	77	21.62	11.17
Glassport	397	114	23.61	17.35
Hazelwood	397	54	18.30	9.85
Liberty	397	126	27.05	21.20
Lincoln	397	189	35.23	28.14
Stowe	397	69	17.81	13.65

N= total number of days of observations during the study period. The maximum and mean PM_{10} is expressed in $\mu g/m^3$.

Table 12: Summary statistics of PM_{10} for Allegheny County: May 2003-May 2004

		Minimum 24-hr	Mean 24-hr	Maximum 24-hr
N		397	397	397
Mean		2.71	24.36	132.93
Std. Dev		4.15	13.65	90.82
Minimum		0.00	4.28	10.00
Maximum		27.00	79.46	447.00
Percentiles	25	0.00	13.63	63.50
	50	1.00	20.93	100.00
	75	4.00	31.61	191.00
	100	27.00	79.46	447.00

N= total number of days of observations. The mean Std. Deviation and percentiles of PM_{10} is expressed in $\mu g/m^3$

Table 13: Correlation coefficients of PM_{10} for the Allegheny County monitoring sites: May 2003-May 2004

	Avalon	Braddock	Flag Plaza	Glassport	Hazelwood	Liberty	Lincoln	Stowe
Avalon	1	.817*	.905*	.800*	.853*	.424*	.721*	.838*
Braddock		1	.785*	.802*	.753*	.411*	.719*	.723*
Flag Plaza			1	.835*	.878*	.473*	.704*	.867*
Glassport				1	.781*	.487*	.837*	.755*
Hazelwood					1	.382*	.641*	.848*
Liberty						1	.456*	.401*
Lincoln							1	.629*
Stowe								1

N=391 for Avalon, 397 for all other sites. * Correlation is significant at $p < 0.01$

Table 14: Summary statistics of meteorological variables: Allegheny County May 2003-May 2004

		DPTP °F	MNRH %	MNTP °F	PRES inHg
N		397	397	397	397
Mean		43.15	53.57	52.16	28.75
Std. Dev.		17.67	15.38	17.42	0.171
Minimum		-2.60	17.00	9.00	28.24
Maximum		69.30	100.00	79.00	29.29
Percentiles	25	28.70	42.00	39.00	28.64
	50	46.40	52.00	56.00	28.76
	75	57.95	64.00	67.00	28.87
	100	69.30	100.00	79.00	29.30

DPTP= average daily dew point temperature in tenths of degree Fahrenheit. MNRH= minimum relative humidity in barometric expressed in whole percent. MNTP= average temperature in degrees Fahrenheit. PRES=average daily station pressure expressed in inches of mercury (inHg). N= total number of days of observations during the study period

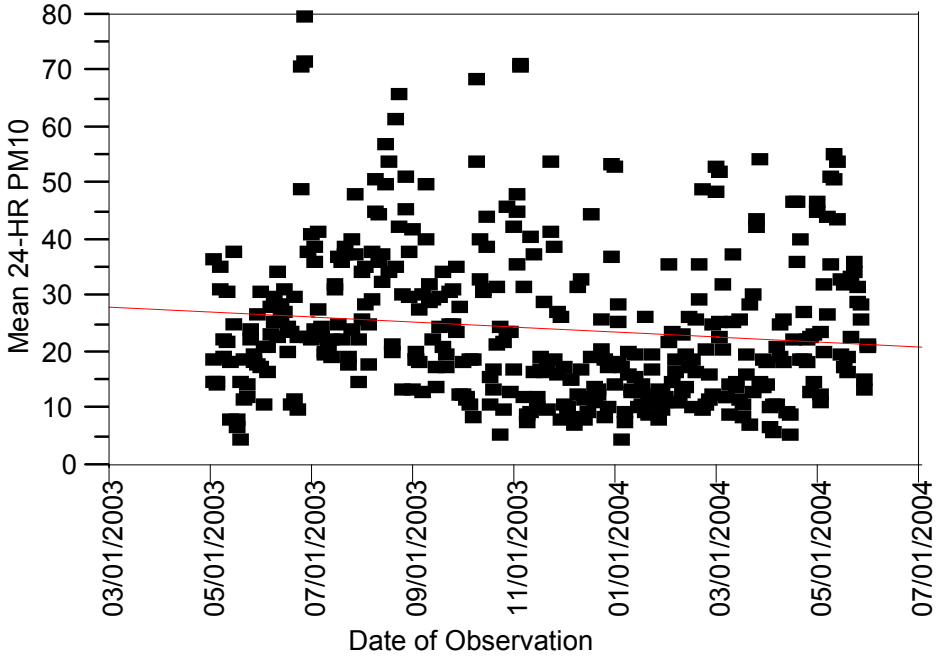


Figure 8: Average PM_{10} by month for May 2003- May 2004

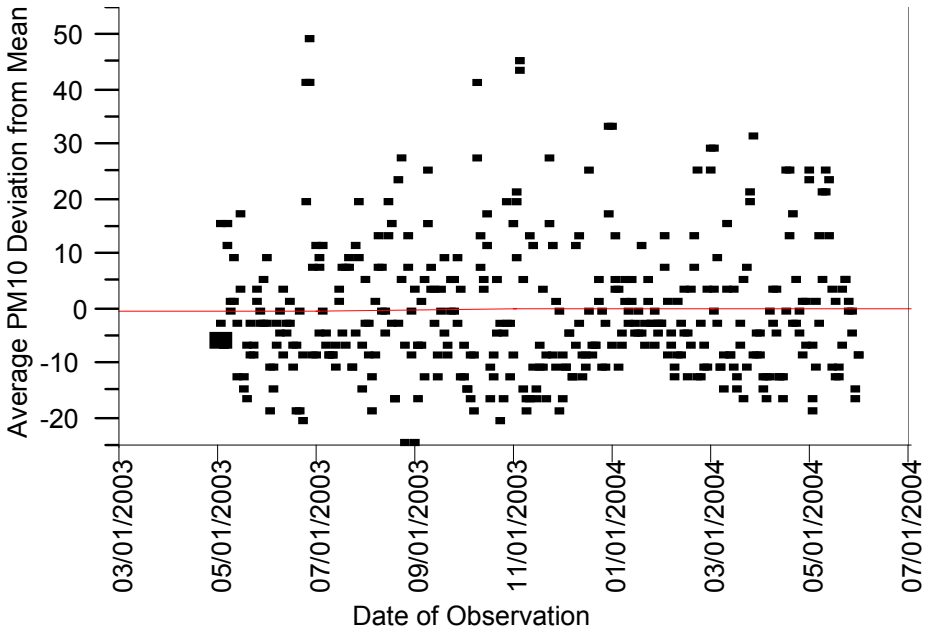


Figure 9: Average deviations from the Mean PM_{10} by month and year

4.4 Association between PM_{10} and Meteorological Conditions

A bivariate correlation of PM_{10} and meteorological variables showed a positive correlation between average 24-hr PM_{10} and mean relative humidity (MNRH) and dew point (DPTP). There was a strong positive linear association between the MNTP and DPTP (r=0.964) and a borderline strong linear association between PM_{10} and mean temperature (MNTP) and DPTP (r=0.502 and 0.413 respectively). There was a negative linear association between DPTP and pressure (PRES) and between MNRH and PRES (Table 15).

Table 15: Correlation coefficients of PM_{10} and meteorological variables: Allegheny County May 2003-May 2004

	Mean PM_{10}	DPTP	MNRH	MNTP	PRES
Mean PM_{10}	1	.413*	.502*	-.067*	.173*
DPTP		1	.209*	.964*	-.239*
MNRH			1	-.022	-.374*
MNTP				1	-.139*
PRES					1

DPTP= average daily dew point temperature in tenths of degree Fahrenheit. MNRH= minimum relative humidity in barometric expressed in whole percent. MNTP= average temperature in degrees Fahrenheit. PRES=average daily station pressure expressed in inches of mercury (inHg). N= total number of days of observations during the study period. The mean PM_{10} is expressed in $\mu g/m^3$. *Correlation is significant at $p < 0.01$

4.5 Physiological Responses

To assess if there is an association between air pollution and the health outcomes among the individuals, four homogeneous groups were created for the study period. Two participants were

omitted from this analysis. The reason for omitting the two participants is because they could not be fitted into any of the groups because of the overlap of their minimum days of participation over two periods of study. The final group of participants resulted in 895 person days (Table 16).

The data from the diaries were analyzed to assess participants' experience of symptoms during the study period. A subject was defined as having presence of symptoms if they reported any one of the symptoms such as shortness of breath, chest pain, fatigue, cough, wheezing related to cardiopulmonary diseases. Participants reported symptoms 59% times during the observation period.

Further, data was analyzed to assess person days (PD) of symptoms reports and number of persons experiencing each of the symptoms. Participants reported high frequency of cough, chest pain, shortness of breath, being awakened by shortness of breath and fatigue during the study period of June, 2003 (Table 18, Figure 10). During the study periods of October, November 2003 and April 2004, participants did not report any symptoms of chest pain. There were no reports of frequent cough during the month of April, 2004.

Figure 11 shows the analysis of total symptoms and use of anti-inflammatory medication for each study period. The results showed that during the study period of April 2004, all the participants were on anti-inflammatory medication and reported 51% symptoms experience. During the study period of October 2003 the participants were on anti-inflammatory medication 71% and they reported experience of symptoms 71% of the time.

Table 16: Study Periods showing frequency and percent of person days contributed

Study Period	Number of Participants	Frequency of Person Days N=895	Percent
June 2003	8	239	26.7
October 2003	9	266	29.7
November 2003	8	240	26.8
April 2004	5	150	16.8

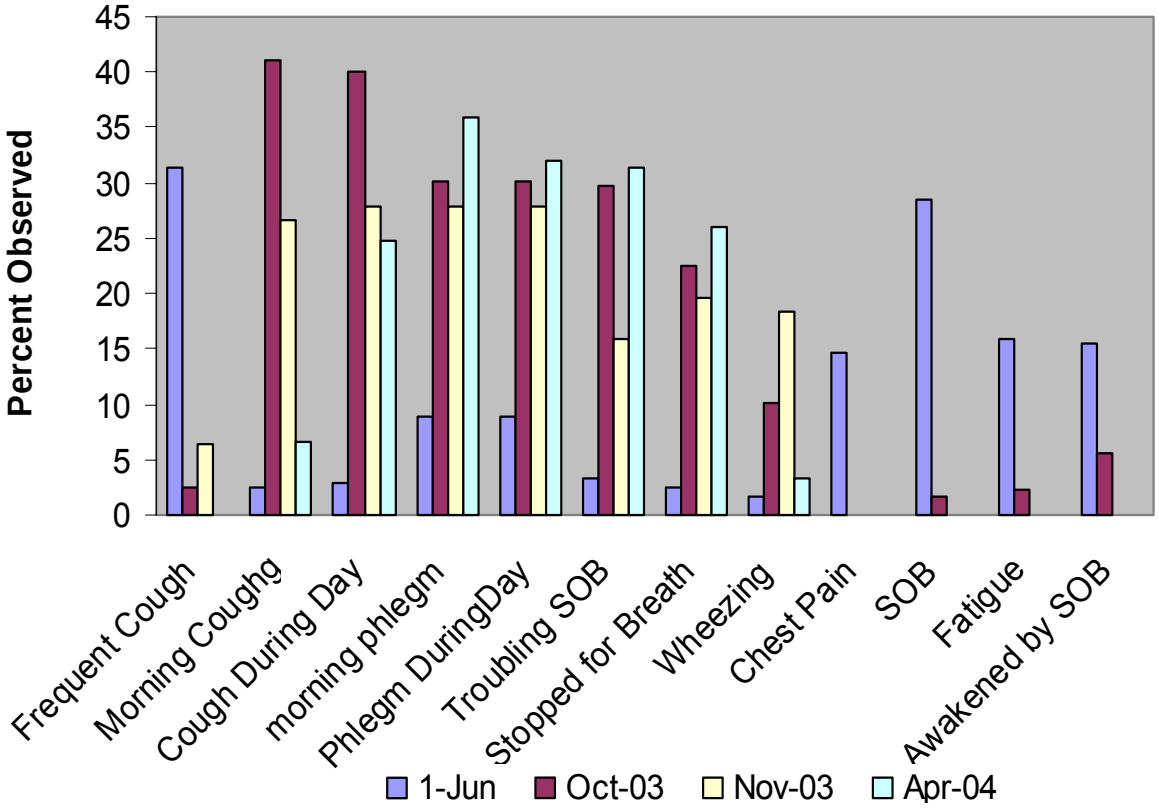


Figure 10: Percent of reported daily symptoms by study period

Table 17: Frequency person-days and percent of reported daily symptoms

Daily Symptoms	June 2003			October 2003			November 2003			April 2004		
	n	PD	%	n	PD	%	n	PD	%	n	PD	%
Any frequent cough	5	75	31.4	1	6	2.5	1	15	6.3	0	0	0
Any cough first thing this morning?	2	6	2.5	5	109	41.0	5	64	26.7	3	10	6.7
Any cough during the day?	2	7	2.9	6	107	40.0	5	67	27.9	3	37	24.7
Any phlegm first thing this morning?	2	21	8.8	4	80	30.1	6	67	27.9	4	54	36.0
Any phlegm during the day?	2	21	8.8	4	80	30.1	5	67	27.9	4	48	32.0
Troubled by shortness of breath?	2	8	3.3	5	79	29.7	5	38	15.8	3	47	31.3
Stopped for breath while walking on level ground?	2	6	2.5	4	60	22.6	3	47	19.6	3	39	26.0
Any wheezing or whistling sound from your chest?	1	4	1.7	4	27	10.2	4	44	18.3	1	5	3.3
Any Chest Pain?	3	35	14.6	0	0	0	0	0	0	0	0	0
Any Shortness of breath?	3	68	28.5	2	31	1.7	0	0	0	0	0	0
Any Fatigue?	3	38	15.9	2	6	2.3	0	0	0	0	0	0
Awakened by shortness of breath?	3	37	15.5	1	15	5.6	0	0	0	0	0	0

The table represents the total number of persons (n) reporting the symptoms, person days (PD) and the percent person days when symptoms were reported during the four study periods during May 21, 2003 to May 31, 2004

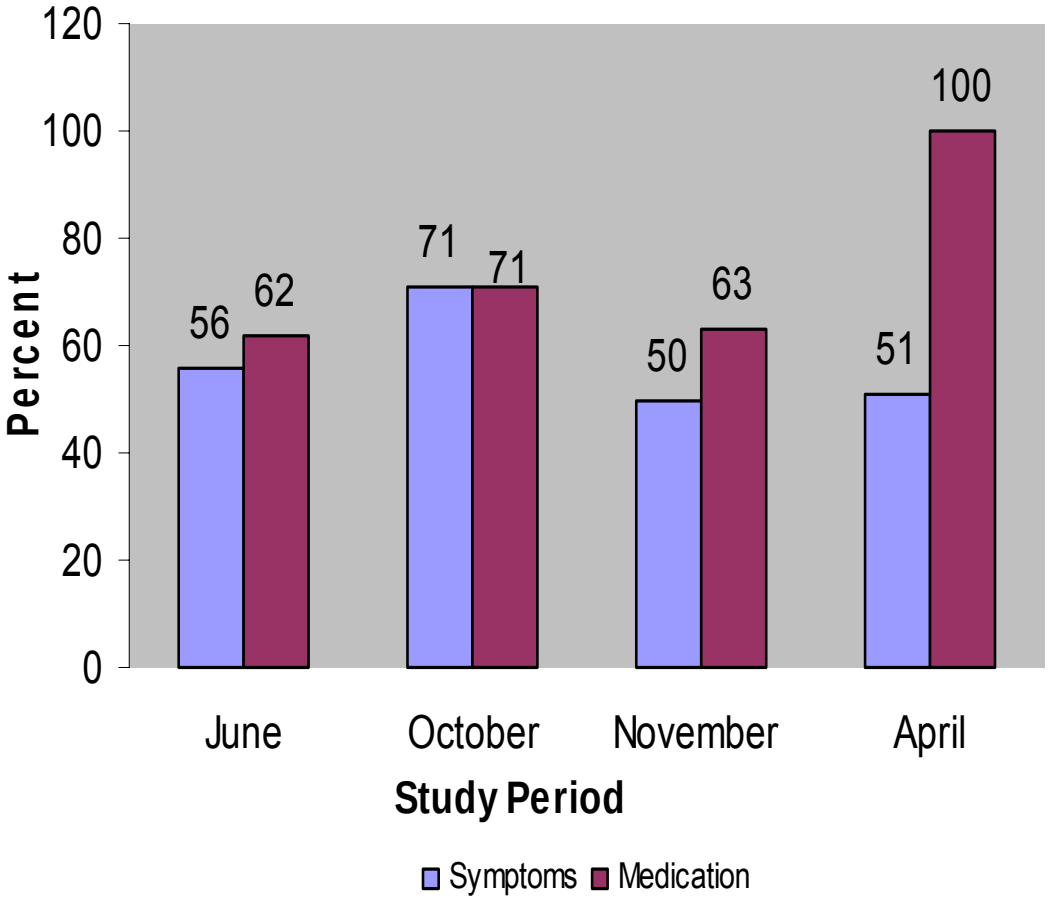


Figure 11: Percent of participants with symptoms and on anti-inflammatory medication

4.6 Peak Flow Rate (PEFR) Measurements

The peak expiratory flow rate (PEFR) records of the participants ranged from a minimum of 100 liters/minute (L/Min) to a maximum of 650 L/Min and an average of 295 L/Min. When the data was examined by study period, the results showed that the mean PEFR for June 2003 were much higher for both the morning and the afternoon rates compared to the other study periods (365 L/Min). The study period of April 2004 had the lowest mean PEFR (Table 18). The morning PEFR and afternoon PEFR were examined further for daily decrements from the mean and calculated for each study period (Tables 19). The PEFR decrements ranged from –40 L/Min to 45 L/Min. The largest mean decrements were observed for months of June (-2.27 L/Min for morning PEFR; -3.39 L/Min for afternoon PEFR).

4.7 Association between PEFR and PM_{10}

To assess a relationship between PEFR and PM_{10}, a liner regression was examined for the morning PEFR deviations and the average 24-hr PM_{10}. The morning PEFR showed more records of complete data compared to the afternoon PEFR and thus was used in the bivariate analysis. A trend analysis was carried out using the JMP statistical package for linear fit. The results of the differences of the morning PEFR (i.e. differences of present day's PEFR minus previous day PEFR) by the average 24-hr PM_{10} changes (i.e. differences of present day's average 24-hr PM_{10} minus previous day's average 24-hr PM_{10}) yielded a non significant statistical levels between the two variables ($p=0.6100$) (Figure 12). A bivariate analysis of the morning PEFR deviations and the average 24-hr PM_{10} results also showed a non significant trend line ($p=0.0640$) (Figure 13).

Both analyses showed no association between daily changes in PM_{10} and daily change in PERF. Thus the PERF appear not to be a sensitive measure of exposure effect assessment.

Table 18: Average morning and afternoon PEFR by study period

Study Period	Time of PEFR Measurements	Missing	N	Min L/Min	Max L/Min	Mean L/Min
June 2003	Morning PEFR	0	239	101	650	365
	Afternoon PEFR	25	214	102	650	365
October 2003	Morning PEFR	2	264	140	450	281
	Afternoon PEFR	9	257	140	430	308
November 2003	Morning PEFR	0	240	120	400	225
	Afternoon PEFR	0	240	120	490	267
April 2004	Morning PEFR	0	150	110	350	242
	Afternoon PEFR	0	150	145	350	256

PEFR= peak expiratory flow rate. N= total number of peak flow tests performed during each of the study periods for both the morning peak flow and the afternoon peak flow. Min=minimum average, Max= maximum average peak flow rates liters per minute (L/Min)

Table 19: Mean minimum and maximum peak flow rate decrements from the daily mean

Study Period	Daily Time of Measurements	Missing	N	Min decrement L/Min	Max decrement L/Min	Mean decrement L/Min
June 2003	Morning PEFR	0	239	-31	44	-2.27
	Afternoon PEFR	25	214	-35	25	-3.39
October 2003	Morning PEFR	2	264	-39	27	-0.37
	Afternoon PEFR	9	257	-26	17	-1.02
November 2003	Morning PEFR	0	240	-33	35	-1.05
	Afternoon PEFR	0	240	-40	31	-0.64
April 2004	Morning PEFR	0	150	-37	39	1.56
	Afternoon PEFR	0	150	-15	45	0.71

PEFR= peak expiratory flow rate. N= total number of peak flow tests performed during each of the study periods for both the morning peak flow and the afternoon peak flow. *Minimum and Maximum average decrements from the mean, liters per minute (L/Min)

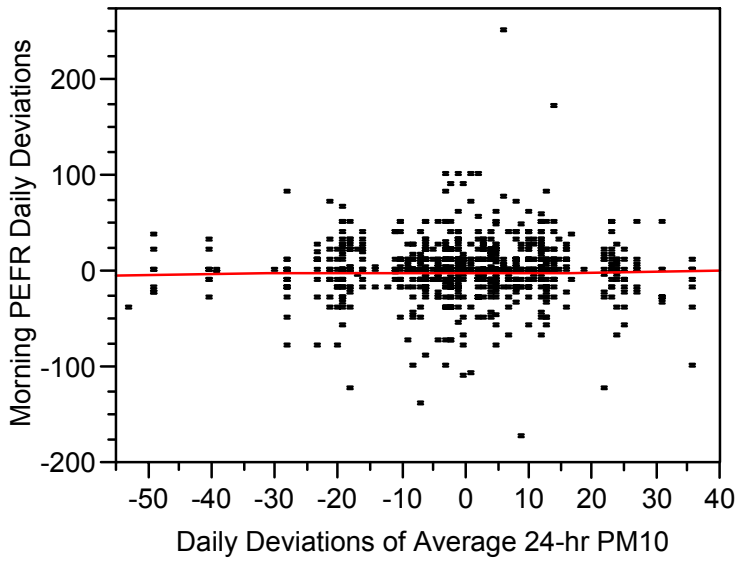


Figure 12: Bivariate Fit of Morning PEFR Day-Day Deviations by Day to Day Deviations of Average 24-hr PM_{10}

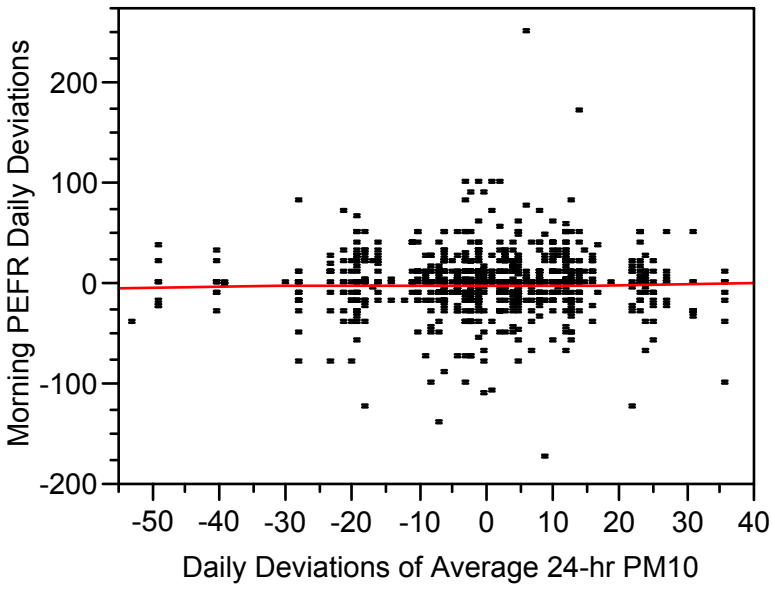


Figure 13: Bivariate Fit of Morning PEFR Day-Day Deviations by Average 24-HR PM_{10}

4.8 Effect of PM_{10} Average Increment on Physiological Responses

Table 20 shows the frequency of the 10-μg/m^3 PM_{10} increments by the study period. The 10 μg/m^3 increments were created to assess a dose response relationship between the reported symptoms and air pollution. The results showed a high frequency of observations at levels ≤20 μg/m^3 to ≤30-μg/m^3 for all of the month months. The extreme levels of ≤10 μg/m^3 and >50 μg/m^3 showed the least frequency of PM_{10}. For further visualization of this result, the percent frequency observations and the PM_{10} increments were plotted (Figure 14) and showed that the month of June 2003 had highest levels of PM_{10} levels between levels ≤20 μg/m^3 to ≤30 μg/m^3. The months of October and November 2003 had the highest peak levels around ≤20 μg/m^3.

To assess a dose-response relationship between PM_{10} and cardiopulmonary symptoms outcomes, a Mantel Haenszel Chi-Square (M-Hχ^2) test was carried out for the ordinal measure of significance. The M-Hχ^2 was applied to assess whether PM_{10} increments of 10μg/m^3 are associated with frequencies of having symptoms. The M-Hχ^2 results showed a significant effect at $p < 0.05$ between the symptoms of cough in the morning (p=0.0419), frequent cough (p=0. 0.0431and being awakened by shortness of breath (p=0.0332) and PM_{10} increments of 10μg/m^3 exposures (Table 21).

A general chi-square (χ^2) cross tabulation analysis was carried out using SPSS version 12.0.1 to assess an association of the10 μg/m^3 increments of PM_{10} on morning PEFR changes and symptoms. The χ^2 analysis showed strong effect at $p<0.05$ with significant association between PEFR decrements ≥10 and cough in the morning (p=0.007), cough during the day (p=0.021) and wheezing (0.051); The results also showed a significant association ($p<0.05$) between PEFR decrements not greater than 10% from the mean and symptoms of cough in the

morning, cough during the day, frequent cough and stopping for breath while walking on level ground (Table 22).

The General Estimating Equation (GEE) analysis GENMOD procedure in SAS was used to estimate the risk the PM_{10} increments of 10 $\mu g/m^3$ (categories) on frequency of the symptoms and by study period (seasonality). The odds ratio for the model was obtained by exponentiation of the parameter estimate for the independent variables in the GENMOD procedure and the output also produces along with the OR, the 95% confidence interval. The probability that participants will report symptoms with changes in PM_{10} was analyzed. The results indicated significant effect for cough in the morning ($p=0.0141$) when PM_{10} increases by 10 $\mu g/m^3$. The odds ratio (OR) and 95% confidence interval (CI) was OR 1.12, (CI= 1.02– 1.23) (Table 23). An analysis of the initial parameter estimates (logistic regressions) showed that the seasonality (study period) had an influence on symptoms outcomes. The study period of October 2003 had a significant effect on cough in the morning ($p= 0.0209$) and the month of November 2003 had a marginal influence ($p= 0.0868$). The study period of June 2003 had a significant influence on being trouble by shortness of breath ($p=0.0121$) and on "stopped for breath while walking on level ground" ($p= 0.0172$).

We performed PROC GENMOD analysis by adding the meteorological variables using a backward elimination in the model to assess the effect of the independent variables on the symptoms. Initially all the independent variables of interest were added into the model followed by elimination from the model in an iterative process of variables with the least significance. Effects of independent variables such as weather and exposures to tobacco are thought to be confounders of ambient air pollution. Cardiopulmonary conditions such as asthma, and chronic obstructive pulmonary disease (COPD), can be triggered by cold and dry air weather conditions,

and seasonal pollen and infectious diseases. Effects such as those of smoke and other indoor pollution are constant during a short-term observation study and therefore are not considered to confound the air pollution. Additionally, the weather variables were significantly correlated to each other and therefore decided to examine only the effects of the weather and seasonality on symptoms in the regression model. The relative risk (odds ratio) and the confidence limits and significant relationship at $p<0.05$ of experiencing cardiopulmonary symptoms when exposed to 10 $\mu g/m^3$ incremental levels of PM_{10} are shown in Table 24. The risk estimates were significant for cough in the morning was ($p< 0.0010$), cough during the day ($p=0.0008$), chest pain ($p<0.0001$), fatigue ($p=0.0153$), stopping for a breath while walking on level ground ($p= 0.0487$) and wheezing ($p=0.0013$).

4.9 Risk Estimates of Cardiopulmonary Symptom and Medication Use

Table 25 shows the characteristics estimate of symptoms and use of anti-inflammatory medication. The effect was explored by carrying out a chi-square (χ^2) analysis and risk estimate using SPSS version 12.0.1 for windows to see if there is an association among the parameters. The relationship between symptoms and anti-inflammatory medication use showed that the risk for cough in the morning (OR 3.99; 95% CI 2.47-6.46) and during the day (OR 5.15; 95% CI 3.13-8.48), phlegm in the morning (OR 5.29; 95% CI 3.20-8.69) and wheezing (OR 1.15; 95% CI 0.78-1.71), was greater if the individual was not on medication.

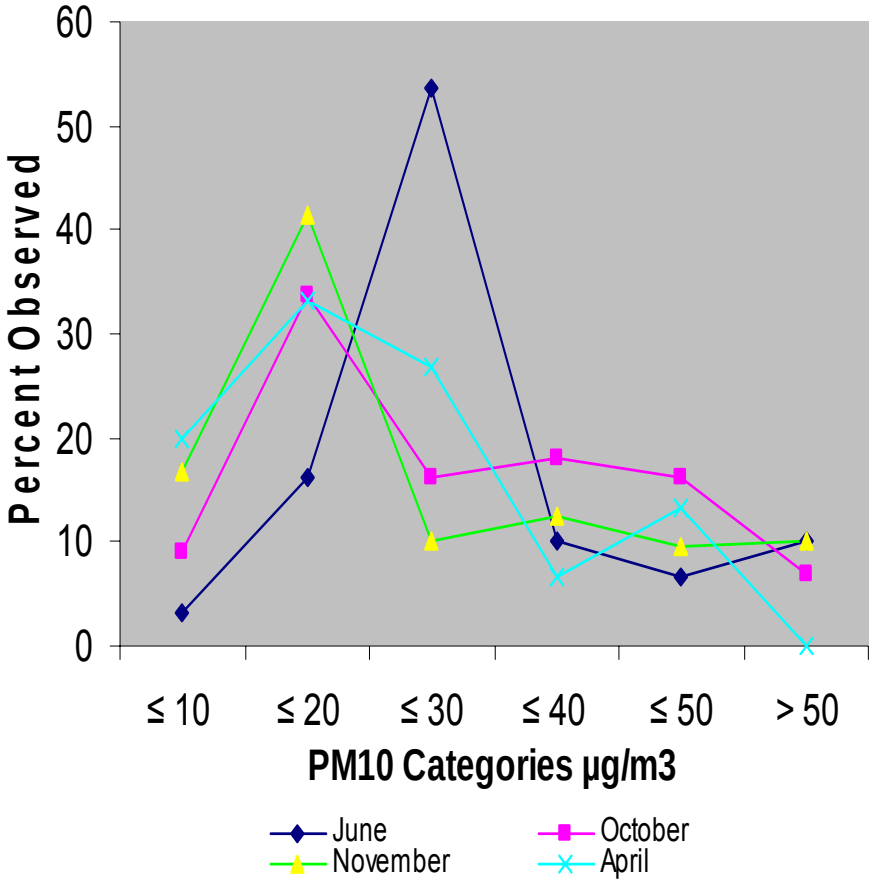


Figure14: Frequency of 10 µg/m^3 PM_{10} increments showing percent observed by study period

Table 20: Frequency of 10 µg/m^3 PM_{10} increments by study period

Mean 24-hr PM_{10} Category	June 2003		October 2003		November 2003		April 2004	
	*n	%	*n	%	*n	%	*n	%
≤ 10 µg/m^3	8	3.3	24	9.0	40	16.7	30	20.0
≤ 20µg/m^3	39	16.3	90	33.8	99	41.3	50	33.3
≤ 30µg/m^3	128	53.6	43	16.2	24	10.0	40	26.7
≤ 40 µg/m^3	24	10.0	48	18.0	30	12.5	10	6.7
≤ 50µg/m^3	16	6.7	43	16.2	23	9.6	20	13.3
> 50µg/m^3	24	10.0	18	6.8	24	10.0	0	0
Total	239	100	266	100	240	100	150	100

Table 21: Summary of association between symptoms and PM_{10} by increments of 10 $\mu g/m^3$

Health Outcomes	**DF	Mantel Haenszel Chi-Square	p-value
Frequent cough	1	4.0931	0.0431*
Cough in the morning	1	4.1403	0.0419*
Cough during the day	1	0.0310	0.8603
Phlegm in the morning	1	0.0279	0.8673
Phlegm during the day	1	2.8626	0.0907
Troubled by shortness of breath	1	1.0520	0.3050
Stopped for breath while walking on level ground	1	1.1972	0.2739
Wheezing	1	0.2343	0.6284
Chest pain	1	0.8872	0.3462
Shortness of breath	1	3.3771	0.0651
Fatigue	1	2.4724	0.1159
Awakened by shortness of breath	1	4.5350	0.0332*
Total symptoms	1	3.1715	0.0749

*Significant at p <. 05. **Degrees of Freedom

Table 22: Summary association of symptoms by morning PEFR changes with PM_{10} increments of 10 µg/m^3

Health Outcomes	PEFR Decrements ≥ 10%			PEFR Decrements ≠ >10%		
	**DF	Chi-Square	p-value	**DF	Chi-Square	p-value
Frequent coughing	5	9.302	0.093	5	12.994	0.023*
Cough in the morning	5	16.030	0.006*	5	18.236	0.003*
Cough during the day	5	13.280	0.019*	5	15.697	0.008*
Phlegm in the morning	5	5.074	0.416	5	9.561	0.088
Phlegm during the day	5	4.550	0.484	5	10.525	0.061
Troubled by shortness of breath	5	7.387	0.193	5	10.003	0.075
Stopped for breath while walking on level ground	5	1.153	0.955	5	10.625	0.059
Wheezing	5	11.018	0.048*	5	6.823	0.232
Chest Pain	-	-	-	5	24.864	0.000*
Shortness of breath	5	13.247	0.021*	5	12.752	0.025*
Fatigue	-	-	-	5	14.054	0.016*
Awakened by shortness of breath	5	32.200	0.001*	5	7.325	0.195

*Significant at $p < .05$. **Degrees of freedom

Table 23: Relative Risks (OR) of the presence of symptoms among participants by PM_{10} exposure increments of 10 μg/m^3 controlling for seasonality

Variable	OR	95% Confidence Interval	p-value
Cough in the morning	1.1216	1.0234-1.2293	0.0141*
Cough during the day	1.0402	0.9593-1.1280	0.3393
Phlegm in the morning	1.0633	0.9746-1.1600	0.1672
Phlegm during the day	0.9483	0.8724-1.0309	0.2132
Troubled by shortness of breath	0.9823	0.9235-1.0448	0.5709
Stopped for breath while walking on level ground	0.9860	0.9346-1.0403	0.6064
Wheezing	0.9895	0.9207-1.0634	0.7737

* Significant at $p < .05$

Table 24: Relative Risk (OR) of symptoms by PM_{10} increments of 10 μg/m^3 and after controlling temperature, relative humidity, pressure and seasonality

Symptoms	OR	95% Confidence Limits	p-value
Frequent coughing	1.0490	0.9178-1.1991	0.4829
Cough in the morning	1.4464	1.2473-1.6773	<0.0001*
Cough during the day	1.2937	1.1129- 1.5038	0.0008*
Phlegm in the morning	1.0721	0.9775-1.1759	0.1395
Phlegm during the day	0.9566	0.8810-1.0386	0.2902
Troubled by shortness of breath	0.9964	0.9429-1.0530	0.8991
Stopped for breath while walking on level ground	0.8940	0.7998-0.9994	0.0487*
Wheezing	1.3077	1.1103-1.5400	0.0013*
Chest pain	0.6563	0.5798-0.7428	<0.0001*
Shortness of breath	1.0190	0.09564-1.0856	0.5607
Fatigue	0.7015	0.5268-0.9341	0.0153*
Awakened by shortness of breath	1.1285	0.9356-1.3611	0.2062

* Significant at $p < .05$

Table 25: Relative risk (OR) of symptoms among participants by anti-inflammatory medication use

Symptoms	Anti-inflammatory Medication use N=640		No Anti-inflammatory Medication use N=255	
	OR	95% Confidence Interval	OR	95% Confidence Interval
Frequent cough	2.44	(1.81 - 3.30)	0.34	(0.29 - 0 .41)
Cough in the morning	0.72	(0.68 - 0.77)	3.99	(2.47 - 6.46)
Cough during the day	0.69	(0.65 - 0.74)	5.15	(3.13 - 8.48)
Phlegm in the morning	0.69	(0.65 - 0 .75)	5.29	(3.20 - 8.69)
Phlegm during the day	0.65	(0.61 - 0.69)	15.91	(6.65 - 38.04)
Troubled by shortness of breath	0 .74	(0.69 - 0.80)	3.33	(2.10 - 5.29)
Stopped for breath while walking on level ground	0.84	(0.77 - 0.92)	1.73	(1.21 - 2.47)
Wheezing	0.95	(0.83 - 1.09)	1.15	(.78 - 1.71)
Chest pain	12.983	(3.378-49.894)	0.274	(0.261-0.315
Shortness of breath	2.937	(2.107-4.095)	0.310	(0.261-0.369)
Awakened by shortness of breath	6.518	(3.068-13.948)	0.280	(0.240-0.327)

5.0 DISCUSSION

5.1 Particulate Matter

The SHAPE study examined an association between ambient air PM_{10} pollution and outcomes of cardiopulmonary symptoms in an adult cohort using a semi-individual longitudinal design approach. The trend of PM_{10} in Allegheny County is shown in Figure 2 for years 1995-2000, and for the period of May 2003 to May 2004 in Figures 8-9. The average 24hr PM_{10} levels ranged from 30.84 $\mu g/m^3$ in year 1995 to 25.57 $\mu g/m^3$ in year 2000. The average 24hr PM_{10} levels for the period of May 2003 to May 2004 was 24.36 $\mu g/m^3$. These results show that the ambient air quality in Allegheny County is improving. In both studies (PACCC data evaluation, SHAPE) the air pollution show low levels of ambient concentrations during the winter months and high levels in the months of October to December. All of the 8 continuous monitoring sites were highly correlated and statistically significant ($p<.01$) during the SHAPE study (Table 13). Liberty monitoring site showed slightly lower correlation coefficients compared to the other 7 monitors. This observation endows an opportunity to evaluate the current regional air pollution monitoring policy. New strategies could integrate programs that include personal monitoring which can efficiently calculate and apportion accurate individual daily exposures of the most susceptible individuals in the community.

The earlier studies have shown that PM_{10} is a risk factor for cardiopulmonary hospital and emergency room visits (Schwartz 1994; Morris 2001; Peters et al., 2001). This could be due to the composition of the inhalable particles of a mixture of combustive by-products and re-suspended crystal material as well as biological materials such as pollen, endotoxins, bacteria

and viruses (Levy et al., 2002; Verrier et al., 2002, Jinsart et al., 2002; Aekplakorn et al., 2003). Additionally, several biological mechanisms both in animals have shown that the particulate matter can induce pro-inflammatory conditions in lung tissue following exposure to variable levels of concentrations. Yeates and Manderly (2001) summarized studies on mechanisms of air pollution on cardiovascular and systemic responses and how non-respiratory organ health outcomes can occur following air pollution deposition in the respiratory tissue. A possible contribution to the mixture of ambient air concentrations in Allegheny County are the power plants and toxic release inventory (TRI) sites (Table 8), and possible combustive by-products and re-suspended crystal material from automobile (Figure 7). It is essential to carry out regional studies because of the differences in chemical mixtures influenced by local emissions.

5.2 Cardiopulmonary Symptoms

In the analysis of the admission data of the Pennsylvania Cost Care Containment (PACCC) of years 1995-2000, we observed that 43% of the adults aged ≥ 65 years are admitted for cardiopulmonary reasons (ICD-9 Codes 390-519, Tables 3&4). The results also showed that the elderly who were admitted multiple times had diagnoses of acute conditions compared to those admitted only one time during the 6 year period. A logistic regression model controlling for weather, seasonality and day of the week of admission and age group showed a significant relationship ($p < 0.0001$) between admission type (multiple admission versus one-time admission) and the average 24-hr PM_{10}. In the SHAPE follow-up study, the results showed relationships between PM_{10} levels and cardiopulmonary symptoms. Significant relationships were shown between frequent cough, cough in the morning and being awakened by shortness of breath and increments of 10 $\mu g/m^3$ PM_{10} (Table 21) and a risk estimate only showed significant

relationships with cough in the morning (Table 23). The study did not show significant relationship between increments in 10 μg/m^3 PM_{10} and wheezing before adjustments for covariates. Other studies (von Klot et al., 2002; Zemp et al., 1999), reported that there was no association with wheezing, chest tightness and air pollution. When a risk estimate was carried out adjusting for weather and seasonality, an association between cardiopulmonary symptoms and increments in 10 μg/m^3 PM_{10}, was strengthened (Table 24). This result shows that after controlling for the weather variable of temperature, relative humidity and pressure and seasonality, the physiological responses appear to be related to PM_{10} exposures. For cough in the morning the OR was 1.12 (95% CI =1.02- 1.23), for an increase in 10 μg/m^3 adjusting for seasonality (Table 23). The SHAPE study showed some consistency with other studies that have shown effects of low-level ambient air pollution and acute adverse cardiopulmonary health effects.

In this study, the average 24-hr PM_{10} was 24.36 μg/m^3, which is far below the federal ambient air quality standard of 150 μg/m^3. The annual arithmetic standard for PM_{10} is 50 μg/m^3. The acute health effects observed are often reversible health conditions (PEFR, phlegm, cough, and shortness of breath) which improve following removal of an exposure or following treatment. This is often seen in occupational settings where a worker who is experiencing the effects of occupational exposures can often recover completely once removed from the nuisance exposure (Nieuwenhuijsen & Burddorf, 2001). Practical short-term intervention studies of ambient air pollution are not common. In an intervention study of the ban of coal use in Dublin, Ireland, Clancy et al., (2002) showed that after 72 months about 116 fewer respiratory deaths and 243 fewer cardiovascular deaths were seen per year. This accounted for 5.7% decrease in respiratory death (95% CI, 4-7, $p<0.0001$) and for the cardiovascular death by 10.3% (95% CI,

8-13, $p<0.0001$). The intervention clearly shows the benefits of dealing first with the bigger contributors to air pollution.

5.3 Peak Expiratory Flow Rate (PEFR)

Scatter plots of PEFR changes were not associated with PM 10 changes (Figure 12-13). It could be that PEFR is not a sensitive tool for evaluation of pulmonary function in adults. A significant relationship was shown between PM10 and increased decrements of 10% pulmonary function as measured by the PEFR and cardiopulmonary symptoms of cough (Table 22). But we also observed a significant relationship ($p<.05$) for PEFR decrements less than 10% for cough in the morning and during the day, frequent cough, and for stopping for breath while walking on level ground. This could be that as PM increases the already vulnerable people react more adversely than healthier people would to even small changes in air quality. PEFR essentially is a surrogate measurement of FEV_1 but FEV_1 is measured often in a pulmonary laboratory, whereas, PEFR is often self-administered and can be prone to errors. Future studies measuring PEFR could also include measurement of a series of FEV_1.

Not many studies have shown a relationship between PM exposures and PEFR. Significant negative associations were reported by Roemer et al., (1998) and Pentinnen et al., (2001). Osunsanya et al., (2001) reported borderline significant ($p< .05$), with 19% increase in the rate of 10% decrements in daytime PEFR with increase in PM_{10} of 10-20 $\mu g/m^3$. Boezen et al., (1998) reported a high significant prevalence of symptoms with increase in PM_{10} in adults who had a greater variability of PEFR. Koeing et al., (1993) showed that an increase in fine particulate was associated with declines in forced expiratory volume in 1 second (FEV_1) by 34 ml for an increase in PM_{10} of 20 $\mu g/m^3$.

A low significant relationship between wheezing and PM_{10}, adjusting for PEFR of 10% from the mean was observed (=0.048) (Table 22). Wheezing is of interest in respiratory symptoms as normally, this is one of the overt signs of changes in breathing patterns of asthma patients. In the Pollution Effects on Asthma Children in Europe (PEACE) studies by Roemer et al., (1998) that involved children, the authors reported that PM_{10} was associated with wheezing outcomes. Boezen, (1998) reported that there was no consistent association between PM_{10}, NO_2, SO_2 and black smoke with respiratory symptoms, but reported an OR of 1.10 (95% CI= 0.81-1.31) for a 5% decrease in PEFR to PM_{10} exposure of average 41.5 $\mu g/m^3$. The SHAPE study showed that individuals who took their anti-inflammatory medication as much as 100 % of the time (Figure11) reported symptoms outcomes 50% of the time. It could be that wheezing symptoms in adult groups is well controlled by use of medication. Conversely, this may not be the case in children who rely on adults to regulate their medication, and hence most studies of children show a significant relationship between air pollution and wheezing. Future studies should explore this medication phenomenon in different age groups.

5.4 Medication Use and Symptoms

Medication has been reported to be protective of symptoms of the cardiopulmonary system. In this study an increased prevalent use of anti-inflammatory medication among participants (Figure 11) was reported. Over 59% of the participants were on anti-inflammatory medication. When medication use was analyzed by study period, the results showed that in October, 2003 individuals reported use of anti-inflammatory medication 71% of the time and also reported having symptoms 71% of the time during the same period. Because the study did not obtain complete data on the patterns of taking the medication it is speculative to discern that the individuals were taking the medication because they needed to take the medication to alleviate

the symptoms. In other cases however, the elderly take their medication simply because the doctor prescribed it, a phenomenon reported by Curtis et al., (2004). In fact, when a risk estimate analysis was performed the results showed that non-users of anti-inflammatory medication were at higher risks of experiencing the cardiopulmonary symptoms compared to those on the medication (Table 25). In a study involving children however, Delfino et al., (2002) reported significant association between symptoms among kids who were not taking anti-inflammatory medication and criteria pollutants of PM_{10}, O_3 and NO_2. Future study analysis should report on the environmental triggers that can influence the study participants to regulate their anti-inflammatory medication use. This can contribute to accurate measurement of the cardio-respiratory response under unpredictable concentrations of air pollution.

5.5 Emergency Room Visits and Hospital Admissions

Longitudinal follow-up studies can contribute a great deal to our understanding of insidious currents that occur before an individual seeks medical help. In this study very few incidences of emergency room visits, doctor's visits and hospitalizations were observed. Undoubtedly, higher ambient air pollution exposures seen in earlier studies can be implicated for hospital admissions or death in different population groups. But, lower levels of ambient air pollution exposures as seen today do not necessarily cause death, accelerate death, or shorten life by a few hours or days, or lead to frequent hospitalization or emergency room visits but can result in repeated acute symptoms that can be reversed once exposures are removed (Nieuwenhuijsen & Burddorf, 2001). Continued exposures at levels that are thought to be safe can aggravate the symptoms and can eventually compromise physiological cardiopulmonary function. This has implications to ambient air quality that can be improved to protect all groups of individuals in a community.

5.6 Conclusion

The SHAPE study followed up individuals who monitored their health by using a self-administered pulmonary function test and keeping records of cardiopulmonary symptoms as well as daily activities. Since short-term exposure are likely to cause overt symptoms, it is important to have knowledge and background health history of study participants in air pollution studies in order to detect these small changes observed and to make correct inferences of any significant outcomes. All the participants had a physician confirmed diagnosis of cardiopulmonary disease. The study showed results that have small estimates to the population but are not insignificant suggesting that the elderly susceptible individuals may be at a greater risk of developing symptoms if exposed to the currently observed low-levels of exposure. There is some consistency between the results of this study and the results of studies performed elsewhere (Table1). Even after controlling for potential confounders we found that the PM_{10} concentrations are significant in exerting cardiopulmonary symptoms in this susceptible population.

Mortality studies on low levels of ambient air particulate exposures have shown that the elderly are significantly at risk of death from cardiopulmonary causes compared to the younger adults (Fischer et al., 2003; Vedal et al., 2003). A few morbidity studies on hospital and ER visits and air pollution studies have also shown that the elderly are especially at risk to low-ambient exposure level (Hwang &Chan, 2002). Follow-up studies that have included the elderly and the disadvantaged communities have shown how the African Americans and those with lower education attainment can experience consequential health outcomes by living close to power plants (Levy et al, 2002).

The SHAPE study restricted recruitment and participation of individual to an area defined by zip codes and within 15 km of known polluting sources. Although we included all the data from Allegheny County continuous monitoring sites, this should not be necessary in future studies because these sites were highly correlated. Individual monitoring can be more benefitial to the communities and also to the advancement of air pollution studies. Individual apportionment of exposure and control of study area improves on the study outcomes inference and is recommended for future studies. More regional research investigations targeting the susceptible populations such as the elderly are needed. Implications of such study findings can influence policy changes that can lead to increased attention to ambient air quality regulations and consequently improved quality of life among different groups of populations. The federal, state and the county agencies should re-evaluate their monitoring strategies to incorporate the best science that protects individuals. It is not important that the industrial companies meet the current standards, but that individuals at risk of being impacted by these low level exposures are protected. The state and federal agencies and environmental and epidemiology scientists should ask the question whether the current USEPA standards are stringent enough to protect those groups of people that are most susceptible such as the sick, elderly, children, those with less educational attainment and different ethnic groups and whether the current monitoring programs are over due for a review.

5.7 Study Limitations and Implications

Sample size for estimation of association was small. Forty-seven percent (47%) of our data was excluded from the final analysis in order to create a homogenous group for comparison. As a result, our study did not consider separate analysis for different diagnosis to see which groups of

people are most affected by air quality. Future longitudinal studies could evaluate separately the effects of air pollution on individuals who have cardiovascular disease and those who have respiratory disease diagnosis. Additionally, this study based exposure of individuals on ecological exposure; the assumption of this type of study is that all participants are exposed to the same levels of particulate matter in a given period. The effect on all participants will be relatively similar regardless of health condition. Future studies may require funding to include individual monitoring to improve on the extrapolation of individual exposure matrix.

The implications of the SHAPE study are that very few hospital or emergency room visits are reported yet a large percent of individuals reported symptoms. This signifies that the susceptible populations may be sensitive to the currently recorded levels of ambient air and that they react adversely but not severe enough to require medical support. These small incidences can eventually burden the body leading to hospitalization or death. Although this study did not assess the outcomes by ethnicity groups or educational level, it is reasonable to conclude that a large percent of population in the study area are employed in the industrial plants and that the population includes different ethnic groups that live and work in the vicinity of the power plants and coke oven plants. Future studies that explore these factors are recommended.

APPENDIX A: ENVIRONMENTAL HEALTH STUDY QUESTIONNAIRE

1. **Study Code identification number** **"CIN"** **1.** □ □□□□□□□□

2. **Name**_____ **2.** □□□□□ □□□□□

Address_____

_____

3. **Telephone number** **3.** □□□ □□□ □□□□

4. **Date of Birth**_____ **4.**□□ □□ □□□□

5 **Sex (M/F)** **5.** □

6. **What is your racial/ethnic background?** **6.** □□

(01) African American/Black; (02) White/Caucasian; (03) Hispanic; (04) American Indian (05) Asian/Pacific Islander; (99) Other

7. **Date of interview (mm dd yyyy)** **7.** □□ □□ □□□□

8. **Have you ever been told by a physician that you have a lung disease such as asthma? NO YES**

If yes, what disease and at what age (in years)?_____ **8.** □□

Codes: (00)if YES; (88)NO; (99)UNKNOWN

9. **Have you ever been told by a physician that you have heart problems? NO YES**

If yes, what disease and at what age (in years)?_____ **9.** □□

Codes: (00)if YES; (88)NO; (99)UNKNOWN

10. **Have you ever been to the emergency room for lung problems? NO YES**

If yes, what lung problem and how many times?_____ **10.** □□

Codes: (88)NO; (number of times)YES; (99)UNKNOWN

11. **Have you ever been admitted to the emergency room for heart problems? NO YES**

If yes, what heart problem and how many times? _____ **11.** □□

Codes: (88)NO; (number of times)YES; (99)UNKNOWN

12. **Have you ever been placed on a ventilator (a machine that breaths for you while you have a plastic tube in your mouth/lung?) (0)NO (1)YES (9)UNKNOWN** **12.** □

13. **What factors aggravate your respiratory or heart problems or bring on an attack?**

13a. cold air (0)NO (1)YES (9)UNKNOWN **13a.** □

13b. humidity (0)NO (1)YES (9)UNKNOWN **13b.** □

13c. exercise (0)NO (1)YES (9)UNKNOWN **13c.** □

13d. medication (0)NO (1)YES specify:_____ **13d** □

13e. change of seasons (0)NO (1)YES (9)UNKNOWN **13e.** □

13f. dust or dander (animal) (0)NO (1)YES (9)UNKNOWN **13f.** □

13g. other (0)NO (1)YES specify:_____ **13g.** □

(9)UNKNOWN

APPENDIX A (Cont'd)

14. Have you ever taken medications for lung problems? (0)NO (1)YES*(9)UNKNOWN **14.** □
If yes, please list for each medication ever used:
Drug Name**;** Route **(nasal spray, oral inhaler, pills);** Dose **(in number of sprays, puffs or mg);**
Frequency **(times per day; less than once a week; etc);** Date started**;** Date stopped

_____

_____

_____

15. Are you still being treated for asthma or lung disease?(0)NO(1)YES (9)UNKNOWN **15.** □
Name of Medications_____

16. Have you ever passed out or had a heart problem? (0)NO (1)YES (9)UNKNOWN **16.** □
If yes, please list:
Date, type of event, triggering factors/circumstances

_____

_____

17. Have you ever taken medications for heart problems? (0)NO (1)YES* (9)UNKNOWN **17.** □
If yes, please list for each medication ever used:
Drug Name**;** Route **(nasal spray, oral inhaler, pills);** Dose **(in number of sprays, puffs or mg);**
Frequency **(times per day; less than once a week; etc);** Date started**;** Date stopped

_____

_____

_____

18. Are you still being treated for heart problems? (0)NO (1)YES (9)UNKNOWN **18.** □
Name of Medications_____ _____

19. Have you been admitted to a hospital for respiratory or heart problems in the past year? **19.** □
(0)NO (1) YES (9) UNKNOWN If yes, please list:
Date, reason, and hospital, county, state

_____

_____

_____

20. How old is the house that you live in now? **20.** □□
(Enter age) YES (99)UNKNOWN

21. How long have you lived in this house. **21.** □□
(Enter years) YES (99)UNKNOWN

22. Are there rooms including basement in the house that are damp?
(0)NO (1)YES **22.** □

APPENDIX A (Cont'd)

23. What is the main source of heating in your home?
(Enter a Number given for each heating source below) **23.** □□
(11) Radiators (steam or water)
(22) Gas- heated forces air (vents)
(33) Electric- heated forced air (vents)
(44) Gas stove/ fireplace/ wall furnace
(55) Electric space heater
(66) Kerosene space heater
(77) Wood burning stove/ fireplace
(99) UNKNOWN

24. How long have you lived in Allegheny County? **24.** □□

25. Has the air pollution gotten better since you first lived in Allegheny County ? **25.** □
(0) NO; (1) YES; (9) UNKNOWN

26. Do you smoke?
(0)NO (1)YES **26.** □

27. Are you exposed to tobacco smoke in your home? **27.** □
(0)NO (1)YES

Thank you for taking time to answer this survey.

28.Form completed by _____ **28a.** □□ □□ □□□□ **28b.** □□□□
Month **day** **year** **Staff Code**

29.Form checked by _____ **29a.**□□ □□ □□□□ **29b.** □□□□
Month **day** **year** **Staff Code**

APPENDIX B: DAILY PEAKFLOW AND SYMPTOMS DIARY

DAILY PEAKFLOW AND SYMPTOMS DIARY {LUNGS}							
Date_____ Peak Flow, Medication and Symptoms	1	2	3	4	5	6	7
Record your best Peak flow this morning (before medication)							
Record your best Peak flow this afternoon? (Between 2 PM and 6PM)							
Did you change your medication today? Please specify medication below. Rank your response as follows: No = 0 Increased = 1 Decreased = 2.							
Did you have any of the following symptoms today? Please rank your response as follows: No =0 Mild =1 Moderate =2 Severe =3							
Any cough first thing this morning?							
Any cough during the day?							
Any phlegm first thing this morning?							
Any phlegm during the day?							
Troubled by shortness of breath?							
Stopped for breath while walking on level ground?							
Any wheezing or whistling sound from your chest?							
Did you have any of these other symptoms today? Y or N							
Muscle aches?							
Nose congestion?							
Runny nose?							
Sore throat?							
Fever or shaky chills?							
Headache?							
Did you have a visit to the ER today? Y or N							
Did you have an unscheduled visit to your doctor today? Y or N							
How long were you outdoors today? Please Enter Number of Hours. If None Enter 0.							
If you smoke, how many cigarettes did you smoke today? If none enter 0							
Were you exposed to tobacco smoke (secondary smoke) today? Y or N							
Were you more than 10 miles away from your home today? Y or N							
If you were more than 10 miles away from home, Enter Number of Hours. If None Enter 0 Hours.							

APPENDIX B (Cont'd)

DAILY PEAKFLOW AND SYMPTOMS DIARY {HEART}							
Date_____ Peak Flow, Medication and Symptoms	1	2	3	4	5	6	7
Record your best Peak flow this morning (before medication)							
Record your best Peak flow this afternoon (Between 2 PM and 6 PM)							
Did you change your medication today? Please specify medication below. Rank your response as follows: No = 0 Increased =1 Decreased = 2							
Did you have any of the following symptoms today? Please rank your response as follows: No =0 Mild =1 Moderate = 2 Severe = 3							
Experienced any chest pain during activities?							
Experienced any shortness of breath during activity?							
Experienced unexplained weakness or fatigue?							
Awakened by shortness of breath?							
Experienced any frequent coughing?							
Did you have any of these other symptoms today? Y or N							
Muscle aches							
Nose congestion/ Runny nose?							
Sore throat?							
Fever or shaky chills?							
Headache?							
Did you have a visit to the ER today? Y or N							
Did you have an unscheduled visit to your doctor today? Y or N							
How long were you outdoors today? Please Enter Number of Hours. If None Enter 0.							
If you smoke, how many cigarettes did you smoke today? If none enter 0							
Were you exposed to tobacco smoke (secondary smoke) today? Y or N							
Were you more than 10 miles away from your home today? Y or N							
If you were more than 10 miles away from home, Enter Number of Hours. If None Enter 0 Hours.							

*The diary comprised of a one calendar to make it easier for participants' record keeping. This diary has been modified here to fit the page.

BIBLIOGRAPHY

Aekplakorn W, Loomis D, Vichit-Vadakan N, Shy C, Wongtim S, Vitayanon P (2003). Acute effects of sulphur dioxide from power plants on pulmonary function of children, Thailand. *International Journal of Epidemiology, 32(5): 854-61.*

Atkinson RW, Bremner SA, Anderson HR, Strachan DP, Bland JM, Ponce de Leon A (1999). Short-term Associations between Emergency Hospital Admissions for Respiratory and Cardiovascular Disease and Outdoor Air Pollution in London. *Archives of Environmental Health, 54 (6): 398-411.*

Basu R, Samet JM (2002). An exposure assessment study of ambient heat exposure in an elderly population in Baltimore, Maryland. *Environmental Health Perspective, 110 (12): 1219-1224.*

Batalha JRF, Saldiva PHN, Clarke RW, Coull BA, Stearns RC, Lawrence J, Murthy GG, Koutrakis P, Godleski JJ (2002). Concentrated ambient air particles induce vasoconstriction of small pulmonary arteries in rats. *Environmental Health Perspectives, 110 (12): 1191-1197.*

Bellander T, Berglind N, Gustavsson P, Jonson T, Nyberg F, Pershagen G, Jarup L (2001). Using geographic information systems to assess individual historical exposure to air pollution from traffic and house heating in Stockholm. *Environmental Health Perspective, 109 (6): 633-639.*

Bernard SM, Samet JM, Grambsch A, Ebi KL, Romieu I (2001). The potential impacts of climate variability and change on air pollution-related health effects in the United States. *Environmental Health Perspectives, 109 (2): 199-209.*

Boezen M, Schouten J, Rijcken B, Vonk J, Gerritsen J, van der Zee S, Hoek G, Brunekreef B, Postma D (1998). Peak expiratory flow variability, bronchial responsiveness, and susceptibility to ambient air pollution in adults. *American Journal of Respiratory and Critical Care Medicine, 158: 1848-1854.*

Braga A, Zanobetti A, Schwartz J (2000). Do respiratory epidemics confound the association between air pollution and daily deaths? *European Respiratory Journal, 16 (4): 723-728.*

Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F (2002). Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. *Circulation., 105 (13): 1534-1536.*

Brunekreef B, Hoek G (1993). The relationship between low-level air pollution exposure and short-term changes in lung function in Dutch children. *Journal of Expo Anal Environmental Epidemiology, 3 (1): 117-128.*

Brunekreef B, Dockery DW, Krzyzanowski M (1995). Epidemiologic studies on short-term effects of low levels of major ambient air pollution components. *Environmental Health Perspective, 103 (2): 3-13.*

Brunekreef B, Hoek G (2002). Air pollution and health. *The Lancet, 360: 1233-1242.*

Bryson (1998). The Donora fluoride fog: A secret history of America's worst air pollution disaster http:/www.fluoridation.com/donora (accessed 5/1/2003).

Burnett RT, Cakmak S, Raizenne ME, Stieb D, Vincent R, Krewski D, Brook JR, Philips O, Ozkaynak H (1998). The association between ambient carbon monoxide levels and daily mortality in Toronto, Canada. *Journal of Air Waste Management Association, 48*(8): *689-700.*

Checkoway H, Levy D, Sheppard L, Kaufman J, Koenig J, and Siscovick D (2000). A case-crossover analysis of fine particulate matter air pollution and out-of-hospital sudden cardiac arrest. *Health Effects Institute, 1-32.*

Chock DP, Winkler SL, Chen C (2000). A study of the association between daily mortality and ambient air pollutant concentrations in Pittsburgh, Pennsylvania. *Journal of Air and Waste Management Association, 50 (8): 1481-500.*

Clancy L, Goodman P, Sinclair H, Dockery D (2002). Effect of air-pollution control on death rates in Dublin, Ireland. *The Lancet, 360: 1210-1214.*

Costa D, Dreher KL (1997) Bioavailable Transition Metals in Particulate Matter Mediate Cardiopulmonary Injury in Healthy and Compromised Animal Models. *Environmental Health Perspectives, 105 (Supplementary 5):1053- 1060.*

Crater D, Heise S, Perzanowski M, Herbert R, Morse CG, Hulsey TC, Platts-Mills T (2001) Asthma Hospitalization Trends in Charleston, South Carolina, 1956 to 1997: Twenty-fold Increase Among Black Children During a 30 year Period. *Pediatrics, 108 (6): 97.*

de Hartog JJ, H**o**ek G, Peters A, Timonen KL, Ibald-Mulli A, Brunekreef B Heinrich J, Tiittanen P, Wijnen JH, Kreyling W, Kulmala M, Pekkanen J (2003). Effects of fine and ultrafine particles on cardiorespiratory symptoms in elderly subjects with coronary heart disease. *American Journal of Epidemiology, 157(7): 613-623.*

Delfino R, Zeiger R, Seltzer J, Street D (1998). Symptoms in pediatric asthmatics and air pollution: Differences in effects by symptom severity, anti-inflammatory medication use and particulate averaging time. *Environmental Health Perspectives, 106*: *751-761.*

Delfino R (2002). Epidemiologic evidence for asthma and exposure to air toxics: Linkages between occupational, indoor, and community air pollution research. *Environmental Health Perspectives, 110 (4): 573-589*.

Delfino R, Zeiger R, Seltzer J, Street D, and McLaren C (2002). Association of asthma with peak particulate air pollution and effect modification by anti-inflammatory medication use. *Environmental Health Perspectives. 110 (10): 607-617.*

Delfino R, Gong Jr H, William L, Pellizzari E, and Hu Y (2003). Asthma Symptoms in Hispanic Children and Daily Ambient Exposures to Toxic and Criteria Air Pollutants. *Environmental Health Perspective, 111 (4): 647-656.*

Desqueyroux H, Pujet J, Prosper M, Squinazi F, Momas I (2002). Short-Term Effects of Low-Level Air Pollution on Respiratory Health of Adults Suffering from Moderate to Severe Asthma. *Environmental Research Section, A89*: *29-37.*

Devlin RB, Ghio AJ, Kehrl H, Sanders G, Cascio W (2003). Elderly humans exposed to concentrated air pollution particles have decreased heart rate variability. *European Respiratory Journal, 40 (21): 76-80.*

Dockery DW (2001). Epidemiologic Evidence of Cardiovascular Effects of Particulate Air Pollution. *Environmental Health Perspective, 109 (4): 483-486*.

Donaldson G C, Keating WR (1997). Early increases in ischemic heart disease mortality dissociated and later changes associated with respiratory mortality after cold weather in south east England. *Journal of Epidemiology Community Health, 51(6): 643-8.*

Donaldson K and Macnee W (2001). Potential Mechanisms of Adverse Pulmonary and Cardiovascular Effects of Particulate Air Pollution. (PM_{10}). *International Journal of Hygiene Environmental Health, 203 : 411-5*.

Donaldson K., Stone V., Seaton A., and Macnee W (2001). Ambient Particle Inhalation and the Cardiovascular System: Potential Mechanisms. *Environmental Health Perspectives, 109 (4): 523-602.*

Eldwood PC, Beswick A, O'Brien JR, Renaud S, Fifield R, Limb ES, Bainton D (1993). Temperature and risk factors for ischemic heart disease in the Caerphilly prospective study. *British Heart Journal, 70 (6): 520-3.*

Fischer P, Hoek G, Brunekreef B,Verhoeff A, van Wijnen J (2003). Air pollution and mortality in the Netherlands: are elderly more at risk? *European Respiratory Journal, 34s-38s.*

Folinsbee Lawrence J (1993). Human Health Effects of Air Pollution. *Environmental Health Perspectives, 100: 45-56.*

Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, Kuller LH, Manolio TA, Mittlemark MB, Newman A, O'Leary DH, Psaty B, Rautaharju P, Tracy RP, Weiler PG (1991). The cardiovascular health study: design and rationale. *AEP, Volume1.*

Geyh A, Xue J, Özkaynak H, and Spengler J (2002). The Harvard Southern California Chronic Ozone Exposure Study: Assessing Ozone Exposure of Grade-School-Age Children in Two Southern California Communities. *Environmental Health Perspectives, 108 (3): 1-14.*

Ghio AJ, Kim C, Devlin RB (2000). Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers. *American Journal of Respiratory Critical Care Medicine, 162*: *981-988.*

Ghio AJ, Hall A, Bassett MA, Cascio WE, Devlin RB (2003). Exposure to concentrated ambient air particles alters hematologic indices in humans. *Inhalation Toxicology, 15(14): 1465-78.*

Gold DR, Litonjua A, Schwartz J, Lovett E, Larson A, Nearing B, Allen G, Verrier M, Cherry R, Verrier R (2000). Ambient pollution and Heart Rate Variability. *Circulation, 101: 1267.*

Godleski JJ, Verrier RL, Kroutakis P, and Catalano, P. Mechanism of Morbidity and Mortality from Exposure to Ambient Air Particles. Health Effects Institute Report Number 91, February 2000.

Godleski JJ, Sioutus C, Verrier RL, Killingsworth CR., Lovett E., Kshna Murthy GG, Hatch V, Wolfson JM, Ferguson FT, Kroutakis P (1997). Inhalation exposure of cannines to concentrated ambient air particles. *American Journal Respiratory and Critical Care Medicine, 155: A246.*

Goldberg MS, Bailar JC 3rd, Burnett RT, Brook JR, Tamblyn R, Bonvalot, Ernst P, Flegel KM, Singh RK, Valois MF (2000). Identifying subgroups of the general population that may be susceptible to short-term increases in the particulate air pollution: a time-series study in Montreal, Quebec. *Rep Health Inst*, *(97).*

Greenbaum DS, Bachmann JD, Krewski D, Samet JM, White R, Wyzga RE (2001). Particulate Air Pollution Standards and Morbidity and Mortality:Case Study. *American Journal of Epidemiology, 154 (12): s78-s90.*

Greenberg MR. (2004). Is public support for environmental protection decreasing? An analysis of U.S. and New Jersey data. *Environmental Health Perspectives, 112(2*): *121-125.*

Helfand WH, Lazarus J, Theerman P. Donora, Pennsylvania: An Environmental Disaster of the 20th Century. *American Journal of Public Health, 91 (4): 553.*

Hernandez-Cadena L, Tellez-Rojo MM, Sanin-Aguirre LH, Lacasana-Navarro M, Campos A, Romieu I (2000). Relationship between emergency consultations for respiratory diseases and air pollution in Juarez City, Chihuahua. *Saluda Publica de Mexica. 42 (4): 288-297.*

Hoek G, Dockery DW, Pope A, Neas L, Roemer W, Brunekreef B (1998). Association between PM_{10} and decrements in peak expiratory flow rates in children: reanalysis of data from five panel studies. *European Respiratory Journal, 11 (6): 1307-1311*.

Hoek G, Brunekreef B, Goldbohm S, Fischer P, Brandt P (2002). Association between mortality and indicators of traffic related air pollution in the Netherlands: A cohort study. *The Lancet, 360:1203-1209.*

Hoyos S, Ballester F, Tenias J.M, Merelles A, Rivera ML (2000). Length of stay in a hospital emergency room due to asthma and chronic obstructive pulmonary disease: Implications for air pollution studies. *European Journal of Epidemiology, 16: 455-463.*

Hwang JS and Chan CC (2002). Effects of Air Pollution on Daily Clinic Visits for Lower Respiratory Tract Illness. *American Journal of Epidemiology, 155 (1): 1-10.*

Ibald-Mulli A, Timonen KL, Peters A, Heinrich J, Wolke G, Lanki T, Buzorius G, Kreyling WG, de Hartog J, Hoek G, ten Brink HM, Pekkamen J (2004). Effects of Particulate Air Pollution on Blood Pressure and Heart Rate in Subjects with Cardiovascular Disease: A Multicenter Approach. *Environmental Health Perspectives, 112 (3): 369-377.*

Jedrychowski W, Flak E, Mroz E (1999). The adverse effect of low levels of ambient air pollutants on lung function growth in preadolescent children. *Environmental Health Perspectives, 107 (8): 669-674.*

Jinsart W, Tamura K, Loetkamonwit S, Thepanondh S, Karita K, Yano E (2002). Roadside particulate air pollution in Bangkok. *Journal of Air Waste Management Association, 52 (9):1102-10.*

Keeler G, Dvonch T, Yip F, Parker E, Israel B, Marsik F, Morishita M, Barres J, Robins T, Brakefield-Caldwell W, Sam M (2002). Assessment of personal and community-level exposures to particulate matter among children with asthma in Detroit, Michigan, as part of community action against asthma (CAAA). *Environmental Health Perspectives, 110 (2): 173-181.*

Koenig JQ, Larson TV, Hanley QS, Rebolledo V, Dumler K, Checkoway H, Wang SZ, Lin D, Pierson WE (1993). Pulmonary Function Changes in Children Associated with Fine Particulate Matter. *Environmental Research, 63: 26-38.*

Koken PJM, Piver WT, Ye F, Elixhauser A, Olsen LM, Portier CJ (2003). Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. *Environmental Health Perspectives, 110 (10): 1312-1317.*

Künzli N, Tager IR (1997). The Semi-individual Study in Air Pollution Epidemiology: A valid Design as Compared to Ecologic Studies. *Environmental Health Perspectives, 105 (10): 1078-1083.*

Kung-Yee L, Zeger SL (1986). Longitudinal data analysis using generalized linear models. *Biometrika, 73: 13-22.*

Leaderer BP, Naeher L, Jankun T, Balenger K, Holford TR, Toth C, Sullivan J, Wolfson JM, Koutrakis P (1999). Indoor, outdoor, and regional summer and winter concentrations of PM_{10}, PM2.5, SO4(2)-, H+, NH4+, NO3-, NH3, and nitrous acid in homes with and without kerosene space heaters. *Environmental Health Perspective, 107(3):223-231.*

Lee J, Schwartz J (1999). Reanalysis of the effects of air pollution on daily mortality in Seoul Korea: A Case-crossover design. *Environmental Health Perspectives, 107* (*8): 633-636.*

Levy J, Greco S., and Spengler J (2002). The importance of population susceptibility for air pollution risk assessment: a case study of power plants near Washington DC. *Environmental Health Perspectives, 110 (12): 1253-1260.*

Liao DP, Creason J, Shy C, Williams R, Watts R, Zweidinger R (1999). Daily variation of Particulate Air Pollution and Poor Cardiac Autonomic Control in the Elderly, *Environmental Health Perspectives, 107 (7): 521-525*.

Mann J, Tager IB, Lurmann F, Segal M, Quesenberry CP, Lugg MM, Shan J, and Van Den Eeden S (2002). Air Pollution and Hospital Admissions for Ischemic Heart Disease in Persons with Congestive Heart Failure or Arrhythmia. *Environmental Health Perspectives, 110* (*1247*-1252).

Mazumdar, Sussman (1983). Relationships of Air Pollution to Health: Results from the Pittsburgh Study. *Archives of Environmental Health, 38 (1).*

Mittlemen, Maclure M, Robins J M (1995). Control sampling strategies for case-crossover studies: an assessment of relative efficiency. *American Journal of Epidemiology, 142(91-98).*

Morris Robert D (2001). Airborne Particles and Hospital Admissions for Cardiovascular Disease: A Quantitative Review of the Evidence. *Environmental Health Perspectives, 109. Suppl. 4. 495-4996*

Morris RD., Naumova EN., and Munasinghe RL (1995). Ambient Air Pollution and Hospitalization for Congestive Heart Failure Among Elderly People in Seven Large US Cities. *American Journal of Public Health, 85 (10); 1361-1365*.

Nemmar A, Hoet PHM, Vanquickenborne B, Dinsdale D, Thomeer M, Hoylaerts MF, Vanbilloen H, Mortelmans L, Nemery B (2001). Passage of Inhaled particles into the blood circulation in humans. *Circulation, 105: 411-414.*

Osunsanya T, Pescott G, Seaton A (2001). Acute respiratory effects of particles: mass or number? *Occupational and Environmental Medicine, 58 (3); 154-159.*

Penttinen P, Timonen KL, Tiittanen P, Mirme A, Ruuskanen J, Pekkanen J (2001). Ultrafine particles in urban air and respiratory health among adult asthmatics. *European Respiratory Journal, 17: 428 – 435.*

Penttinen P, Timonen K, Tiitanen P, Mirme A, Ruuskanen J, Pekkanen J (2001). Number concentration and size of particles in urban air: effects on spirometric lung function in adult asthmatic subjects. *Environmental Health Perspectives, 109: 319-323.*

Perez-Hoyos S, Ballester F, Tenias JM, Merelles A, Rivera M (2000). Length of stay in a hospital emergency room due to asthma and chronic obstructive pulmonary disease: implications for air pollution. *European Journal of Epidemiology, 16 (5): 455-63.*

Peters A, Sigfried P, Angela D, Jutta, S, Wolfgag K, Erich WH (1999). Increases in Heart Rate during an Air Pollution Episode. *American Journal of Epidemiology, 150 (10): 1094-1098.*

Peters A, Liu E, Verrier R, Schwartz J, Gold D, Mittleman M, Baliff J, Oh J.A, George A, Monahan K, Dockery DW (2000). Air Pollution and Increase of Cardiac Arrhythmia. *Epidemiology, 11(1); 11-17.*

Peters A, Dockery DW, Muller JE (2001). Increased Particulate Air Pollution and the Triggering of Myocardial Infarction. *Circulation, 102: 2810-2815.*

Pope III CA (2001) Particulate Air Pollution, C - reactive protein, and Cardiac Risk. *European Heart Journal, 22 (14): 1149-50.*

Pope III CA, Burnett RT, Thun MJ, Calle E, Krewski D, Ito K, Thurnston GD (2002). Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA, 287: 1132-1141.*

Pope III CA, Verrier RL, Lovett E G, Larson A C, Raizenne ME, Kanner RE, Schwartz J, Villegas G M, Gold D R, and Dockery DW (1999). Heart Rate associated with Particulate Air Pollution. *American Heart Journal, 138: 890-899.*

Pope C A III, Hansen ML, Long RW, Nielsen KR, Eatough NL, Wilson WE, Eatough DJ (2004). Ambient Particulate Air Pollution, Heart Rate Variability, and Blood Markers of Inflammation in a Panel of Elderly Subjects. *Environmental Health Perspectives, 112 (3); 339-345.*

Rochon J (1998). Application of GEE procedures for sample size calculations in repeated measures experiments. *Statistics in Medicine, 17: 1634-1658.*

Roholm K (1937). The fog disaster in the Meuse Valley, 1930. A fluorine intoxication. *The Journal of Industrial Hygiene and Toxicology, 19 p. 126-137.*

Rosero SZ, Zareba W, Moss AJ, Robinson JL, Hajj Ali RH, Locati EH, Benhorin J, Andrews ML (1999). Asthma and the risk of cardiac events in the Long QT syndrome. Long QT Syndrome Investigative Group. *American Journal of Cardiology, 15;84(12):1406-11.*

Schwartz J. Dockery DW (1992) Particulate Air Pollution and Daily Mortality in Steubenville, Ohio. *American Journal of Epidemiology, 135: No.1. 12-19.*

Schwartz J, Slater D, Larson TV, Pierson WE, Koeing JQ (1993). Particulate air pollution and hospital emergency room for asthma in Seattle. *American Review of Respiratory Diseases, 147: 826-831.*

Schwartz J (1994). Air Pollution and Hospital Admissions for the Elderly in Birmingham, Alabama. *American Journal of Epidemiology, 139 (6): 589-598.*

Schwartz J (1999). Air pollution and hospital admissions for heart disease in eight U.S counties. *Epidemiology, 10: 17-22.*

Slauhgter JC, Lumley L, Koeing JQ, Shapiro G (2003). Effect of ambient air pollution on symptoms severity and medication use in children with asthma. *Annals of Allergy, Asthma and Immunology, 91: 346-353.*

Simoyi P, Wilson N, Ducatman A, McCauley M (1995) "Childhood Asthma Risk Factors and Intervention"; *Fifth Annual Prevention Center Conference, CDC, Atlanta, GA, Feb. 16-18. 1995.*

Stevens J (1986). Applied multivariate statistics for the social sciences. Third edition, ISBN: 0-898-59568-1, Lawrence Erlbaum Associates, Inc., Mahwah, NJ, USA.

Stokes ME, Davis CS, Koch GG (2001). Categorical analysis using the SAS systems, 2d ed. Cary, NC: SAS Institute Inc.

Stone PH, Godleski JJ (1999). First Steps toward Understanding the Pathophysiologic Link between Air Pollution and Cardiac Mortality. *American M Heart Journal, 138: 804-807.*

Timonen KL, Pekkanen J (1997).Air pollution and respiratory health among children with asthmatic or cough symptoms. *American Journal of Respiratory Critical Care Medicine, 1997 Aug; 156 (2 Pt 1):546-52.*

US Census Bureau, American Fact Finder. Allegheny County, Pennsylvannia, http://factfinder.census.gov/servlet/SAFFFacts

U.S. Environmental Protection Agency (1997). National Ambient Air Quality Standards for Particulate Matter; Final Rule, 40 CFR. Part 50. Federal Register 38652, Vol. 62, No 138. Washington DC.

Verrier RL, Mittleman MA, Stone PH (2002). Air Pollution: An Insidious and Pervasive Component of Cardiac Risk. *Circulation, 106 (8): 890-892.*

Vedal S, Brauer M, White R, Petkau J (2003). Air Pollution and Daily Mortality in a City with Low Levels of Pollution. *Environmental Health Perspectives, 111 (1): 45-51.*

Vichit-Vadakan N. Ostro BD, Chestnut LG, Mills DM, Aekplakorn W, Wangwongwatana, and Panich N (2001). Air Pollution and Respiratory Symptoms: Results from Three Panel Studies in Bangkok, Thailand. *Environmental Health Perspectives, 109: Supplement 3: 381-387.*

von Klot S, Wolke G, Tuch T, Heinrich J, Dockery DW, Schwartz J, Kreyling WG, Wichmann HE, Peters A (2002). Increased asthma medication use in association with ambient fine and ultrafine particles. *European Respiratory Journal, 20: 691-702.*

Watkinson WP., Campden M J., Nolan JP., and Costa DL (2001). Cardiovascular and Systemic responses to Inhaled Pollutants in Rodents: Effects of Ozone and Particulate Matter. *Environmental Health Perspectives, 109; Supplement, 4, 539-546.*

Yeates DB, Mauderly JL (2001). Inhaled environmental/occupational irritants and allergens: mechanisms of cardiovascular and systemic response. *Environmental Health Perspectives, 109: 479-481.*

Yu O, Sheppard L, Lumley T, Koeing J, Shapiro G (2000). Effects of ambient air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP Study. *Environmental Health Perspective, 108: 1209-1214.*

Zanobetti A, Schwartz J, Gold D (2000). Are there sensitive subgroups for the effects of airborne particles? *Environmental Health Perspectives, 108 (9)*: *841-845.*

Zanobetti A, Schwartz J (2002). Cardiovascular damage by airborne particles: are diabetics more susceptible? *Epidemiology, 13: 588-592.*

Zanobetti A, Schwartz J, Samoli E (2003). The temporal pattern of respiratory and heart disease morality in response to air pollution. *Journal of the National Institute of Environmental Health Sciences, 1-29.*

Zemp E, Elsasser S, Schindler C, Kunzli N, Perruchoud AP, Domenighetti G, Medici T, Ackermann-Liebrich U, Leuenberger P, Monn C, Bolognini G, Bongard JP, Brandli O, Karrer W, Keller R, Schoni MH, Tschopp JM, Villiger B, Zellweger JP..(1999). Long-term ambient air pollution and respiratory symptoms in adults (SAPALDIA Study). *American Journal of Respiratory and Critical Care Medicine, 159:1257-1266.*