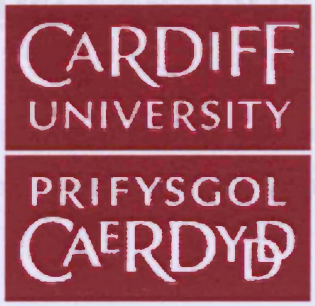

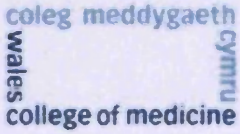

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PhD 2006

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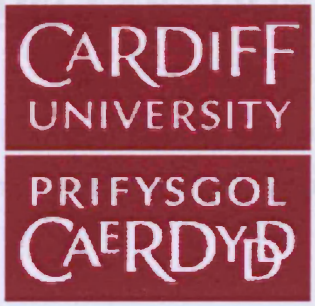

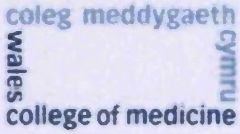

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DECLARATION

This work has not previously been accepted in substance for any degree and is not concurrently being submitted in candidature for any degree.

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Date.....13/09/06.....

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This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged by footnotes giving explicit references.

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SUMMARY

Epidemiological evidence has shown that increased levels of respirable particulate air pollution leads to adverse cardiorespiratory health effects although the exact mechanism of damage is unknown. In the UK the largest single source of respirable air particulates is road transport. Currently the background levels of respirable air particulates are measured by stationary monitoring stations. However, traffic volumes often vary considerably within a city and hotspots of densely trafficked areas may give rise to microenvironments with increased respirable particulate levels.

The primary objective of this thesis was to investigate whether a high density of local motor traffic would give rise to microenvironments with increased levels of respirable air particulates. A selection of streets in Cardiff city were allocated into exposed and control group according to traffic volumes. Levels of respirable air particulates were measured for each residential location both indoor and outdoor, and individual residents provided blood, urine, and hair samples for the analysis of trace elements, which may serve as biomarkers of exposure to air particulates from motor vehicles. Results showed that for both indoor and outdoor respirable air particulate concentrations, the levels were found to be higher in exposed areas than controls, and there was a moderately high correlation between indoor and outdoor concentrations. However, the study failed to demonstrate any differential uptake of trace elements as reflected by the lack of differences in the levels of biomarkers in the biological samples of subjects residing in different exposure areas.

A separate study was carried out to investigate whether short-term changes in respirable air particulate levels would lead to acute exacerbation of disease symptoms in individuals with asthma, chronic respiratory diseases excluding asthma, and chronic cardiac diseases. Subjects were recruited through specialist hospital outpatient clinics located in South Wales and disease specific questionnaires were sent out during different episodes of respirable particulate air pollution. Results showed that symptoms of most subjects were not affected by short-term changes in air particulate levels, although individuals with more severe asthma and cardiac disease appeared to have benefited relatively more from lower levels of respirable air particulates than those with less severe disease symptoms as well as those suffering from chronic respiratory disease.

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ABSTRACT

In the UK levels of respirable air particulates in a city are measured by one or more stationary monitoring stations. While this method provided information regarding the background levels of respirable air particulates in the sampled area, it did not take into account that hotspots of densely trafficked areas may give rise to microenvironments with increased respirable particle concentrations. Also, evidence from epidemiological studies have shown that short-term increase in the levels of respirable particles increased hospital admissions and mortality in compromised individuals suffering from chronic cardiorespiratory disease. However, relatively few studies have examined the effects of respirable air particulates on disease symptoms in subjects from the community.

This thesis was divided into two separate sections. Section 1 investigated the possible existence of microenvironments in terms of increased levels of respirable air particles caused by local traffic, and its relationship with the levels found in indoors. In addition, biomakers of exposure were also analysed to find out whether individuals residing in densely trafficked areas would result in higher levels of personal exposure and subsequently uptake of respirable air particulates. Section 2 examined the acute effects of short-term changes in the levels of respirable particulate air pollution on disease symptoms in individuals with chronic cardiorespiratory disease, using air quality data from stationary monitoring stations.

Methods: Section 1

Streets from heavily trafficked areas and from sub-urban areas with minimal traffic were chosen from the city of Cardiff and assigned to the exposed group and the control group respectively. Recruitment of subjects was carried out by sending letters to all houses in the target streets, and a permanent male resident aged 50-70yrs was selected from each participating household. A total of 123 individuals took part in the study, of which 73 were from the exposed group and 50 were from the control group. Indoor and outdoor levels of air particles were measured on the same occasion and biological samples including blood, hair, and urine were collected and analysed to study the uptake of biomarkers that may be related to exposure to respirable particles from motor vehicles.

Methods: Section 2

Individuals with asthma, chronic respiratory disease excluding asthma, and chronic cardiac disease were recruited via specialist hospital outpatient clinics in South Wales. Daily levels of particulate pollution were monitored throughout the 12-month study period through databases accessible via the Internet. Disease specific questionnaires were sent out on four separate occasions subsequent to episodes of high and normal particulate air pollution. Each questionnaire contained items extracted form validated instruments that focused on changes in symptoms, medication use, and emotional well-being. Each answer given by the subjects corresponded to a "symptoms score" and from this the magnitudes of changes in symptoms between high and normal pollution episodes were calculated.

Results: Section 1

Mean levels of outdoor air particulates between exposed and control groups were compared and tested by Independent-Samples T-Test, and the difference in median indoor levels was tested by Mann-Whiney test. In addition the relationship between indoor and outdoor particulate levels were also examined by calculating the correlation coefficient. Levels of exposure markers to motor traffic measured in biological samples provided by individual subjects were compared and the differences in medians were tested by Mann-Whitney test. The presence of a dose-response relationship was also investigated by sub-dividing the exposed group into high and medium exposure groups. Results showed that the mean outdoor level of respirable air particulates was approximately 50% higher in the exposed group than the controls ($17.5\mu g/m^3$ v $11.8\mu g/m^3$), and the median indoor level was approximately 40% higher in the exposed group than the controls ($13.2\mu g/m^3$ v $9.4\mu g/m^3$). There was a significant correlation between the levels of indoor and outdoor respirable particles ($r = 0.64$; $p<0.01$). However, no differential uptake of biomarkers that may be associated with motor traffic were found in any of the biological samples collected.

Results: Section 2

Answers of all items in the questionnaires given by each subject were converted into symptoms score. Means of symptoms score were calculated for all asthma questionnaires and the differences observed were expressed as the percentage of net

change. Because neither means nor medians could be calculated for both the cardiac and respiratory questionnaires, changes in symptoms score were evaluated by calculating the percentage of net changes, and changes in symptoms score at individual levels were also examined graphically. A sub-group of patients classified as more severe cases were chosen to find out if short-term changes in particulate levels will differentially affect individuals with more severe symptoms. Results showed that while most subjects had reported no changes in symptoms score between episodes of high and normal pollution levels, individuals suffering from more severe asthma and cardiac symptoms in overall obtained higher symptoms scores on occasions when particle concentrations were normal. In contrast, subjects with chronic respiratory disease had obtained low symptoms score throughout the study that were not greatly influenced by the levels of air pollution.

Conclusions: Section 1

Evidence obtained in the study showed that microenvironments exist within a city, based on the observation that higher levels of respirable particles were found in areas where traffic volume was high. The moderately high correlation between indoor and outdoor particle concentrations suggested that particles generated from motor vehicles outside entered the indoor environment, meaning exposure to respirable particles was higher in subjects residing within proximity to motor traffic. However, the study did not find any evidence of human uptake of exposure biomarkers, as reflected by the null findings that none of the levels of biomarkers measured in biological samples varied between different exposure groups.

Conclusions: Section 2

Results showed that the majority of patients in the study reported no changes in disease symptoms between episodes of high and normal respirable particulate air pollution. However, a subgroup of asthma and cardiac patients who suffered from more severe disease symptoms appeared to be more vulnerable to short-term increase in respirable particle concentrations, as reflected by the exacerbation of their disease symptoms during episodes of high pollution level. In contrast, symptoms reported by individuals suffering from chronic respiratory disease were generally worse than those with asthma and cardiac disease, and short-term changes in particle levels seem to have little effects on their respiratory symptoms.

AIMS AND OBJECTIVES

This thesis aimed primarily to investigate whether the levels of respirable air particulates vary within a city due to differences in local traffic volumes, and whether for individuals residing in proximity to dense traffic there was evidence of personal uptake of markers of air particulates associated with motor vehicles. Three objectives relating to this aim were:

1. To measure the levels of respirable air particulates in outdoor environments in areas with different traffic flow to investigate the possible existence of microenvironments in terms of increased levels of respirable air particulates emitted from local traffic.

2. To investigate whether indoor levels of particles were associated with the outdoor particle concentrations.

3. To examine whether individuals residing in densely trafficked microenvironments show evidence of increased biomarkers of such exposure.

A separate study examined whether short-term changes in the levels of respirable particulate air pollution, as measured by stationary air quality monitoring stations, would lead to acute exacerbations of disease symptoms in chronically ill individuals. The objectives of this study were to detect any changes in an individual's disease symptoms, medication use, and emotional well-being between episodes of high and normal pollution, using questionnaires that were specific to asthma, chronic respiratory disease excluding asthma, and chronic cardiac disease.

FIGURE LISTING

TABLE LISTING

CHAPTER 1 - INTRODUCTION
ENVIRONMENTAL AIR POLLUTION

1.1 History of air pollution and pollution control in the UK

The industrial revolution in the late 18th century and early 19th century brought major technological, socio-economic and cultural changes to Europe. Production was increased significantly through the use of fossil fuels as energy sources, but at the same time also brought in a new problem - air pollution. Large numbers of factories built within cities attracted workers and cities became densely populated. Soot and toxic gases from factory chimneys and residential burning of solid fuel for cooking and heating severely polluted the atmosphere.

In the last half of the twentieth century, several acute episodes of smog alerted us the danger of air pollution and consequently led to the birth of epidemiological research on air pollution and the introduction of legislated control strategies. One of the first documented episode of air pollution happened in the Mueuse Valley in Belgium between 1 December and 5 December 1930. During that period, high levels of sulphur dioxide (SO_2), sulphuric acid mists, and fluoride gases released from steel mills, coke ovens, foundries, and smelters in the region were trapped in the atmosphere by stable atmospheric conditions. This led to the death of more than 60 people, which was more than 10 times the normal mortality rate of that area [Nemery *et al* 2001]. Later in the United Sates between 27 October and 30 October 1948, an intense meteorological inversion settled on the valley of Donora in southwestern Pennsylvania. Fuelled by air pollutants released from local industries and coal burning, 20 people died within the week and one-third of the population of 14,000 required medical attention [Schrenk *et al* 1949]. The fog of December 1952 in London, or "The Great Smog", was one of the most infamous episodes of air pollution which ever took place and led to the premature deaths of thousands of people [Met Office 2005]. The term "smog", being a portmanteau word meaning "fog intensified by smoke" was coined almost half a century earlier by HA Des Voeux, who first used it in 1905 to describe the conditions of sooty fog that occurred all too often over British urban areas. During the early hours on 5 December 1952 nothing was unusual except the cold weather that had existed for some weeks. However when nightfall came, a thick layer of fog appeared and visibility dropped to a few meters. In central London, the visibility remained

below 500 meters continuously for 114 hours and below 50 meters continuously for 48 hours. This fog was triggered by a natural phenomenon called temperature inversion, which happens when the night time temperature drops and cold air close to the ground is trapped by a layer of warm air above. Normally this can be dispersed by the morning sun but in December 1952 the accumulation of smoke close to the ground was so great that the sun never broke through. As a result pollutants emitted from local industries and residential coal burning were trapped in the atmosphere with the stagnant layer of air. This "pea soup-like" yellowish-black colour smog filled with black soot, particles, and SO_2 stayed for 5 days until 10 December, when eventually winds from the west blew it down the Thames Estuary and out into the North Sea. The recorded levels of smoke and SO_2 in the air were approximately 10 and 12 times higher respectively than the normal levels recorded at that period. It was estimated that on each day during the foggy period 1,000 tonnes of smoke particles, 2,000 tonnes of carbon dioxide, 140 tonnes of hydrochloric acid and 14 tonnes of fluorine compounds were released into the atmosphere. In addition, and perhaps most dangerously, 370 tonnes of SO_2 were converted into 800 tonnes of sulphuric acid. The destruction caused by this episode of smog was devastating – road, rail, and air transport were brought to a stand still and theatre performances had to be cancelled. But most importantly the smog had led to a total death toll of 12,000 people and caused illness to many others. The majority of the deaths occurred in people suffering from chronic respiratory and cardiovascular conditions. In response to this tragedy the British government legislated the Clean Air Act in 1956 and produced legislation again in 1968. Both were later revised and combined to form the Clean Air Act 1993, which covered a number of air pollution control strategies including the control of chimney heights, prohibition of dark smoke emission from chimneys and industrial premises, as well as the declaration of smoke control areas by local authorities. However, air pollution control strategies did not stop here and more legislation and regulations were introduced in the coming years as shown in table1.1. Thanks to the introduction of the Clean Air Acts and other legislations on air pollution control, emission of pollutants has been largely reduced since the 1952 London Smog. Nowadays, episodes of serious air pollution similar to the Great Smog are unlikely to occur again in the UK. However in 1991 another episode of London smog took place between 12 and 15 December. Although not as severe as the 1952 London smog it was still responsible for an estimated 160 excess deaths due to cardiorespiratory

complications. Because there were no official figures recorded for the non-fatal cases, the total effects it caused on human health was unknown. The 1991 London smog was a warning sign of the potential damage air pollution can cause despite the implementations of active and tightened pollution control strategies.

Motor Vehicles Regulation	1973	Regulation of motor vehicles constructions and usage
Control of Air Pollution Act	1974	Regulation of motor fuel composition and limited the sulphur content in fuel oil
Air Quality Standards Regulation	1989	EU regulations for air pollutants
Environmental Protection Act	1990	Integrated control for significant industrial sources of pollution. Inclusion of small emission sources under control by local authorities
The Road Vehicle Regulation	1991	Inclusion of carbon monoxide and hydrocarbons emissions tests in the MOT test for petrol cars and light goods vehicles
The Environmental Act	1995	To improve local air quality managements. Publication of National Strategy for setting air quality standards and targets for the most concerned pollutants
The National Air Quality Strategy	1997	Commitments to achieve new air quality objectives in the UK, reviewed periodically
The National Air Quality Strategy for England, Scotland, Wales, and Northern Ireland	2000	Second National Air Quality Strategy published with new air quality objectives for local authorities

Table 1.1: List of air pollution control strategies introduced in the UK after the Clean Air Act 1968.

Since the introduction of the Clean Air Acts and other legislations, the type of emissions that caused air pollution has changed considerably. While black smoke and SO_2 from coal combustion for industrial and domestic usage have been significantly

reduced, a six-fold increase in road vehicle number between 1955 and 2001 means that emissions from the transport sector have huge impact on urban air quality. The main pollutants of concern are nitrogen oxides, respirable air particles, carbon monoxide, and volatile organic compounds. In addition, despite the use of cleaner fuel such as natural gas for power generation, the ever increasing demand in electricity usage and the dependence on fossil fuel means that the industrial sector still contributes a significant proportion of these air pollutants nowadays.

Each year the National Atmospheric Emission Inventory (NAEI), which is co-funded by the Department for Environment, Food and Rural Affairs (DEFRA), The National Assembly for Wales, The Scottish Executive, and the Department of Environment, Northern Ireland, compiles estimates of annual atmospheric emissions in the UK from a wide range of sources including those from the industrial, residential, and road transport sectors. These pollutants are divided into various groups including greenhouse gases, regional pollutants leading to acid deposition and photochemical pollution, persistent organic pollutants and other toxic pollutants such as heavy metals. Amongst them, the National Air Quality Strategy (NAQS) has set national objective standards under the Environment Act 1995 for several key pollutants including benzene, 1,3-butadiene, carbon monoxide, lead, nitrogen dioxide, air particulates, sulphur dioxide, and ozone to be met by Dec 2005. For "hotspots" of air pollution areas in which air quality standards objectives are unlikely to be achieved by the end of 2005, the corresponding local authorities are required to designate Air Quality Management Areas (AQMA) and set up an Air Quality Action Plan (AQAP) to assess, monitor, and control the air pollution levels in those target areas. The city of Cardiff currently has 4 declared AQMA zones dedicated to reduce the levels of nitrogen dioxide in accordance to the NAQS objectives.

Levels of air pollutants in the UK are monitored by a network of over 1,300 national air quality monitoring stations set up across the country. One hundred and twenty of these sites are fully automatic and provide hourly data on several key pollutants of interest, while the non-automatic sites measure mean concentrations over a specified timeframe which is typically a week or a month. Together they provide invaluable information to build a larger picture of the levels and the impacts of air pollution in the UK. The type of pollutants being monitored varies from site to site but may

include one or more of the following: respirable particles, nitrogen dioxide, ozone, sulphur dioxide, carbon monoxide, metals, volatile organic compounds and other toxic air pollutants.

In the automatic monitoring stations respirable particles are measured by TEOM (tapered element oscillating microbalance). Briefly, the TEOM draws air from its surrounding environment through a size-specific inlet head onto an oscillating quartz tube with a known frequency. Particles present in the air will change the frequency of oscillation of the quartz tube, which is proportional to the changes in the mass of the particles collected. Air drawn into the TEOM is heated to 50°C in order to remove water vapour which may confound the result. Inevitably, this causes the loss of some volatile compounds which are often attached on particle surfaces. Gaseous pollutants are measured by optical methods such as ultraviolet (UV) and infrared (IR).

1.2 Common air pollutants

This section summaries some of the most commonly seen air pollutants in the UK, together with their physical/chemical properties, effects on the environment/human health, and emission sources and trends.

1.2.1 Gaseous pollutants

Carbon Monoxide

Carbon monoxide (CO) is a colourless and odourless gas formed from incomplete fuel-combustion and is of concern mainly because of its effect on human health and its role in tropospheric ozone formation. CO is a very dangerous gas because once breathed in it reacts strongly with the oxygen-carrying protein haemoglobin, thereby preventing oxygen from binding to the red cells and causing oxygen starvation throughout the body. Excess inhalation will lead to hypoxic injury, neurological damage, and possibly death. Even at low levels CO will result in the decreased exercise capacity in individuals with ischaemic heart disease and lead to a lower threshold for ischaemia. In the environment, CO indirectly contributes towards the formation of tropospheric ozone by reacting with hydroxyl radicals (OH) in the atmosphere which would otherwise remove other pollutants in the air. Through

natural processes in the atmosphere CO is eventually oxidised into carbon dioxide (CO_2) which is one of the main constituents of greenhouse effects.

Road transport and in particular petrol driven vehicles is the most important source of CO in the UK. Despite a slight reduction in CO emission from road transport which was seen between 1970 and 1990, and more significantly from the early 1990s, it was still the single largest source of CO emission accounting for 59% (1916 kilotonnes) of the total UK emission in 2002. Other emission sources of CO are small compared with transport, they include industrial (12%) and domestic (7%) fuel combustions, and power generation (2%). Overall, CO emission in the UK is decreasing and there was a 56% reduction observed in 2002 compare with the emission level in 1990, mainly due to reduction in emissions from the road transport sector after the introduction of catalytic converters.

Nitrogen oxide

The term nitrogen oxide (NO_x) is imprecise and can be used to refer to any of the oxides of nitrogen. Many of the nitrogen oxides are colourless and odourless. However, one common pollutant, nitrogen dioxide (NO_2) along with particles in the air can often be seen as a reddish-brown layer of smog over many urban areas and impair visibility. NO_x is also a precursor of acid rain that will contaminate the environment and damage plants and buildings. One member of the NO_x, Nitrous oxide (N_2O) is a greenhouse gas that contributes towards global warming. The formation of smog by NO_x and its association with air particulates can lead to a number of adverse health effects including reduction in lung functions, lung tissue damage, and worsen symptoms of individuals who suffer from chronic cardiorespiratory diseases.

Road transport is the most significant source of NO_x, with approximately one-third of the emissions deriving from major sections of roads. In 2002, 45% of the total UK emission equivalent to 711 megatonnes of NO_x was contributed by motor traffic alone. Because NO_x emission is the greatest when travelling at high speeds, high levels of NO_x are measured along motorways and major roads. In urban areas, high volumes of motor traffic together with residential and commercial combustions released a significant amount of NO_x into the atmosphere. Power generation is the second largest source of NO_x in the UK (24% in 2002). Industrial combustion

contributed approximately 10% to total UK emissions in 2002. Overall, UK emissions of NO_x have fallen significantly from 2.5 megatonnes to 1.6 megatonnes in 2002, representing a 43% reduction in the 1990 emissions estimate. This was primarily due to emission control in the road transport sector and increased use of other fuels for power generation.

Sulphur dioxide

Sulphur dioxide (SO_2) is a colourless gas with a smell of burning sulphur. High concentrations of SO_2 can result in temporary breathing impairment for asthmatics who are active outdoors. Short-term exposures of asthmatic individuals to elevated SO_2 levels during moderate activity may result in breathing difficulties that can be accompanied by symptoms such as wheezing, chest tightness, or shortness of breath. In conjunction with high levels of air particulate it may lead to the exacerbation of respiratory and cardiovascular symptoms of susceptible groups.

In the UK the largest contribution to SO_2 emissions is from power generation and accounted for 68% (680 kilotonnes) of the total emission in 2002. Historically coal combustion has been the most important source and estimation of SO_2 emissions was directly proportional to the sulphur content of coal. The increase in the use of nuclear energy and gas for power generation has led to a gradual decline in SO_2 emission in the UK. Industrial combustion of coal and oil, as well as some refinery processes and the production of sulphur-related chemicals contributed 149 kilotonnes (15%) of SO_2 released in 2002. In contrast, SO_2 emission from road transport is relatively insignificant and accounted for less than 1% of the total emission in 2002. Overall, UK emissions of SO_2 have fallen from 3.72 megatonnes in 1990 to 1 megatonne in 2002, representing a decrease of 73%. This was a result of decreasing use of coal in favour of cleaner fuel in power generation as well as in the industrial and residential sectors.

Tropospheric ozone

Ozone (O3) is a gas composed of three oxygen atoms and is a key constituent of the troposphere, which is the lowermost portion of the atmosphere where greenhouse effect occurs. O_3 is not directly emitted by motor vehicles or industrial processes and has therefore no significant anthropogenic sources. Instead, it is created by chemical

reactions between NO_x, CO, and volatile organic compounds in the presence of sunlight. Ozone occurs naturally in the stratosphere approximately 10 to 30 miles above the earth's surface and forms a layer to absorb biologically harmful ultraviolet (UV) radiation from the Sun. However, at ground level ozone contributes towards the formation of smog. The health effects of ozone include lung airways irritation, asthma exacerbation, reduced lung functions, and increase susceptibility to respiratory illnesses such as pneumonia and bronchitis. Repeated exposure to ozone pollution can also lead to permanent lung damage.

1.2.2 Volatile organic compounds

Volatile organic compounds (VOC) are organic chemical compounds that have a high tendency to evaporate under normal conditions. Examples include aldehydes, ketones, and hydrocarbons. Some of the VOC are involved in the formation of ozone and while some others are capable of causing adverse health effects in humans such as benzene and 1,3-butadiene.

When estimating the national emissions of VOC, NAEI measures methane separately from the other members of VOC and as a result they are referred as non-methane volatile organic compounds (NMVOC). Unlike SO_2 and NO_x in which the contribution from combustion is much higher, only 22% (284 kilotonnes) of the NMVOC emissions arose from combustion sources in 2002. The largest sources of NMVOC in the UK were solvent production and solvent use in industrial and domestic applications. NMVOC are mainly released from the chemical industry, petroleum refining, and food and drink manufacture as well as minor sources such as iron and steel production and road construction. Road transport is currently responsible for 16% of the national NMVOC emissions, equivalent to 171 kilotonnes in 2002. NMVOC emission rate is increased when vehicles are idle or travelling at low speed, which is reflected by the higher concentrations of the pollutant in urban major roads than on high-speed motorways. Overall, UK emissions of NMVOC have decreased from 2.6 megatonnes in 1990 to 1.4 megatonnes in 2002, representing a 46% reduction. The observed decrease arose primarily from the road transport and industrial sectors.

Benzene

Benzene (C_6H_6) is classified as VOC and is a colourless flammable liquid with a sweet, pleasant smell. It is carcinogenic and has been shown to increase the risk of leukaemia development in occupationally exposed individuals [Glass *et al* 2003] and caused DNA damage in animal model [Lee *et al* 2005, Vestergaard *et al* 2002].

Benzene is released from petroleum products via combustion and also evaporation because it is a component of petrol. The road transport sector is the largest source of benzene emission in the UK and accounted for approximately 33% of the 2002 emission estimate total. At lower speeds motor vehicles release relatively higher levels of benzene thus higher emission densities can be found in densely populated areas. Benzene escaped during its manufacture and use in the chemical industry is also one of the major sources of emission (16% in 2002). Overall, benzene emissions have decreased by 75% between 1990 and 2002, giving an emission of 13.5 kilotonnes in 2002. This was mainly due to the reduced emissions from road transport after the introduction of catalytic converters and the decreased content of benzene in petrol.

1,3-butadiene

1,3-butadiene (C_4H_6) is classified as VOC and is a colourless gas with a mildly aromatic odour. Its ability to damage DNA means that it is a potent carcinogen, i.e. capable of causing cancers, as demonstrated in the increased risks of cancer in both occupational exposure studies and animal experiments [EPA 2002]. Having said that, the risk of adverse impact caused by the atmospheric concentrations of 1,3-butadiene seen in the UK is considered to be acceptably small [NAEI 2004].

Similar to benzene, 1,3-butadiene is released from the combustion of petroleum products and its manufacture and use in the chemical industry. However, because 1,3-butadiene is not present in petrol but rather a by-product of combustion, it is therefore not present in road transport evaporative emissions. In the UK the single largest source of 1,3-butadiene is road transport which contributed 75% of the total emission in 2002. As with benzene, the introduction of catalytic converters has a significant impact on the emissions from the road transport sector. Emission of 1,3-butadiene from its manufacture and usage is relatively small (8% in 2002) in contrast to motor

traffic emissions. Overall, emission of 1,3-butadiene has reduced by 73% between 1990 and 2002.

Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAH) are organic chemical compounds that consist of fused rings formed entirely from carbon and hydrogen. They are classified as VOC and are produced from incomplete combustion of carbon-based fuels. There are over 100 species of PAH identified and some are known to be carcinogenic in nature. A dedicated section on PAH can be found in chapter 1.4.

1.2.3 Heavy metals

Heavy metals are defined as elements between copper and bismuth on the periodic table of elements, or more strictly as those metals heavier than the rare earth metals. Living organisms require trace amounts of some heavy metals such as copper and zinc but excessive levels can cause damage to health. Some heavy metals including mercury, lead, and cadmium are not required by living organisms and their accumulation in the bodies of mammals can cause serious health issues. The health effects of each heavy metal are different. Some are able to cause minor and short-term effects such as irritations of the respiratory tract caused by cadmium, copper, and selenium. However some can cause severe and long-term health effects such as damage to the central nervous system by mercury and lead. In some cases prolonged exposure to heavy metals such as arsenic and nickel can also increase the risks of cancer. The NAEI currently reports emissions of nine heavy metals in the UK including arsenic, cadmium, copper, lead, mercury, nickel, selenium, tin, and zinc. In addition to the heavy metals, four other metals including beryllium, chromium, manganese, and vanadium are also monitored.

Metal emissions arise from a number of different sources, but in general fuel combustion and certain industrial processes that produce dust are the main contributors. In the case of combustion, metals are emitted either as vapour or particles or both. Volatile metals such as mercury and selenium are mostly emitted as vapour. Whereas metals such as cadmium and lead are emitted as both with some of the vapour condensing onto ash particles. Other metals such as chromium do not vaporise and may be emitted in ash particles. Metal emissions can be reduced by

cleaning equipment which removes particulates from waste gases. This abatement equipment can be fitted to large coal-fired industrial boilers and power station boilers and also industrial processes which produce large amounts of dust. Table 1.2 below shows the annual national emission estimates of various metals in 2002, and the percentage of which were emitted from road transport.

		Total UK emission 2002 (tonnes)	Emission from road transport
Heavy metals	Arsenic	24	0%
	Cadmium	4.5	4%
	Copper	50	<1%
	Lead	162	1%
	Mercury	8	0%
	Nickel	98	1%
	Selenium	32	<1%
	Tin*	65	1%
	Zinc	583	2%
Non-heavy metals	Beryllium*	15	36%
	Chromium	44.8	<1%
	Manganese	232	no data
	Vanadium	161	<1%

* Accuracies on these data are uncertain.

Table 1.2: Estimated metal emissions in the UK, 2002 [NAEI 2004].

1.2.4 Particulate matter

Particulate matter (PM) is a complex mixture of extremely small particles or liquid droplets. Particulate pollution is made up of a number of components such as acids, organic chemicals, metals, and soil or dust particles. Emission sources of air particulates are wide and they can be generated naturally such as abrasion, sea salt, forest fires, and anthropogenically such as road traffic, power generation, and industrial processes. Health effects of air particulates are well documented and there is a large amount of evidence relating exposure to elevated levels of air particulates and acute exacerbation of cardiorespiratory symptoms, increased medication use as well as increased number of deaths. Studies carried out in the United States also

demonstrated the chronic health effects of long-term exposure to airborne particles including cancer.

1.3 Particulate air pollutants

1.3.1 Physical properties and lung deposition of air particulates

Air particulates have diverse physical and chemical properties. These particles are typically very small and can be a few nanometers (nm) in diameter to 100 or more micrometers (μm). Particles have irregular shapes and their aerodynamic properties determine how they are transported in the air and how far they can penetrate into the respiratory system. The aerodynamic behaviour is expressed in terms of the diameter of an idealised sphere, and the sampling and description of particles are based on their aerodynamic diameter. Because the potential for particles to cause health effects is related to size, therefore it is important to define the size of the particles that are to be measured with a universal standard. One of the standardised methods is the International Standard IS 7708 which comprises four main fractions and are summarised in table 1.3 below.

IS 7708 standard	Definition	Median aerodynamic diameter
Inhalable fraction	The mass fraction of total airborne particles which is inhaled through the nose and/or mouth	>10μm
Thoracic fraction	The mass fraction of inhaled particles penetrating the respiratory system beyond the larynx	10μm
Respirable fraction	The mass fraction of inhaled particles which penetrates to the unciliated airways of the lungs, i.e. alveolar region	4μm
High risk respirable fraction	The respirable fraction for the sick and infirm, or children	2.5μm

Table 1.3: IS 7708 definitions of different airborne particle sizes

In addition to the IS 7708 standards, there is also the US Environmental Protection Agency (USEPA) definition of the thoracic aerosol fraction known as PM_{10}. It is defined as the particulate fractions with a median aerodynamic diameter of less than 10μm, and with a 50% efficiency when sampled by a PM_{10} sampling device. Strictly speaking PM_{10} is slightly different from the ISO thoracic fraction due to the differences in the upper cut-off size, although in practice such difference is not significant. Moreover, USEPA also has a definition of particle size equivalent to the high risk respirable fraction and is known as $PM_{2.5}$ (particulate matters with a median aerodynamic diameter of less than 2.5μm). This would separate the larger particles that are generated mostly from natural sources from the finer particles of anthropogenic origin.

Generally, air particulates are often being referred to as coarse, fine, and ultrafine – coarse particles include those that are within PM_{10} with a size ranging from 2.5-10μm. On the other hand, $PM_{2.5}$ is known as the fine particles and contains smaller particles with a size up to 2.5μm. The particles in the fine fraction which are smaller than 0.1μm are called ultrafine particles. Table 1.4 summarises various particle sizes under different definitions, and figure 1.1 shows a graphical comparison of particles with different sizes in contrast to a human hair.

	Median aerodynamic diameter	IS 7708	USEPA
Coarse	2.5 - 10μm	Thoracic fraction	PM_{10}
Fine	0.1 - 2.5μm	High risk respirable fraction	$PM_{2.5}$
Ultrafine	<0.1μm		$PM_{0.1}$

Table 1.4: Sizes of air particulates under different definitions.

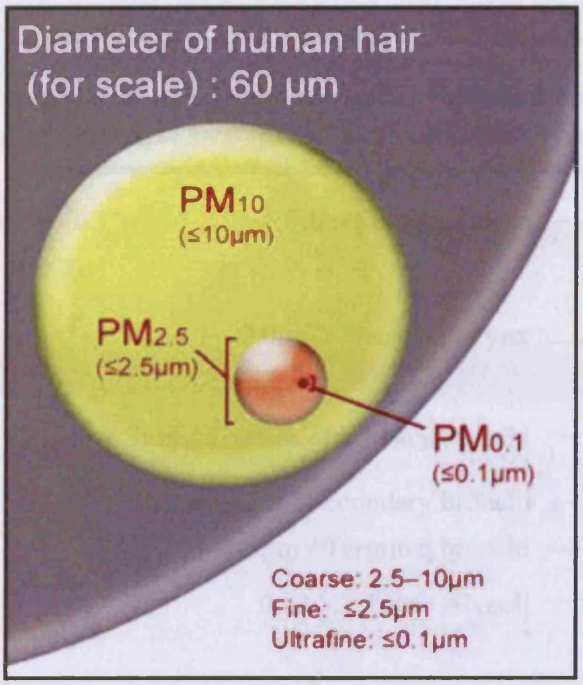


Figure 1.1: Comparisons between different particle sizes and a strand of human hair *(Source: www.greenfacts.org).*

Deposition of particles within the respiratory system is mainly determined by particle size, although other factors such as breathing pattern, airway diameter, and the anatomy of the nasal, oral, and pharyngeal areas also play important roles. Generally, the smaller the particle size the further it can penetrate into the lungs, as seen in figure 1.2 which shows the deposition of particles of different sizes in various regions within the respiratory system. Once inhaled, particles are removed from the lungs by several mechanisms. For larger particles deposited in the upper nasopharyngeal areas, clearance is often by entrapment in the mucous lining and removed either by reflex responses, such as sneezing and coughing, or through the continuous movement of mucus up the mucociliary escalator, where the particles are then swallowed or spit out. For smaller particles that penetrated as far as the terminal bronchioles and alveoli, clearance is carried out primarily by phagocytosis by pulmonary macrophages. Some particles may actually be solubilised by body fluids and absorbed into the bloodstream. Deposition and clearance of particles in the body can be affected by smoking or the presence of an underlying respiratory condition such as chronic obstructive pulmonary disease (COPD), which increases particle deposition in the lungs and reduces the rate and efficiency of the mucociliary escalator [Lourenço *et al* 1971, Anderson *et al* 1990, Svartengren *et al* 1996, Brown *et al* 2002].

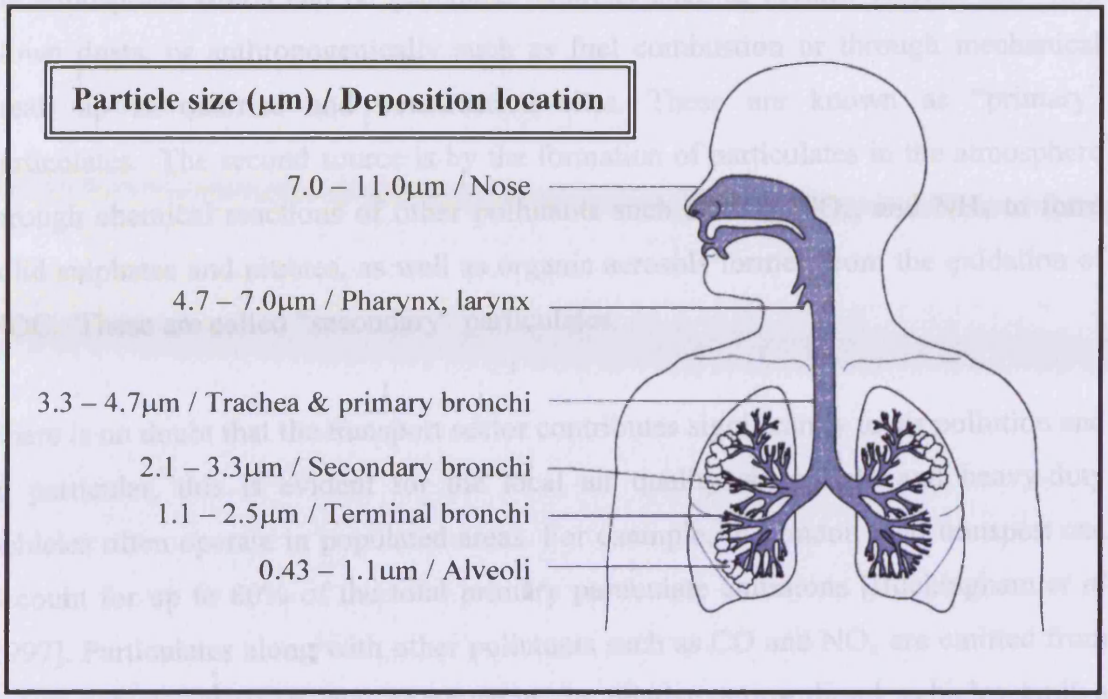


Figure 1.2: Particle deposition by size distribution in various regions of the respiratory system *(Source: Rosenstock et al. Textbook of clinical occupational and environmental medicine, 2nd edition. Philadelphia, USA: Elsevier Saunders, 2005).*

For many years the levels of ambient air particulates have been measured by the levels of black smoke. Briefly, black smoke estimates the levels of air particulates by a simple non-gravimetric method in which air is sampled through a filter and the resulting blackening measured. The method was calibrated for domestic coal smoke when most of the emissions came from coal combustion in the past. However, smoke from different sources has a different blackening effect and so there is no simple relationship between black smoke and the mass of particulate emissions. Although in some places black smoke is still being used an indicator of particulate levels nowadays, its use is limited and has been generally replaced by PM_{10} and $PM_{2.5}$. Sometimes ambient air particles are also measured as TSP, or total suspended particulates, which measures the total mass of airborne particles irrespective of their sizes. The lack of size-specificity means that TSP is less favourable to be used for air pollution studies.

1.3.2 Sources, formation, and fate of air particulates

Air particulates found in the atmosphere arise from a variety of sources and can be classified into two general groups. The first is the direct emission of particulates into

the atmosphere which can be generated naturally such as surface erosion and wind blown dusts, or anthropogenically such as fuel combustion or through mechanical break up in quarries and construction sites. These are known as "primary" particulates. The second source is by the formation of particulates in the atmosphere through chemical reactions of other pollutants such as SO_2, NO_x, and NH_4 to form solid sulphates and nitrates, as well as organic aerosols formed from the oxidation of VOC. These are called "secondary" particulates.

There is no doubt that the transport sector contributes significantly to air pollution and in particular, this is evident for the local air quality since light and heavy-duty vehicles often operate in populated areas. For example, in London road transport can account for up to 80% of the total primary particulate emissions [Buckingham *et al* 1997]. Particulates along with other pollutants such as CO and NO_x are emitted from motor vehicles through fuel combustion. In relative terms diesel vehicles emit a greater concentration of particles per vehicle kilometre than those running on petrol [NAEI 2004]. Concerns have been raised that modern diesel engines, which emit a low mass of particles, have high emission of particles in the nanometer range that are capable of reaching the deepest regions of the lungs and have relatively large surface areas [AQEG 2005]. Despite this the market penetration for light duty diesel cars has been increasing in most European market and has reached over 30% in 2001 [Ahlvik 2002]. A number of factors determine the emission levels of motor vehicles, including the age of the vehicle, condition of the engine, load, driving speed, operating temperature, and fuel quality. In Europe the introduction of catalytic converters in all new cars with spark ignition engines in January 1993 has contributed towards the decreased levels of CO, NO_x and PAH. At optimal operating conditions the main emissions from an engine is water and CO_2, although CO_2 itself is also of great concerns as a greenhouse gas. However, in urban areas the predominance of short journeys and cold starts as well as slow or idle engine operating speed rendered the catalyst less efficient. In 2000 the Committee on the Medical Effects of Air Pollutants (COMEAP) discussed the relative merits of diesel and petrol light vehicles in terms of health-damaging pollutants [COMEAP 2000]. The committee concluded that the comparison between the two fuel types was difficult and they were unable to provide a definite answer as to the preferability of diesel or petrol fuel on health grounds, but they suggested that concerns about the effects of particles on health in urban areas

seem to be more in favour towards petrol. Particles are also released through brake and tyre wear. It has been estimated that the wear rate of brake linings for passenger cars to be around 1-9mg/km and for heavy duty vehicles around 20-40mg/km [USEPA 1995, TNO 1997]. For tyre wear the typical wear rates have been reported to be 10-90mg/km per tyre [AQEG 2005]. In addition, although not strictly caused by traffic, turbulences of moving motor vehicles also cause settled dust on road surfaces to re-entrain. These dust particles are often generated from erosion of road surfaces, exhaust emissions, and brake and tyre wear which contributed a significant proportion of air particulates in the atmosphere.

In the industrial sector, air particulates are formed in the production processes of metals, cement, lime, coke, and chemicals, and released during bulk handling of dusty materials, construction, mining and quarrying. Emissions from these sources are difficult to quantify due to the contribution of the so-called "fugitive emissions", meaning those diffused emissions which are released directly into the atmosphere from a process rather than being collected in a controlled manner and then vented to the atmosphere. Usually a major fraction of the particles from these sources is larger than 10μm but the large quantities emitted ensure that the fraction less than 10μm is still substantial. In contrast particles emitted from combustion are much smaller in size. Burning of fossil fuels including coal, wood, gas, and oil in both industries and domestic sectors all contributed significantly toward the total PM_{10} emission in UK. Note that although the use of coal for domestic combustion has been restricted by the Clean Air Acts, domestic coal is still being used in Northern Ireland and certain smaller towns and villages.

The mechanism of how air particulates are formed is crucial in determining particle size. The finest particles within 1-10nm in size are often result from the condensation of small numbers of involatile molecules formed in combustion processes or in evaporation from hot surfaces. This mechanism is known as nucleation. For slightly larger particles within the range of 0.05-2μm, they are often formed by the accumulation mode in which the finest particles adhere to form larger droplets or long chains of particles. Finally the coarsest particles with the size of ~10μm-100μm are often produced through mechanical break-up of solids and liquids. In a mixture of air

particulates, the greatest numbers of particles are those formed by nucleation, although they only represent a small fraction of the total mass due to their small sizes.

Particles in the atmosphere are removed in two ways known as dry deposition and wet deposition. In dry deposition particles are retained by surface forces and remain on the ground, whereas in wet depositions they are removed from the atmosphere through precipitation. In the UK, about 7% of the 1μm size particles are removed by wet deposition per day, and 15-30% for those 3-5μm or larger [Harrison *et al* 1996]. Particles in the nucleation mode are often very short-lived (~10mins) because they rapidly adhere to other particles and grow into the accumulation size range. Coarse particles are short-lived (10-20hrs) and are likely to travel distances from a few metres to a few hundred kilometres depending on their size and wind speed. Finally, particles formed in the accumulation mode are long-lived (~10days) because both dry and wet depositions are least efficient in this size region. They are also capable of travelling long distances in the range of several thousand km.

1.3.3 Chemical constituents of air particulates

Apart from their size range, the complexity of air particulates is also demonstrated by their diverse chemical compositions. As discussed previously, specific sources give rise to particles of a certain size range, therefore the chemical constituents of particles in certain extent are also related to its size. For example, suphate produced from the oxidation of SO_2 is typically present in fine particles, whereas silicon from the resuspension of soil and surface dust is normally found in coarse particles. However, particles of different sources can sometimes be internally mixed via the process of condensation and coagulation, and give rise to a mixture of particles containing components that have arisen from different sources. Table 1.5 below shows the typical components that are often found in particulates. The list is divided into major and minor components, with the former comprising at least a few percent of the mass of particles.

	Component	Source
Major component	***Sulphate***	Atmospheric oxidation of SO_2
	Nitrate	Atmospheric oxidation of NO_x
	Ammonium	Atmospheric oxidation of NH_3
	Sodium and chloride	Sea salt
	Elemental carbon	High temperature combustion of fossil and biomass fuels
	Organic carbon	Automotive, industrial, or oxidation of volatile organic compounds
	Mineral components	Earth's crust or anthropogenic activities such as quarrying and construction
	Water	Taken up by the water soluble components of particles
Minor component	***Trace metals***	Combustion of fuel and metallurgical processes
	Trace organic compounds	Combustion and oxidation of organic compounds

Table 1.5: Typical components found in air particulates and their sources.

1.3.4 Emission trends of air particulates in the UK

Each year NAEI measures the emission sources of PM_{10} in the UK. Figure 1.3 shows the annual emission of PM_{10} in the UK since 1970 [NAEI 2004]. Overall emissions of PM_{10} in the UK have declined since 1970, and between 1990 and 2002 the total national PM_{10} emission has declined by 48%, measured as 160 kilotonnes in 2002. A trend away from coal use has also been seen, in which in 1970 over 65% of the total PM_{10} emission was from the use of solid fuel and approximately 16% from the use of petroleum. Over the years this trend has changed and in 2002 the burning of coal only contributed approximately 23% of the total emission, whereas emissions from petroleum was increased to 27%. The trend reflects the reduction in coal use especially in the domestic setting, and replacement by other fuel type such as gas.

Domestic burning of coal contributed more than 40% of the total PM_{10} emission in UK in 1970 and released 222 kilotonnes of PM_{10} into the atmosphere. In 1980 this was reduced by more than 50% to 103 kilotonnes, and further reduced to 52 kilotonnes in 1990. Since then the level of PM_{10} emission by domestic burning of coal has remained at around 30 kilotonnes per year. Similarly in the industrial sector, the reduced use of coal and the installation of particles abatement equipment has led to the reduction in PM_{10} emission caused by industrial combustion processes. Emissions from electricity generation have also recently been declining since 1991 despite a significant growth in the electricity generated between 1970 and 2002. This is due to the move away from coal to natural gas and nuclear power for electricity generation and to improvements in the performance of particulate abatement plant at coal-fired power stations. Also the installation of flue gas desulphurisation plants at two power stations in Drax and Ratcliffe in 1994 have reduced particulate emissions further. Emissions from road transport have not seen any significant changes in the past 30 years or so in terms of total mass, but the contribution to the total emission has increased with time due to other sectors decreasing. The contribution to the total UK emission has risen from 8% in 1970 to 24% in 2002. The main source of road transport emissions is exhaust from diesel engine vehicles. Emissions from diesel vehicles have been growing due to the increased number of heavy duty vehicles and the move towards more diesel cars. Since around 1992, however, emissions from diesel vehicles have been decreasing due to the penetration of new vehicles meeting tighter PM_{10} emission regulations, such as the Euro Standards for diesel vehicles introduced in 1992. Although the resuspension of road dust is not monitored routinely, an estimation based on the deposition of primary particles from all UK sources, including vehicle tailpipes and from brake and tyre wear that are returned to the air from the turbulence of passing vehicles has been provided by NAEI (table 1.6). In 1970 approximately 8.2 kilotonnes of resuspended dust was caused by the turbulences of passing motor vehicles. Since then the trend has been increasing and accounted for 20.3 kilotonnes in 2002, which reflects the increased number of road vehicles in the UK in the past 30 years. Among the non-combustion and non-transport sources, the major emissions are from industrial processes, the most important of which is quarrying whose emission rates have remained fairly constant. Other industrial processes, including the manufacture of steel, cement, lime, coke, and

primary and secondary non-ferrous metals, are collectively important sources of air particulates although emissions from individual sectors are relatively insignificant.

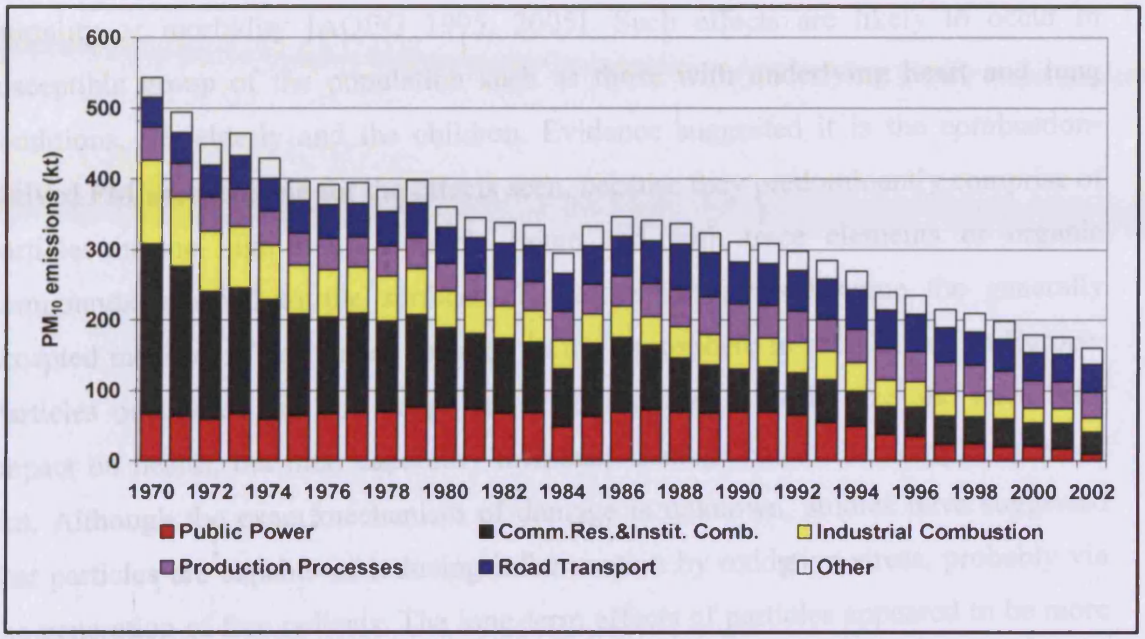


Figure 1.3: Time-series of UK annual PM_{10} emissions by category, 1970, 1980, 1990 & 1996-2002 *(Source: NAEI)*.

Year	PM_{10} resuspension (kilotonnes)
1970	8.2
1980	11.2
1990	16.9
1996	18.2
1997	18.6
1998	19.0
1999	19.3
2000	19.3
2001	19.6
2002	20.3

Table 1.6: UK PM_{10} emission estimates from resuspension, 1970, 1980, 1990 & 1996-2002.

1.3.5 Health impact of air particulates

The epidemiological evidence of the effects of air particulates shows good correlation between short-term and long-term exposure to PM_{10} and increased cardiorespiratory mortality or morbidity [AQEG 1995, 2005]. Such effects are likely to occur in susceptible group of the population such as those with underlying heart and lung conditions, the elderly and the children. Evidence suggested it is the combustion-derived PM_{10} responsible for the effects seen, because they predominantly comprise of particles in the high risk respirable range and with trace elements or organic compounds attached to the surfaces. Therefore PM_{10} has become the generally accepted measure of particulate material in the atmosphere in the UK and in Europe. Particles outside of this size range are relatively very large in size and have little impact on health, but their capability to induce damage cannot be completely ruled out. Although the exact mechanism of damage is unknown, studies have suggested that particles are capable of inducing inflammation by oxidative stress, probably via the generation of free radicals. The long-term effects of particles appeared to be more significant for mortality due to cardiovascular disease than respiratory disease. It is estimated that there will be a gain of 0.2-0.5 million life years in 2000 for every $1\mu g/m^3$ decrease in $PM_{2.5}$ over the lifetime of the current population of England and Wales [COMEAP 2001]. However, such gain is not spread evenly over the whole population and thus it is not possible to calculate the distribution of life gain in each individual. In the UK each adult is estimated to have approximately $250\mu g$ of PM_{10} particles deposited in their body daily. Having said that, there is no convincing evidence to show that the levels of ambient particulates found in the UK have significant health impact on healthy individuals [AQEG 2005]. It is important to note that, such estimations were calculated based on studies carried out in the United States which has a different particle composition and population lifestyle.

1.4 Polycyclic aromatic hydrocarbons

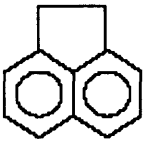
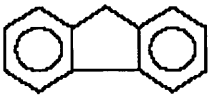
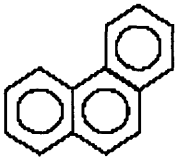
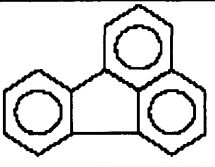
The significance of polycyclic aromatic hydrocarbons (PAH) as a major air pollutant is due to their ability to cause cancer as well as their close association with air particulates. For PAH that are absorbed onto the surfaces of air particulates, approximately 90% of them are associated with particles less than 3.3μm in diameter, with a peak distribution between 0.4 and 1.1μm [Venkataraman 1994]. Particles of this size range are often deposited deep in the lungs. Moreover, research has shown that carcinogenic PAH are mostly associated with air particulates [Lyall *et al* 1988, Hart *et al* 1994].

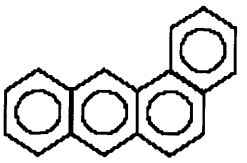
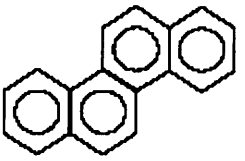
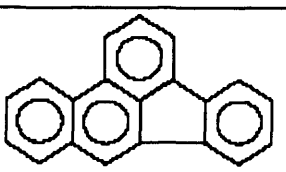
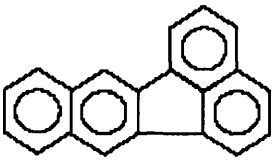
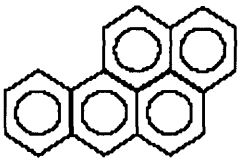
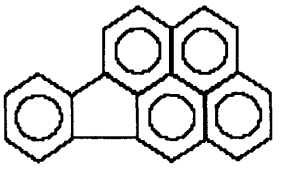
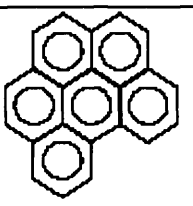
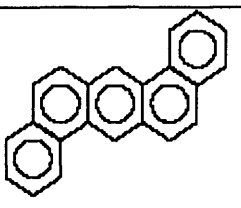
1.4.1 Physical and chemical properties of PAH

Polycyclic aromatic hydrocarbons are a large group of organic chemical compounds that consist of two or more fused aromatic rings which can be in linear, angular, or cluster arrangements. Although PAH consist of aromatic rings made entirely from carbon and hydrogen, the physical and chemical properties of individual PAH vary and the semi-volatile properties of some PAH make them highly mobile throughout the environment. There are over 100 different PAH identified but 16 of them were designated by the USEPA as compounds of interest (table 1.7). From these 16 PAH the International Agency for Research on Cancer (IARC) identified a subset of 6 compounds which included benzo[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, indeno[123cd]pyrene, benzo[ghi]perylene, and dibenz[ah]anthracene as "probable" or "possible" human carcinogens [IARC 1983, 1987].

PAH can either be present in ambient air in the form of gases or associated with air particulates. Generally, PAH that contain up to 4 fused benzene rings are know as light PAH and those containing more than four benzene rings are known as heavy PAH. The lighter PAH such as phenanthrene are found almost exclusively in the air in gaseous form, while heavy PAH such as benzo[a]pyrene (B[a]P) are absorbed onto particle surfaces [DERFA 1999]. PAH that are associated with particles can remain in the air for a longer period than gaseous PAH because firstly they have a slower dry deposition and take longer to settle to the ground, and secondly they have less efficient wet depositions and are thus less likely to be lost by precipitation [Baek *et al* 1991]. These PAH-bound air particles deposit slowly from the atmosphere, and

depending on atmospheric conditions they may be airborne for a long period of time and travel long distances. This is supported by evidence that PAH have been detected in a remote area situated in the Mediterranean Sea distance from any major sources [Masclet *et al* 1988]. Degradations of PAH are more efficient under summer conditions because of higher sunlight intensities, temperatures, and ozone concentrations [Menichini *et al* 1999]. PAH are lipophiclic in nature, i.e. they are relative insoluble in water but dissolves in fats and oils.

PAH	Molecular weight	Chemical formula	Chemical structure
Napthalene	128	$C_{10}H_8$	
Acenapthylene	152	$C_{12}H_8$	
Acenapthene	154	$C_{12}H_{10}$	
Fluorene	167	$C_{13}H_9$	
Anthracene	178	$C_{14}H_{10}$	
Phenanthrene	178	$C_{14}H_{10}$	
Fluoranthene	202	$C_{16}H_{10}$	
Pyrene	202	$C_{16}H_{10}$	

Benz[a]anthracene*	228	$C_{18}H_{12}$	
Chrysene	228	$C_{18}H_{12}$	
Benzo[b]fluoranthene#	252	$C_{20}H_{12}$	
Benzo[k]fluoranthene#	252	$C_{20}H_{12}$	
Benzo[a]pyrene*	252	$C_{20}H_{12}$	
Indeno[123cd]pyrene#	276	$C_{22}H_{12}$	
Benzo[ghi]perylene	276	$C_{22}H_{12}$	
Dibenz[ah]anthracene*	278	$C_{22}H_{14}$	

*IARC Group 2A *"probably carcinogenic to humans"*
IARC Group 2B *"possibly carcinogenic to humans"*

Table 1.7: Molecular weight, formulae, and structure of the sixteen PAH classified by the USEPA as compounds of interest.

1.4.2 Emission sources and trends in the UK

PAH found in the environment are formed both naturally and through human activities. Natural sources of PAH include thermal geological reactions, natural fires, biosynthesis of algae, bacteria, and plants, and synthesis from degraded biological matters such as fossil fuels [Harrison *et al* 1996]. Human activities are the more significant sources of PAH and they are formed in all processes that involve the incomplete combustion of carbon-based fuels such as coal, oil, wood, and gas. In addition PAH are also produced through a process known as pyrolysis, which is when organic materials are heated in the absence of oxygen or any other reagents. The major anthropogenic sources of PAH can be divided into industrial, automobile, domestic, and agricultural. The most important industrial sources include cokeries and aluminium production in particular to plants using the Vertical Stud Söderberg (VSS) process [NAEI 2004].

Figure 1.4 shows the annual PAH emission by source in the UK since 1990. Note that only the 16 PAH classified by the USEPA were included. Back in 1990 the annual national emission was 8326 tonnes. Approximately 42% were contributed by the production processes of non-ferrous metals which were mainly aluminium production and anode baking. The second largest source was road transport which contributed 28% of the estimated emission total. Except emissions of PAH from domestic combustion have slightly increased between 1997 and 1999, emission levels from other sources have been declining in a steady rate throughout the years between 1995 and 2002. In contrast, emissions from non-ferrous metals production processes have undergone dramatic changes. Aluminium production and anode baking was the largest source of PAH emissions in the UK until 1996, which contributed nearly half of the total emission. However, since then they have declined and in 2002 these sources accounted for only 6% of the total UK emissions. According to NAEI, this was a consequence of the closure of the production plant at Kinlochleven and investment in abatement equipment following the regulations of the Environmental Protection Act 1990. Since then one of the anode baking plants has dramatically reduced its emissions and as in 2002 the other was timetabled to follow shortly. On the other hand, although the total PAH emissions in tonnage by motor transport have been reduced by more than 50% since 1990, it has become the largest single source of PAH in the UK due to decreased emissions in the other sectors. In 2002, PAH emission

from motor transport was approximately 52% of the total annual emission. While industrial sources most strongly influence the PAH levels in the vicinity of the plant, road traffic emissions are a dominant source in towns and cities. In a study conducted in Birmingham UK using B[a]P as indicator, traffic emissions were estimated to associate with 80-82% and 61-67% of the PAH concentrations in the city centre and outskirt respectively [Lim *et al* 1999]. Moreover, the authors estimated that of the total PAH emissions contributed from motor traffic at the city centre site, approximately 60-84% were originated from diesel vehicles.

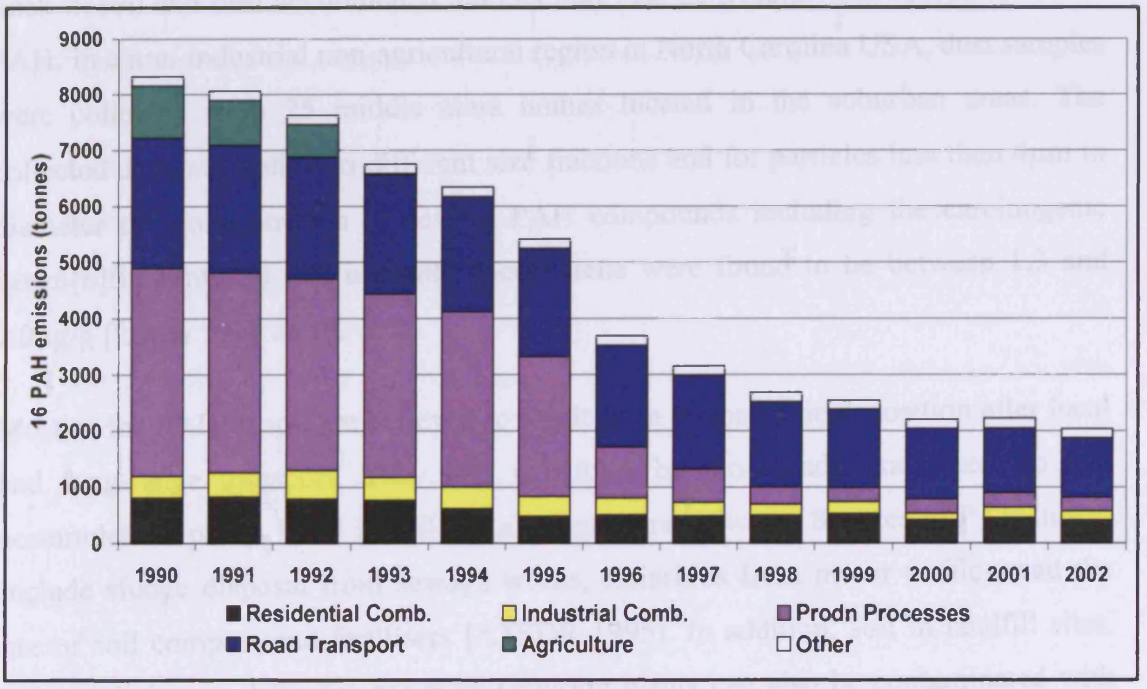


Figure 1.4: Time-series of 16 PAH Emissions (tonnes) in the UK, 1990-2002 ***(Source: NAEI).***

During combustions and industrial processes mixtures of PAH are formed which are varied by the combustion source. For example, PAH in diesel and petrol exhaust are predominantly consist of phenathrene, fluoranthene, pyrene, and benzo[ghi]perylene [Rogge *et al* 1993, Westerhold *et al* 1994], and in primary aluminium production involving the VSS process, the main PAH are anthracene, phenanthrene, and pyrene [Wenborn *et al* 1999]. Nonetheless, naphthalene is the most predominant compound of all PAH in both industrial and motor vehicle emissions [Wenborn *et al* 1999].

Indoor levels of PAH are likely to be contributed from both indoor and outdoor sources. According to the USEPA report on indoor concentrations of environmental

carcinogens, smoking has the greatest effect on PAH concentrations indoors [Gold *et al* 1990]. In a smoke-polluted environment, the concentrations of some PAH including the carcinogenic benzo[a]pyrene, benzo[ghi]perylene, dibenz[ah]anthracene, and fluoranthene were found to be within the range of 0.1 to 99ng/m^3 [WHO 1983]. The effect of smoking on indoor PAH levels was evaluated in a study involving 8 US homes, and it was estimated that the effect of smoking 10 cigarettes in an 8-hr period produced an increase in the level of B[a]P by 110% of the overall average level observed in the study [Chuang and Mack 1991]. Sometimes track-in soil and dust accumulated indoors may also be a significant source of indoor PAH. In a non-industrial non-agricultural region in North Carolina USA, dust samples were collected from 25 middle class homes located in the suburban areas. The collected dust was split into different size fractions and for particles less than 4μm in diameter the concentration of several PAH compounds including the carcinogenic benzo[b]fluoranthene and indenol[123cd]pyrene were found to be between 1.3 and 2.0μg/g [Lewis 1999 *et al*].

Most of the PAH in soil are believed to result from atmospheric deposition after local and long-range transport. They can volatilise, be biodegraded or taken up and accumulate in plants. PAH in soil can also enter groundwater. Sources of PAH in soil include sludge disposal from sewage works, emissions from motor traffics, and the use of soil compost and fertilisers [ATSDR 1995]. In addition, soil in landfill sites, industrial sites, and former gas manufacturing plants can also be contaminated with PAH [Bewley *et al* 1989, Tumey and Goerlitz 1990, ATSDR 1995]. For example, soils collected from a former charcoal production facility were found to contain concentrations of up to 80mg/kg of PAH [Snow-Ashbrook and Erstfeld 1998]. Levels of PAH found in sewage sludge may be higher in industrialised regions than in non-industrial regions [Bodzek 1999].

Small amount of PAH can often be found in food and water through contaminations of soil and water and be taken up by plants, and food is considered to be one of the major non-occupational sources of exposure to the compounds [WHOROE 2000]. A report by the World Health Organisation (WHO) showed that the typical levels of PAH in meat, fish, dairy products, vegetables and fruits, cereals and their products, sweets, beverages, and animal and vegetable fats and oils are within the range of 0.01-

10μg/kg [IPCS 1998]. According to a Dutch study, the largest contribution to the daily PAH intake came from sugar and sweets, cereals, oils, fats, and nuts, and the estimated mean daily intake was between 5 and 17μg/day [De Vos *et al* 1990]. Food processed by certain cooking methods such as smoking and barbecuing contain a more substantial amount of PAH since they are formed in the process of flaming combustion.

1.4.3 Exposure to PAH and health risks

It is now well known that some PAH compounds are capable of causing cancer, which were demonstrated in men exposed to high occupational levels of these compounds with increased incidence and mortality of cancers of the lung [Armstrong *et al* 1994, Constantino *et al* 1995], bladder [Bonassi *et al* 1989, Claver *et al* 1994], and other sites [Berger and Manz 1992, Chau *et al* 1993]. The carcinogenic ability of PAH varies between different compounds but through animal studies three potent carcinogenic PAH compounds namely benzo[a]pyrene, benz[a]anthracene, and dibenz[ah]anthracene have been classified as "probably" carcinogenic in humans [IARC 1987]. The qualification of "probably" reflects the lack of any data on the risks associated with human exposure to these compounds in isolation [EPAQS 1999]. Carcinogenic PAH compounds in their natural state are incapable of inducing tumours. Instead, they are dependent on their conversion in the body into compounds that are able to react with and subsequently damaging the genetic material DNA in the nuclei of cells. Such activation process is mediated by various enzyme systems in susceptible target tissues. In fact, it is known that once inhaled PAH compounds are rapidly absorbed and can be activated in the lungs [IARC 1983].

Epidemiological studies of the health effects of PAH is often difficult because individual PAH compounds have different toxicities, and exposure is always to a complex mixture of PAH and not individual compounds. Moreover, the most significant endpoint of PAH toxicity is cancer which takes a significantly long period of time to develop and is likely to be due to long-term exposures to the compounds. The average level of PAH an individual is exposed to is unknown due to the variations between background PAH levels and each individual's activities. Exposure to PAH can be through active or passive inhalation of tobacco smoke, wood smoke,

and contaminated air, ingestion of the compounds in food and drinking water, and through skin contact with soot and tars. The US Agency for Toxic Substances and Disease Registry (ATSDR) estimated that the average total daily intake of PAH by a member of the general population in the United States to be 0.207μg from air, 0.027μg from water, and 0.16-l.6μg from food. In addition, the total potential exposure to carcinogenic PAH for adult males in the United States was estimated to be 3μg/day [ATSDR 1995]. The annual mean concentrations of B[a]P in major European urban areas are in the range of 1 to 10ng/m^3, and in rural areas <1ng/m^3 [WHOROE 2000].

Risks of lung cancer due to exposure to PAH compounds have been calculated using three different methods as shown in the WHO report on Air Quality Guidelines for Europe 2000 [WHOROE 2000]. The first approach was based on epidemiological data from studies in coke oven workers. Using the typical levels of coke oven PAH emissions, the most plausible upper-bound individual lifetime risk of developing respiratory cancer associated with a continuous exposure to 1μg/m^3 of benzene-soluble compounds of coke-oven emissions in ambient air was approximately 6.2×10^{-4} per ng/m^3. The second approach was to use B[a]P as the indicator of general PAH mixtures from emissions of coke ovens, and using the reported value of 0.71% as the concentrations of B[a]P in the benzene-soluble fraction of coke oven emissions, the lifetime risk of respiratory cancer was estimated to be 8.7×10^{-5} per ng/m^3. The third approach was based on the lung tumour development rate obtained in a rat inhalation study with coal tar/pitch condensation aerosols, and the lifetime cancer risk of $2x10^{-5}$ per ng/m^3 for B[a]P as a constituent of a complex mixture was calculated [Heinrich *et al* 1994]. Overall, the estimated corresponding concentrations of B[a]P producing excess lifetime cancer risks of 1/10,000, 1/100,000 and 1/1,000,000 were 1.2, 0.12 and 0.012 ng/m^3, respectively.

Currently there are no specific guideline values recommended by WHO regarding the levels of PAH in air. This is due to the fact that PAH are often present in the form of complex mixtures and is further complicated by their interactions with a number of other compounds and air particulates, which on their own may also play a role in cancer development. Food containing PAH is considered as one of the major sources of human exposure to the compounds. However, the presence of PAH in food is in

part due to contamination from air pollution, therefore WHO recommended that the levels of PAH in air should be kept as low as possible [WHOROE 2000]. In the UK, the Expert Panel on Air Quality Standards (EPAQS) recommended an air quality standard of 0.25ng/m^3 of B[a]P as an annual average [EPAQS 1999]. This recommendation was intended to reduce any risk to the UK population from exposure to PAH to one, which the panel believed would be so small as to be undetectable.

1.4.4 Exposure biomarkers of PAH in humans

There are a number of ways to monitor uptake of PAH by different biomarkers, such as the detection of metabolites in urine, urinary thioethers, urinary mutagencity, PAH-protein adducts, and PAH-DNA adducts [Jongeneelen 2001]. However, both urinary thioethers and urinary mutagenicity are non-specific indicators of exposure to mutagenic agents, and PAH-protein adducts and PAH-DNA adducts lack sensitivity in the case of occupational exposure to PAH and that results are often strongly confounded by smoking [Clonfero *et al* 1989, Reuterwall *et al* 1991, Ferreira *et al* 1994]. Thus these methods are not suitable for routine applications. In the search of a reliable human exposure biomarker to PAH, a specific metabolite of pyrene, 1-hydroxypyrene (1-HP), has been suggested [Jongeneelen *et al* 1985]. The non-carcinogenic pyrene is an abundant PAH compound that is often present in mixtures of PAH [Jongeneelen *et al* 1985, Buchet *et al* 1992]. It is metabolised by various enzyme systems in the body into 1-hydroxypyrene–glucuronide, which is then excreted [Jongeneelen *et al* 1987]. Pyrene is rapidly distributed, metabolised, and eliminated from the body, this makes 1-HP a reliable indicator of systemic exposure to this PAH compound. Furthermore, because pyrene is always present in PAH mixtures it is therefore not just an indicator of uptake of pyrene, but also an indirect indicator of all PAH. The half-life for the urinary excretion of 1-HP in occupational exposed workers is 18hrs [Buchet *et al* 1992] and the individual half-life ranges from 6 to 35hrs [Jongeneelen *et al* 1990]. The presence of 1-HP in urine is determined by high-pressure liquid chromatography (HPLC). At present, urinary 1-HP is a widely used biological indicator of exposure to PAH and studies using this biomarker is well documented [Jongeneelen 2001]. Despite the widely use of 1-HP as an exposure marker of PAH, its use is not without drawbacks. Although pyrene is often found in high abundance in PAH mixtures, the composition of the PAH mixture in different environment often varies. As stated earlier in this chapter, mixtures of PAH formed

are varied by the combustion source, and thus the relative proportion of individual PAH in the PAH mixture can vary from time to time and place to place. Therefore the specificity of 1-HP as an exposure marker for a PAH mixture is not absolute. And as with all PAH exposure analysis techniques, the use of 1-HP as an exposure marker is subject to confounding by the active and passive inhalation of tobacco smoke.

CHAPTER 2 – LITERATURE REVIEW
HEALTH EFFECTS OF AIR PARTICULATES

There is a body of scientific evidence regarding the epidemiological relationships between the levels of respirable air particulates and cardiorespiratory morbidity and mortality which has been well documented in recent years. Studies suggested that these particles may lead to both short- and long-term adverse health effects. The scale of the effects varies from acute changes in respiratory disease symptoms to increased mortality rates due to exacerbations of pre-existing cardiorespiratory disease. Despite this overwhelming evidence the exact pathophysiological mechanisms of how air particulates may lead to adverse health effects is largely unknown.

The evidence base of population health effect assessment with respirable air particulates is extensive. This chapter summaries the key findings based on the information found from a number of keyword searches using Scirus, which were undertaken at various times to furnish a complete listing of primary research papers for review assessment. Scirus is a comprehensive science-specific search engine on the Internet. It searches over 250 million science-specific web pages and covers a large number of scientific databases such as MEDLINE, Science Direct Online, and BioMed Central.

2.1 Evaluation of short-term effects using acute exposure studies

2.1.1 Increased mortality

Since the early 1930s many studies have been carried out to investigate the acute effects of air pollution on mortality. The earliest studies were, compared to more recent studies, methodologically simple and evaluated the changes in mortality before, during, and after pollution episodes that lasted a few days or weeks. Associations between increased deaths and severe air pollution were demonstrated by several well-known episodes such as the Meuse River valley fog in Belgium in 1930 [Nemery *et al* 2001], the Donora smog in Pennsylvania in 1948 [Schrenk *et al* 1949], and the London Smog in 1952 [Ministry of Health 1954]. These studies showed a clear linkage between cardiorespiratory mortality and morbidity with episodes of extremely elevated concentrations of air particulates and/or other toxic chemicals such as

sulphur dioxide. Later studies have also shown that less extreme pollution could also trigger an increased mortality but with smaller effects. For example, in 1985 a smog episode took place in parts of North Rhine-Westfalia, West Germany for 5 days. The authors compared mortalities in the effected areas with control areas that were not affected by the smog [Wichmann *et al* 1989]. Maximum 24hr average TSP during the episode was 600μg/m^3 in the affected areas, which was 3 times higher than the control. Mortality data in the studied areas were collected and a total of 24,000 deaths during the episode were recorded. Results showed a larger increase in total mortality in the smog areas compared with the control area (8% v 2%). In contrast to an earlier study in the same region in 1962, in which a 5-day smog episode with an average TSP concentration of 2400μg/m^3 has led to an increase of 19% in total mortality [Schmitt 1986], this 1989 study has demonstrated that less severe episode of air pollution would still be able to trigger an increased death rate though at a smaller scale.

In the 1970s and through to the 1980s, various researchers began to adopt time-series analysis to investigate the association between daily mortality and air pollution at relatively low levels. A time-series is a set of observations being recorded at a specific time. When studying air pollution, the dependent and independent variables are measured over time to identify the possible short-term changes in mortality related to the short-term fluctuations in air pollution levels. In a time-series study, levels of pollution within an area of interest serve as indicators of exposure whereas daily health data, such as mortality rate, serve as indicator of the effects. Time-series studies have the major advantage of being able to provide a large set of observational data across a long period of time, rather than a few days before, during, or after an episode. This gives the analysis more statistical power to evaluate the mortality effects of less extreme levels of pollution episodes. Other environmental factors such as meteorological changes or illnesses such as a flu outbreak may confound the results and must be taken into account in the analysis. The disadvantages of time-series studies are their incapability in estimating the effects of air pollution on a longer-term exposure scale. This is because they cannot provide direct information on the loss of person-time associated with the extra deaths, and they are unable to demonstrate the effects of exposure to transient peaks of air pollution have on long-term disease processes. Moreover, exposure data is based on measurements from centrally located

monitoring stations, which means it lacks a direct link between exposure of the pollutant and the resulting health outcome at the individual level. This renders the judgement of causality difficult. Nonetheless, time-series studies can compensate for these weaknesses by examining a very large population of individuals and their responses to the pollutant of interest, thereby gaining an understanding of the public health impacts and risks to the population as a whole. Early time-series studies were limited by inadequate pollution data and a variety of time-series approach was applied to these data that made direct comparison difficult [Holgate *et al* 1999]. Nevertheless, associations between daily mortality counts and air pollution were generally observed.

In the early 1990s, some investigators began to report time-series analysis based on Poisson regression modelling, which evaluates the rate or frequency of an outcome event in a sample that is followed through time. With the help of sophisticated statistical software and computerised records of air pollution, counts of mortality, and weather data, researchers were able to analyse more appropriate and complicated statistical models of the daily counts of death, particularly in small communities with small number of deaths per day. In addition, the widespread use of the same statistical method used in the analysis made direct quantitative comparisons of effects estimates between studies possible. The following are some of the later time-series studies carried out the in the early 1990s.

Pope studied the association between daily mortality and particulate pollution in Utah County between April 1985 and December 1989 [Pope 1992]. Poisson regression models controlled for weather was used to regress daily death counts on PM_{10} pollution levels. During the study period, mean PM_{10} concentration was 47μg/m^3 with a maximum 24hr average of 365μg/m^3. A total of 4,649 non-accidental deaths were recorded, which distributed across 1,736 days and resulted in an average daily death of 2.7. Results showed a significant positive assoication between non-accidental mortality and PM_{10} concentrations. The strongest association was with 5 day moving average PM_{10} levels, including the concurrent day and the preceding 4 days – for every 100μg/m^3 increase in PM_{10} concentrations, an increase of 43%, 20%, and 5% excess deaths due to respiratory, cardiovascular, and all other causes was observed respectively. This is equivalent to 16% excess in total mortality. In addition, relatively

low levels of SO_2, aerosol acidity, and ozone during the study period suggested an independent association between mortality and PM_{10}. Fairley studied the effects of air particulates on mortality in the Santa Clara county of California, United States [Fairley 1990]. The studied area was characterised by its relatively low level of SO_2 compared with other eastern or midwestern U.S. cities, thus eliminating the combined effects of SO_2 in the analysis. Daily mortality counts were obtained from the California Department of Health Services for the years 1980-1986 and counts of daily total non-accidental mortality were extracted. Because PM_{10} levels were not monitored at that time, the author used the coefficient of haze (COH) along with NO_3 as an indicator of the level of pollution. Using a Poisson regression model controlled for seasons, meteorological variables, and other gaseous pollutants such as ozone, the relative risk of non-accidental mortality was 1.05 ($p<0.01$) per 0.9 units increase in COH. In 1999 the author examined all non-accidental deaths as well as respiratory deaths and cardiovascular deaths between 1989 and 1996 in the same area, but this time included PM_{10} and $PM_{2.5}$ data. It was found that for every 50μg/m^3 increase in PM_{10} concentrations, the relative risk (RR) for non-accidental mortality was 1.08 ($p<0.01$), and cardiovascular mortality was 1.09 ($p<0.05$). However, the increased risk seen in respiratory deaths was statistically insignificant (RR = 1.11). As for $PM_{2.5}$, for every 28μg/m^3 increase in its concentrations, the relative risk of non-accidental mortality was 1.09 ($p<0.05$), but no statistically significant associations were found between cardiovascular mortality (RR = 1.07) and respiratory mortality (RR = 1.13).

Using Poisson regression modelling, Schwartz carried out several individual studies in different parts of the United States and identified positive associations between exposure to air pollution and increased mortality. In Detroit, all non-accidental deaths between 1973 and 1983 were regressed for the levels of TSP in the city. After controlling for season, weather, and time trends, a significant correlation ($p<0.01$) was found between predicted TSP and daily mortality, which was independent of SO_2 [Schwartz 1991]. It was found that for each 100μg/m^3 increase in TSP there would be a 6% increase in mortality. The same research methodology was applied in Steubenville, Ohio [Schwartz and Dockery 1992]. All non-accidental deaths were studied over an 11-yr period between 1974 and 1984. Being an area with small

population, the average total number of deaths per day in Steubenville over the study period was only about 1% of the deaths in a typical London winter. Despite the reduced statistical power, TSP was found to be significantly associated with increased daily mortality in Poisson regression analyses controlling for season and temperature. For every 100μg/m^3 increase in particulate levels there was a 4% increase in mortality on the succeeding day, and was independent of SO_2. In Birmingham, Alabama, mortality was studied from August 1985 through 1988. Poisson regression analyses controlled for weather, time trends, day of the week, and year of study, showed a significant association between PM_{10} and daily mortality [Schwartz 1993]. For every 100μg/m^3 increase in particulate level there was an increased mortality risk of 1.11 (95% CI 1.02-1.20). Following Detroit and Birmingham, Schwartz replicated the analysis in Cincinnati, Ohio. Daily TSP concentrations were studied in Cincinnati from 1977 to 1982 and were matched to daily counts of non-accidental deaths [Schwartz 1994]. Poisson regression analysis controlled for seasonal and monthly variations and meteorological variables showed that for every 100μg/m^3 increase in TSP the estimated relative risk of death was 1.06 (95% CI 1.03-1.10), and was increased even further for the elderly (RR = 1.09; 95% CI 1.05-1.14) and subjects with cardiovascular disease (RR = 1.08; 95% CI 1.03-1.14). The results obtained in this study had a striking similarity to the reported results in Philadelphia – using data extracted between 1973 and 1980, the relative risks for a 100μg/m^3 increase in TSP were 1.07 (95% CI 1.04-1.10) for all-cause mortality, 1.10 (95% CI 1.06-1.13) for deaths in the elderly, and 1.10 (95% CI 1.06-1.14) for cardiovascular deaths [Schwartz and Dockery 1992]. At the time when the Philadelphia study was published, critics suggested that the authors did not have sufficient controls on the time-varying variables [Li and Roth 1995, Moolgavkar *et al* 1995], despite seasonal and meteorological factors such as season, year, previous day's mean temperature, dew point, winter temperature, and indicators of hot and humid days had been accounted for. In 1999 Neas together with the two original authors carried out a reanalysis of the Philadelphia data of 1973 to 1980 [Neas *et al* 1999]. Using conditional logistic regression analysis with a case-crossover design, the researchers managed to reproduce very similar results from those estimated in 1992. The case-crossover design is an adaptation of the case-control design in which cases serve as their own controls, meaning the characteristics of a subject and status of exposure at the time of a health event (i.e. case period) are compared with another time period

when the health event of interest is absent (i.e. control period). The regression model which controlled for season and day of week, showed that for a 100μg/m^3 increment in the 48-hr mean level of TSP was associated with increased all-cause mortality (OR = 1.06; 95% CI 1.03-1.09), increased deaths in the elderly (OR = 1.07; 95% CI 1.04-1.11), and increased deaths due to cardiovascular disease (OR = 1.06; 95% CI 1.02-1.11). The similarity of the results confirmed the conclusion of the previous Poisson regression analysis. In another study, concentrations of PM_{10} and $PM_{2.5}$ were measured in six eastern U.S. cities for eight years and daily mortality for these metropolitan areas were combined with particulate air pollution and weather measurements [Schwartz *et al* 1996]. Using Poisson regression models adjusted for time trends and weather, both PM_{10} and $PM_{2.5}$ were each significantly associated with increased daily mortality. The strongest association was found in $PM_{2.5}$, in which for every 10μg/m^3 increase in two-day mean $PM_{2.5}$ was associated with a 1.5% (95% CI 1.1-1.9%) increase in total daily mortality. The risk further increased with deaths caused by chronic obstructive pulmonary disease (3.3%) and by ischemic heart disease (2.1%). Recently this study was reanalysed by Klemm and colleagues [Klemm *et al* 2000]. The authors used the particulate air pollution data supplied by the original investigators, and daily weather and daily counts of total and cause-specific deaths were reconstructed from original public records. The reconstructed data were consistent with the summaries presented in the original paper except for daily counts of deaths, of which the reconstructed data set were lower than in the original paper due to restrictions on residence and place of death. Results from the reconstructed data resembled those of the original paper. For example, the estimated association of a 10μg/m^3 increase in 2-day mean particulate air pollution on total mortality was 1.3% (95% CI 0.9-1.7%) for $PM_{2.5}$ based on the reconstructed dataset, compared to the originally reported association of 1.5% (95% CI 1.1-1.9%). These results from the reconstructed dataset confirmed the validity of the original findings and shown that they could be replicated. Using mortality and pollution data obtained from St Louis and eastern Tennessee, Dockery together with Schwartz and co-workers investigated the mortality of all non-accidental deaths in those areas for a 1-yr period from September 1985 through August 1986 [Dockery *et al* 1992]. Using Poisson regression models which controlled for possible meteorological and seasonal influences, total mortality in St. Louis was increased by 16% (95% CI 1-33%) per 100μg/m^3 increase in PM_{10}, and by 17% (95% CI 12-57%) in eastern Tennessee. No

statistically significant associations were found with gaseous pollutants including SO_2, NO_2, and ozone. Despite the relatively short monitoring period of the study, which may have limited its ability to detect associations, it nevertheless generated consistent results with other US studies and showed a positive association between air particulates pollution and mortality.

Ostro added further evidence of the association between particulate air pollution and mortality by studying death counts and $PM_{2.5}$ in two Southern California counties with a population of approximately 2.8 million people [Ostro 1995]. For the years 1980 through 1986, daily non-accidental death data were collected along with $PM_{2.5}$ concentrations, weather, and meteorological information. Poisson regression models generated results that showed a positive association between $PM_{2.5}$ levels and mortality, although such relationship was affected by seasons. When the full years' data were included in the model, relationships were found between $PM_{2.5}$ concentrations and total mortality (RR = 1.004; 95% CI 0.99-1.02), respiratory mortality (RR = 1.03; 95% CI 0.99-1.06), cardiovascular mortality (RR = 1.01; 95% CI 0.99-1.02), and mortality in those aged 65 or above (RR = 1.01; 95% CI 0.99-1.02) per 36μg/m^3 change in $PM_{2.5}$ concentrations, although they all marginally failed to reach statistical significance. However, when only data from the summer quarters were applied to the model, the effects of $PM_{2.5}$ on total mortality and respiratory mortality were increased to 1.03 (95% CI 1.00-1.05) and 1.08 (95% CI 1.01-1.14) respectively. There were no significant changes for cardiovascular mortality nor mortality in individuals aged 65 or above.

The National Mortality, Morbidity and Air Pollution Study (NMMAPS) was a large-scale time-series study carried out in 20 major US cities covering a total population of 50 million people [Samet *et al* 2000]. Daily mortality rates were obtained from the National Centre of Health Statistics between 1987 and 1994, and all deaths due to natural causes were classified according to age group (≤65yrs, 65-74yrs, and ≥75yrs) and cause of death (cardiorespiratory and other). Weather data and air pollution data were obtained from the Environmental Protection Agency. To avoid potential consequences of outlying values the highest and lowest 10% of air pollution values were excluded in the analysis, and the mean PM_{10} levels throughout the duration of the study ranged from 23.8μg/m^3 to 46.0μg/m^3 across the cities after the 10%

trimming was applied. Results showed that the levels of PM_{10} had greater effects on the rate of deaths from cardiorespiratory causes than all causes. The estimated increase risks of death were 0.51% (95% CI 0.07-0.93) for all causes and 0.68% (95% CI 0.20-1.16) for cardiorespiratory causes per 10μg/m^3 increase in PM_{10}. No significant differences were seen across different age groups. After adjustment for other pollutants including ozone, nitrogen dioxide, sulphur dioxide, and carbon monoxide, the effects of PM_{10} on mortality rates did not change considerably, suggesting that the findings were not affected by confounding by other pollutants.

Goldberg *et al* examined the relationships between particulate air pollution and daily mortality in Montreal, Quebec [Goldberg *et al* 2000a]. Between 1984 and 1993, 140,939 non-accidental deaths occurred in the region along with air pollution data and weather data were analysed by Poisson regression models. Amongst all the pollutants studied, namely COH, TSP, PM_{10}, and $PM_{2.5}$, only COH showed significant associations with total mortality. For every 1.85 units increase in COH, the mean percentage changes in total mortality were 1.44% (95% CI 0.75-2.14%), 1.12% (95% CI 0.42-1.82%), and 1.98% (95% 1.07-2.90%) for the concurrent day, 1 day following an increase in pollution, and 3-day average running mean respectively. For cause-specific mortality, the mean percentage changes in death counts from respiratory diseases in subjects aged >65 were 4.06% (95% CI 1.59-6.59%), 4.65% (95% CI 2.24-7.11%), and 6.9% (95% CI 3.69-10.21%) per 1.85 units increase in COH for the concurrent day, 1 day following an increased in air pollution, and 3-day moving average respectively [Goldberg *et al* 2000b]. No statistically significant associations were found between cardiovascular disease and COH level.

Studies carried out in Europe also generated consistent results. In Valencia, Spain, Ballester *et al* examined the non-accidental and cause-specific mortality occurred between 1991 and 1993 [Ballester *et al* 1996]. Concentrations of daily black smoke in the city were monitored by three stationary monitoring stations and the mean daily level in the study was 67.7μg/m^3. Poisson regression models showed significant positive associations between black smoke and mortality. The estimated relative risk of dying corresponding to a 10μg/m^3 increase in mean daily black smoke over the whole period was 1.009 (95% CI 1.003-1.015). For mortality in the group aged >70

years and for cardiovascular mortality, the relative risks were 1.008 (95% CI 1.001-1.016) and 1.012 (95% CI 1.003-1.022) respectively. No significant associations were found between mortality from respiratory diseases and black smoke. In East Berlin of Germany, non-accidental mortality occurred in the winters of 1981-1989 were studied [Rahlenbeck and Kahl 1996]. Using regression analysis including daily mean levels of suspended particulates controlled for temperature, humidity, day of week, month, and year, the authors found that pollution caused by suspended particulates was a significant contributor to excess mortality. The strongest association was found for mortality 2 days after an increase in particles level. When omitting days with pollutant concentrations above 150μg/m^3, the pollutant-mortality relationship became linear. For every 100μg/m^3 increase in suspended particulates it was associated with a 6.1% increase in mortality 2 days later. When SO_2 levels were included in the model, the effects of particles on mortality was reduced to 4.6%, suggesting there was a combined effect from both pollutants.

A large-scale multi-centre European project, the APHEA project (Air Pollution and Health: a European Approach), investigated the effects of particulate matters on daily mortality across 12 European cities [Katsouyanni *et al* 1997]. The length of the study period varied between cities, but the overall duration was from 1975 to 1992 covering over 23 million populations. Poisson regression modelling was used to analyse the effects of particles measured as black smoke as well as PM_{10}, and controlled for confounding factors such as seasonal and long term patterns, daily temperature, humidity, day of the week, holidays, and influenza epidemics. Because of the difference in geography, the participating cities showed a high degree of variation in air pollution concentrations, seasonal patterns, and meteorological and climatic conditions. Mean winter concentrations of black smoke varied from 10 to 290μg/m^3. Typical patterns of winter and summer type smog were observed, with some cities having particularly high winter type smog, dominated either by sulphur dioxide (e.g. Milan, Italy) or particles (e.g. Cracow, Poland), while others had relatively high air pollution of both types (e.g. Athens, Greece). Results of each city were pooled into two groups namely western European cities and central eastern cities. The estimated relative risks associated with a 50μg/m^3 change in 24hrs were 1.029 (95% CI 1.021-1.037) for black smoke and 1.021 (95% CI 1.012-1.030) for PM_{10} in the western European cities. In central eastern cities, the relative risks were 1.006 (95% CI 0.997-

1.011) for black smoke and 1.043 (95% CI 1.003-1.085) for PM_{10}. When results from all cities were pooled together, the relative risk of death due to black smoke was 1.013 (95% CI 1.009-1.017) and 1.022 (95% CI 1.013-1.031) due to PM_{10}. All relative risk estimates were calculated as the cumulative effects of 24hr moving average. The authors commented that, despite the variations between the western European cities, the consistency of results supported a causal association between exposure to particulate matter and mortality from all causes. As part of the APHEA project Aga and colleagues investigated the short-term effects of ambient particles on mortality in the elderly aged 65 or above [Aga *et al* 2003]. Using Poisson regression models and pooled data of all cities, results showed an increased relative risk of death in the elderly population of 0.8% (95% CI 0.7-0.9%) and 0.6% (95% CI 0.5-0.8%) for every $10\mu g/m^3$ increase in PM_{10} and black smoke respectively. The estimated effect sizes could be modified by the long-term mean level of nitrogen dioxide (higher levels were associated with larger effects), temperature (larger effects were observed in warmer countries), and by the proportion of elderly in each city (a larger proportion was associated with higher effects).

Results of a meta-analysis carried out by the WHO to evaluate the health effects of particulate air pollution was published in 2004 [Anderson *et al* 2004]. Estimates of all-cause mortality were extracted from 33 European cities and the summary relative risk was 1.006 (95% CI 1.004-1.008) for every $10\mu g/m^3$ increase in PM_{10} concentrations. For disease-specific mortality, estimates were pooled from 17 and 18 European cities for cardiovascular and respiratory deaths respectively, and the corresponding summary relative risks were 1.009 (95% 1.005-1.013) and 1.013 (95% CI 1.005-1.020) per every $10\mu g/m^3$ increase in PM_{10} levels. The estimate for all-cause mortality was very similar to those obtained in the NMMAPS carried out in 20 major US cities (RR = 1.005 for every $10\mu g/m^3$ increase in PM_{10}).

For all of the studies reviewed so far none of them have shown a particular threshold of effect, and the estimated relative risk of mortality always increased monotonically with particulate concentrations and usually in an almost linear fashion. Results from these time-series studies were controversial, partly due to the fact that the lack of biological mechanisms to explain the observed mortality, especially at low levels of particulate air pollution. Some suggested that the observed associations might be due

to the selection of modelling technique, or due to confounding by other factors such as season, weather, other pollutants, or some other unknown factors [Lipfert and Wyzga 1995, Moolgavkar and Luebeck 1996].

2.1.2 Changes in respiratory symptoms in children

In comparison with the number of studies investigating how air particulates increase mortality in short-term, relatively few studies have been carried out to demonstrate how disease symptoms change prior to, during, and after an air pollution episode. Most of these studies were panel-based and involved small groups of participants, with the majority of them carried out in children. Symptoms of respiratory or other diseases are recorded using daily diaries, which is an easy and inexpensive way to evaluate acute changes in respiratory health studies. While some studies focused on asthmatics and exacerbation of asthma symptoms caused by air pollution, many followed non-asthmatics and evaluate changes in acute respiratory health status more generally. Reported symptoms were often divided into upper respiratory illness (URI) including runny or stuffy nose, sinusitis, sore throat, wet cough, and irritated eyes, and lower respiratory illness (LRI) including wheezing, dry cough, phlegm, shortness of breath, and chest discomfort or pain. In addition to these, cough was the most frequently reported symptom and was often analysed separately. Often, small if statistically significant associations were observed between particulate air pollution and respiratory symptoms.

One of the earliest studies investigating the acute effects on children's respiratory symptoms was carried out by Vedal and colleagues in 1987 [Vedal *et al* 1987]. The study location was the Chestnut Ridge region of western Pennsylvania of the United States, where air pollution was generated from a large number of coal-fired power plants. A panel of 351 school children living in the most polluted areas in the region were recruited into the study. However, throughout the 8-month study period only 128 participated in the completion of symptoms diary recording daily changes in respiratory symptoms. The pollutant of interest was the CoH measured by a single monitoring station within the study region. Using multiple regression models which controlled for temperature and other gaseous pollutants, no statistically significant associations were found between CoH levels and URI and wheeze. Although other LRI excluding wheeze showed stronger associations with CoH, the relationships

found were statistically insignificant. For every 0.5 units increase in CoH, the odds ratios of the occurrence of URI, wheeze, and LRI excluding wheeze on days with higher levels of pollution were 0.9 (95% CI 0.76-1.07), 1.0 (95% CI 0.97-1.06), and 1.3 (95% CI 0.93-1.82) respectively.

Most respiratory symptoms studies were undertaken in the 1990s and they provided evidence that air particulates were capable of triggering acute respiratory symptoms. Again in Pennsylvania, United States, Neas and colleagues recruited 108 children and asked their parents to complete diaries twice daily of their children's symptoms and hours spent outdoors [Neas *et al* 1996]. Regression models showed that for a $20\mu g/m^3$ increment in 24-hour mean respirable particles, there was an increase in the incidence of cough episodes that evening or the subsequent morning (OR = 1.37; 95% CI 1.13-1.66). Increased incidence of cold episodes on the same evening or the subsequent morning was found for 12-hour day time levels of particles with strong acidity (OR = 1.35; 95% CI 1.14-1.61). Similarly in northern Mexico City, Mexico, 71 children aged 5-7yrs with mild asthma were enrolled in a study to find out the relationship between air pollution and exacerbation of childhood asthma [Romieu *et al* 1996]. Daily changes in symptoms including cough, phlegm production, wheezing, and difficulties in breathing were recorded in daily diaries. Regression analysis showed that an increase of $20\mu g/m^3$ in 24-hour average PM_{10} was related to an 8% (95% CI 4%-15%) increase in LRI on the same day, and an increase of $20\mu g/m^3$ in the weekly mean $PM_{2.5}$ was related to a 21% (95% CI 8%-35%) increase in LRI.

Yu *et al* observed a panel of 133 children aged 5-13yrs with asthma residing in Seattle, United States [Yu *et al* 2000]. Between 1993 and 1995, information on respiratory symptoms the children experienced were obtained via daily symptoms diary. The average number of days of diary data provided by each child was 58, with a range of 28-112 days. Daily levels of PM_{10} and PM_1 were monitored by 3 different sites in the greater Seattle area. In addition, meteorological data were also collected. Logistic regression models were used for the analysis which were controlled for age, sex, race, baseline height, and other potential time-dependent factors such as day of week, season, and temperature 2 days after an air pollution episode. Results showed significant associations between the levels of air particulates and exacerbation of

asthma symptoms. For a 10μg/m^3 increase in PM_{10} level, the odds ratios of short-term asthma symptoms were 1.09 (95% CI 1.01-1.18), 1.11 (95% CI 1.03-1.20), and 1.08 (95% CI 1.01-1.17) for the same day, 1 day after, and 2 days after an air pollution episode respectively. As for PM_1, the odds ratios were 1.18 (95% CI 1.05-1.33), 1.17 (95% CI 1.04-1.33), and 1.09 (95% CI 0.98-1.21) per 10μg/m^3 increase in its level. Vedal *at al* studied the health effects of particulate air pollution on 200 school children aged 6-13yrs from Port Alberni, Canada [Vedal *et al* 1998]. Due to the geographical location of the area it is frequently subjected to thermal inversions that trap air pollutants in the atmosphere, particularly during winter. The main sources of air particulates were the boilers of a local pulp mill and residential wood burning. Data were recorded daily by respiratory symptoms diaries for up to 18 months between 1990 and 1992, during which time when ambient PM_{10} concentrations were monitored by an automated monitoring site located to the north of the pulp mill. Throughout the study period, the 24hr average concentration of PM_{10} was 22.1μg/m^3, with a maximum of 159μg/m^3. Logistic regression analysis controlled for meteorological factors showed associations between PM_{10} and a range of respiratory symptoms in the children. For every 10μg/m^3 increase in PM_{10} above the mean daily concentration of 27.3μg/m^3, the odds ratios were 1.07 (95% CI 1.02-1.11) for cough, 1.07 (95% CI 1.00-1.13) for phlegm production, 1.04 (95% CI 1.00-1.08) for nose symptoms, 1.06 (95% CI 1.01-1.11) for throat soreness, and 1.06 (95% CI 1.02-1.10) for both cough and phlegm. These odds ratios were calculated using cumulative estimates of 1-4days following an air pollution episode. In addition, positive but statistically insignificant associations were also found between PM_{10} and other symptoms including those of the eyes (OR = 1.05; 95% CI 0.97-1.13), wheeze (OR = 1.03; 95% CI 0.96-1.10), chest tightness (OR = 1.06; 95% CI 0.97-1.16), and dyspnoea (OR = 1.01; 95% CI 0.94-1.08).

Studies carried out in Europe also generated results that were consistent to their American counterparts. van der Zee and co-workers investigated the effects of air particulates on acute respiratory symptoms in children in the Dutch cities Rotterdam and Amsterdam [van der Zee *et al* 1999]. Rotterdam is an industrialised city with about 600,000 inhabitants at the time of the study; in contrast, Amsterdam with a population of 720,000 has few industrial developments and local air pollution was

caused primarily by emissions from motor traffic. Three non-urban areas close to Rotterdam and Amsterdam were selected as control areas, which had no major traffic emissions, no large industrial sources, and had sufficient size to select enough children. Groups of children from urban and non-urban areas were further divided into two groups depending on whether or not they suffer from chronic respiratory symptoms. Throughout the study period between 1993 and 1995, parents of 630 children aged 7-11yrs old completed daily respiratory symptoms diaries and provided the data for analysis. Symptoms included in the diary were cough, phlegm, runny or stuffed nose, eye irritations, sore throat, woken up with breathing problems, shortness of breathe, wheeze, and attacks of shortness of breathe with wheeze and fever. Information on medication use were also collected. Twenty-four hour-measurements of PM_{10}, black smoke, gaseous pollutants, and meteorological data of all study areas were obtained through fixed monitoring sites. Regression analysis showed positive associations between air particulates and acute respiratory symptoms in both the exposed and control groups, but the effects were greater in those already suffering from chronic symptoms. For example, children residing in urban areas were more likely to report LRI than their non-urban counterparts (OR = 1.48 v 1.04, per $100\mu g/m^3$ increase in PM_{10} in the day after an air pollution episode). In addition, children from urban areas also reported a higher usage of bronchodilator (OR = 1.29 v 0.82, per $100\mu g/m^3$ increase in PM_{10} on the day of an air pollution episode), and that residing in non-urban areas seemed to have a protective effect. No associations were found between pollution level and acute cough and URI in either group. For children without chronic symptoms, they appeared to be less affected by air pollution than symptomatic children, and neither URI nor cough were shown to have any associations with PM_{10} levels. The only exception was cough in non-urban children, with an odds ratio of 0.88 (95% CI 0.80-0.97) per $100\mu g/m^3$ increase in PM_{10} in the day after an air pollution episode, suggesting a protective effect of living in non-urban areas. Finally, children who suffered from chronic respiratory symptoms were also compared based on whether or not they use any medications for their conditions. Children on medication for asthma residing in urban areas were more likely to suffer from LRI than any other children in the study (OR = 1.80, 95% CI 1.17-2.75, per $100\mu g/m^3$ increase in PM_{10} on the day of an air pollution episode), suggesting that

children with severe underlying respiratory conditions were particularly vulnerable to the acute effects of air particulates.

Peters *et al* studied a small panel of 89 school children for 7 months between 1991 and 1992 in the Czech Republic [Peters *et al* 1997a]. The city of Sokolov was chosen for the study because of its large coal-fired power plant. The wide use of brown coal or lignite with high sulphur and ash content, for both domestic heating and small scale industries further contributed to the high levels of air pollution. The children participated in the study were aged 6-14yrs, and were either asthmatics or suffered from chronic respiratory disease who regularly attended outpatient clinics. Pollutants including TSP, PM_{10}, and particles with strong acidity together with meteorological variables were routinely measured at one central site in the city. Throughout the study period the average TSP and PM_{10} concentrations were 88μg/m^3 and 55μg/m^3 respectively. For particles with strong acidity, the levels were below the minimum detection limit on 79% of the days despite high SO_2 concentrations. Regression models adjusted for temperature, day of week, and other gaseous pollutants have shown significant associations between respiratory symptoms reported in the children and various air pollutants. For TSP, every 70μg/m^3 increase in concentration was associated with a 6% increase (95% CI 1%-11%) in phlegm production on the same day, and the effect was larger with PM_{10} with a 9% increase (95% CI 3%-16%) in odds per 45μg/m^3 increase in its level. Associations were also found between TSP and dyspnoea (OR = 1.01; 95% CI 0.96-1.07) as well as PM_{10} and cough (OR = 1.01; 95% CI 0.97-1.06), and runny nose (OR = 1.03; 95% CI 0.99-1.07) on the same day of an air pollution episode, although the results marginally failed to reach statistical significance. Increased use of asthma medication was also found to be associated with TSP, with an odds ratio of 1.14 (95% CI 1.02-1.28) on the same day.

In Paris, France, Just *et al* followed a panel of 82 medically diagnosed asthmatic children for 3 months from April to June 1996 [Just *et al* 2002]. These children were recruited from an outpatient clinic of a local children's hospital and their age range was 7-15yrs. Parents of the children kept daily symptoms diary during the study period, and at the end of each day they were to record the presence or absence of asthma attacks, upper or lower respiratory infections with fever, and the frequency of

medication use of their children. Daily black smoke and PM_{13} concentrations were collected from 5 monitoring stations within the city together with meteorological information and pollen counts. Logistic regression models adjusted for other factors such as meteorological variables, levels of pollens and other gaseous pollutants were used in the analysis. Results showed that for every $10\mu g/m^3$ increase in black smoke, the odds ratios of developing nocturnal cough in a child who had been free from any asthma symptoms the day before an air pollution episode, were 1.22 (95% CI 0.99-1.51) and 1.36 (95% CI 1.00-1.86) on the day and within 2 days of an air pollution episode respectively. For respiratory infections, the odds were larger at 1.96 (95% CI 1.35-2.84) and 2.08 (95% CI 1.03-4.21) on the day and within 2 days of an air pollution episode respectively. No associations were found between black smoke and asthma attacks, nor PM_{13} and any of the studied symptoms.

So far the reviewed studies have shown some evidence suggesting associations between exacerbation of respiratory symptoms and air particulates pollution, even though the effects were often small, and sometimes only marginally significant. However, not all studies have yielded positive findings. For example, Hoek and Brunekreef recruited 1,000 children from 3 Dutch non-industrial communities and followed them from 1987 to 1990 [Hoek and Brunekreef 1992]. They found no associations between PM_{10} and any of the respiratory symptoms studied including cough (OR = 1.10; 95% CI 0.67-1.79), LRI (OR = 0.88; 95% CI 0.40-1.91) and URI (OR = 1.06; 95% CI 0.71-1.57). Similarly in Sydney, Australia, 125 children were studied for 11 months in 1994 and no associations were found between pollution and symptoms [Jalaludin *et al* 2002]. For every $12\mu g/m^3$ increase in daytime ambient PM_{10} concentration, the odds ratios were 1.01 (95% CI 0.99-1.03), 1.00 (95% CI 0.98-1.03), 1.01 (95% CI 0.99-1.04), and 0.99 (95% CI 0.98-1.01) for wheeze, dry cough, wet cough, and increased medication use on the day of an air pollution episode respectively. Although it is arguable that the odds ratios of wheeze and wet cough were only statistically marginally insignificant, the fact that the effects were so small in such a small group of children (n = 125) it is doubtful whether the associations were real or were found by chance.

2.1.3 Changes in respiratory and cardiovascular symptoms in adults

Short-term changes in cardiorespiratory symptoms caused by particulate air pollution have also been studied in adults, although the number of studies available for reference is fewer compared with those carried out in children. In Southern California, United States, Ostro and colleagues followed 321 non-smoking adults over 6-month period [Ostro *et al* 1993]. The participants were asked to fill in daily symptoms diaries, which were then used in logistic regression analysis to find out the associations between symptoms and ambient sulfates and CoH. Significant association was found between ambient sulfates and LRI, with an odds ratio of 1.30 (95% CI 1.09-1.54) per $10\mu g/m^3$ change in the concentration. However for CoH, which is a more general measure of particulates, the authors have found no associations with any of the symptoms reported.

Changes in respiratory symptoms in adults were also examined in the Dutch study by van der Zee as discussed previously [van der Zee *et al* 2000]. For the adult study, the authors recruited a total of 489 participants aged 50-75yrs from the same regions as the children study. Since the two studies were carried out simultaneously, therefore all air pollution and meteorological data were identical to one another. In symptomatic adults, the effects of PM_{10} in URI were greater in urban adults, although regression analysis marginally failed to show statistical significant associations. For every $100\mu g/m^3$ increase in PM_{10}, the odds ratios of developing URI on the same day was 1.09 (95% CI 0.93-1.29) in urban adults and 0.99 (95% CI 0.85-1.14) for non-urban adults. Black smoke however, showed a stronger effect than PM_{10}. For example, the odds ratio of developing URI on the same day was 1.18 (95% CI 1.01-1.38) for urban adults, and 0.96 (95% CI 0.82-1.12) for non-urban adults. There were no significant evidence linking particulate air pollution to LRI or increased use of bronchodilator in any of the subject groups, and no associations were found between URI and air pollution in healthy adults without chronic respiratory symptoms.

Another study carried out in Paris, France, selected a panel of 60 adults with severe asthma that required frequent medical consultations [Desqueyroux *et al* 2002]. They were followed for 13 months between 1995 and 1996, during which time the levels of PM_{10} and other gaseous pollutants were recorded through a network of urban

background monitoring stations. Every time when the subjects visited their physicians, whether it was regularly scheduled or an emergency, the physicians noted if the patients were enduring an asthma attack as well as other information such as medication use. In addition, the patients also kept a symptom dairy that included information such as the presences of an infection, stress, exposure to allergen etc, which could help to explain the unusual cause of an attack. Logistic regression models were used to estimate the effects of air particulates pollution on asthma symptoms, and the results showed that for every $10\mu g/m^3$ increase in ambient PM_{10} levels, the odds ratio of severe asthma attacks in the patients was 1.21 (95% CI 1.04-1.40) over a period between 3 to 5 days after an air pollution episode. No figures suggested any effects on asthma patients one (OR = 0.87; 95% CI 0.71-1.06) or two days (OR = 0.93, 95% CI 0.80-1.08) after an air pollution episode.

One possible way to examine the acute cardiovascular effects of particulate air pollution is by studying the occurrence of ventricular arrhythmias detected by implantable cardioverter defibrillators (ICD) and ambient air pollution concentrations in the hours immediately before the arrhythmia. ICD devices continuously monitor for ventricular arrhythmias and record the date and time of each detected arrhythmia, which can then be linked to air pollution data to identify any associations between the two. Rich *et al* studied 203 patients with an ICD in Boston, United States [Rich *et al* 2005]. During the follow-up period, 798 ventricular arrhythmias were confirmed in 84 subjects. By matching with the 24-hour average concentrations of ambient $PM_{2.5}$, it was found that for a $7.8\mu g/m^3$ increase in $PM_{2.5}$, the odds ratios of ventricular arrhythmia were 1.08 (95% CI 0.95-1.21), 1.11 (95% CI 0.98-.126), and 1.19 (95% CI 1.02-1.38) within 2hrs, 6hrs, and 23hrs after an air pollution episode respectively. In contrast, Peters *et al* followed 100 cardiac patients with ICD devices in eastern Massachusetts, United States for over 3 years but did not find any significant associations between the levels of $PM_{2.5}$ and cardiac arrhythmia [Peters *et al* 2000].

2.2 Evaluation of long-term effects using chronic exposure studies

While results from time-series studies showed evidence of the acute effects of exposure to increased levels of air particulates, little information is provided as to how particles effect mortality rates in longer-term nor their ability to induce chronic

diseases that may lead to increased mortality. When studying long-term effects, exposure classification uses spatial differences in air pollution as their outcome across communities and neighbourhoods with different levels of air pollution. These studies use longer-term pollution data which varies from a year to decades. Chronic exposure studies allow the examination of the long-term effects of constant exposures to low or moderate level of air particulates over a long period of time, as well as the cumulative effects of repeated exposure to elevated levels of pollution.

2.2.1 Increased mortality

Based on several historic events of severe air pollution such as the 1942 Donora smog and 1952 London smog, a temporal correlation between air pollution and acute increases in mortality was well established. However, subsequent epidemiological studies have reported adverse health effects even at a much lower level of particulate air pollution [Pope and Dockery 1999]. Three large-scale cohort studies all carried out in the United States have shown that prolonged exposure to air particulates increased mortality rate in the long-term. Although most epidemiological studies were focused on short-term effects, results from these long-term studies provided information that exposure to air particulates over a long period of time may be more important in terms of overall public health. Of the three long-term exposure studies the earliest one was the Harvard Six-Cities Study [Dockery *et al* 1993]. Random samples of adults were selected from six US communities, first started from Watertown in Massachusetts in 1974 and gradually including other communities in the subsequent years until 1977. A total sample of 8,000 white subjects aged 25 to 74yrs at enrolment was recruited. Information on vital status were collected from all subjects each year until June 1991. The total duration of follow up was 14 to 16 years, which was equivalent to 111,076 person-years. Death certificates were obtained for 1,401 subjects who died throughout the course of the study, of which 8.4% were due to lung cancer and 53.1% were due to cardiorespiratory disease. Air pollution data were collected from central monitoring stations which measured $PM_{2.5}$ and PM_{10} and other gaseous pollutants. The average concentrations of ambient particulates recorded for the cities ranged from 11.0 to 29.6$\mu g/m^3$ and 18.2 to 46.5$\mu g/m^3$ for $PM_{2.5}$ and PM_{10} respectively. Cox proportional hazards models adjusted for age, sex, smoking, education and body-mass index were used for the analysis and examined the adjusted mortality rates across the range of

exposure for each pollutant among the six cities. The Cox proportional hazards model is a regression model commonly used for analysing survival data, and allows the estimation of survival curves in the presence of covariates. Using $PM_{2.5}$ as an indicator of air pollution, results showed increased risk of death (RR = 1.37; 95% CI 1.11-1.68) due to cardiopulmonary causes in communities with the highest levels of pollution. Results also showed higher risks of lung cancer deaths (RR = 1.37; 95% CI 0.81-2.31) and all other deaths (RR = 1.01; 95% CI 0.79-1.30) but were both statistically insignificant. Similar results were generated when PM_{10} concentrations were studied instead of $PM_{2.5}$. The authors concluded that because the six cities were chosen as representative range of particulate air pollution in the United States, these ratios should therefore roughly represent the relative risk associated with that range.

A second large-scale American cohort study on the time line was the Adventist Health Study of Smog (AHSMOG Study). In 1977 a total sample of 6,338 non-smoking white adults were recruited into the study [Abbey *et al* 1999]. The participants, aged between 27 and 95yrs at enrolment were residents of the Seventh-day Adventists (SDAs) of California. The study consisted of relatively old subjects, with a mean age of 58.5 years for men and 59.2 years for women. The cohort was followed-up through to 1992 in which information on respiratory symptoms, lifestyle, and housing characteristics were obtained periodically to classify individuals according to their health status as well as estimates of exposures to both ambient and indoor air pollution. Concentrations of PM_{10} prior to 1987 were estimated using site- and season-specific regressions based on TSP. Since 1987 PM_{10} had replaced TSP as the particulate pollutant monitored throughout California, so monitored PM_{10} levels were available in the following years. Air pollution exposures were estimated based on the level of TSP / PM_{10} concentrations recorded in nearby monitoring stations not more than 50km away from the residences' zip code centroids. The monthly mean PM_{10} concentration throughout the study was 51.2$\mu g/m^3$ with the maximum recorded value of 83.9$\mu g/m^3$ and an interquartile range of 24.1$\mu g/m^3$. During the follow-up period, 1,628 deaths were identified through record linkage with the state and national death certificate files, as well as the authors' own tracing through the church records. Sex-specific adjusted mortality relative risks were estimated using Cox proportional hazard models adjusted for exposure to passive smoking, education, occupation, and

body mass index. Since air pollution data were not available prior to 1973, the authors had to omit the first 3 years of cancer deaths (1977-1979) in the analysis to allow the relatively long latency period between exposure and cancer development. In the single-pollutant analysis, results showed for men only an increased exposure of 43days/yr to PM_{10} concentrations exceeded $100\mu g/m^3$, the relative risks of death were 1.12 (95% CI 1.01-1.24) for all natural causes, 1.28 (95% CI 1.03-1.57) for non-malignant respiratory diseases, and 2.38 (95% CI 1.42-3.97) for lung cancer. Increased risk of death from cardiorespiratory diseases was also seen but marginally failed to achieve statistical significance (RR = 1.09; 95% CI 0.95-1.24). In contrast, no statistically significant associations were found in women for all natural causes (RR = 0.94; 95% CI 0.86-1.03), cardiopulmonary diseases (RR = 0.90; 95% CI 0.80-1.01), non-malignant respiratory diseases (RR = 1.10; 95% CI 0.91-1.33), and lung cancer (RR = 1.08; 95% CI 0.55-2.13). As part of the AHSMOG study, McDonnell *et al* studied a subset of samples of 3,700 males who resided near airports. However, this time no statistically significant associations were found between particulate air pollution and mortality of all natural causes, lung cancer, and respiratory disease [McDonnell *et al* 2000].

The third large-scale cohort study was carried out based on data collected by the American Cancer Society (ACS) Cancer Prevention Study (CPS-II), involving approximately 1.2 million adults [Pope *et al* 2002]. Recruitment of subjects was carried out with the assistance of 77,000 ACS volunteers in 1982 from all 50 US states, the District of Colombia, and Puerto Rico, and were generally their relatives, friends, neighbours, or acquaintances [Thun *et al* 2000]. Enrolment was restricted to individuals who were 30yrs of age or above and who were members of households with at least one individual aged 45yrs or older. Basic background information of the participants such as demographic characteristics and disease history were obtained through the completion of a self-administered questionnaire. Deaths were recorded via a linkage to the US National Death Index as well as reports from relatives and friends of the deceased individuals. The analysis of the relationship between mortality and air pollution was restricted to a subset of adults where pollution data were available in their areas of residence. As a result the authors included only 295,000 adults in the final analysis. Estimated concentrations of $PM_{2.5}$ based on the levels of

TSP and PM_{10} were used in the analysis, because $PM_{2.5}$ was not monitored in the United States until 1999 as a consequence of the new air particulates monitoring standard. Between the period of 1979 and 1983, daily concentrations of $PM_{2.5}$ were estimated to be 21.1μg/m^3. A total of 20,765 deaths were recorded in this sub-sample and death certificates were obtained for 96% of the total deaths. Using Cox proportional hazard models stratified by sex, race, and 5-year age groups, risk ratios of all-cause and cause-specific mortality were estimated after adjusting for smoking, education, body mass index, alcohol consumption, and occupational exposure to a number of substances. Results showed that for all cause mortality due to exposure to $PM_{2.5}$ between 1979 and 1983, the adjusted relative risk associated with a 10μg/m^3 change in $PM_{2.5}$ was 1.04 (95% CI 1.01-1.08). The relative risks of death were 1.06 (95% CI 1.02-1.10) for cardiorespiratory diseases and 1.08 (95% CI 1.01-1.16) for lung cancer. No association was found for all other causes (RR = 1.01; 95% CI 0.97-1.05).

In 2000, the Health Effects Institute (HEI) of the United States commissioned a reanalysis of the Harvard Six-cities study and the ACS study [Krewski *et al* 2003]. Raw data of the Harvard study and the regenerated data of the ACS study were audited. A few minor errors were discovered but once corrections were made they did not have any marked effects on the original results. The reanalysis also extended to cover some key questions raised when the results were first published, including physical activity, lung function, population mobility, martial status, measures of income, unemployment, maximum temperature, hospital beds per unit of population, water hardness, and a more detailed examination of smoking, occupation, education and age, but no confounders were discovered that would otherwise significantly change the associations found. The reanalysis also found that when age group was stratified the risk per unit measurement of particulate matter did not vary markedly between the <50, 50-65 and >65 years old, nor in subjects with pre-existing heart or lung diseases or in smokers and non-smokers.

After the HEI reanalysis was published, the Institute of Occupational Medicine (IOM) developed a methodology for quantifying the long-term effects of air pollution in the UK [COMEAP 2000, COMEAP 2001]. The analysis linked the result of the US

cohort studies and adapted it with the age and mortality characteristics of the UK population. This allowed an estimate of the possible life loss due to long-term exposure to particles. Based on the population of England and Wales alive in 2000, COMEAP made the following estimations; if a $10\mu g/m^3$ reduction in PM_{10} was maintained for the rest of the lives of this population, then the population would gain between 4 and 26 million life years with a mid-estimate of 7.5 to 17.5 million life years, which is equivalent to about 1 to 6 months per person; if the $10\mu g/m^3$ reduction was maintained for 5 years, the population would gain 10,000 to 350,000 life years with a mid-estimate of 20,000 to 240,000 life years, which can be expressed in another way as a reduction of 1,500 to 48,000 deaths over 5 years. However, it should be noted that the gains in life expectancy are unlikely to be equally distributed amongst the whole population. The benefits of reduction in PM_{10} have also been calculated in the APHEIS study (Air Pollution and Health: A European Information System) [Medina *et al* 2002]. For long-term risks, it was estimated that a decrease of $5\mu g/m^3$ in ambient PM_{10} levels with other factors unchanged in 9 French cities would prevent 1,561 anticipated deaths. When the same scenario is applied in 19 European cities with a total population of 32 million people, 5,547 deaths would be prevented. Finally if the annual PM_{10} limit of $20\mu g/m^3$ set by the European Commission were achieved in those 19 European cities, a total of 11,855 deaths would be prevented.

A European study carried out in the Netherlands investigated the long-term consequences of exposure to traffic-related air pollution in a cohort of 5,000 people aged 55 to 69yrs [Hoek *et al* 2001, Hoek *et al* 2002]. Subjects were chosen from the full cohort of the Netherlands Cohort Study on Diet and Cancer (NLCS) started in 1986 and involved 120,000 participants aged 55-69 years at enrolment. Exposure to traffic-related black smoke was estimated based on the subjects' areas of residences and the regional and urban background concentration. The authors estimated that local motor traffic emissions would lead to spatial variations between areas resulting in a higher concentration of pollutants at short distances from major road. As a result geographic information system (GIS), which is a computer system for managing spatial data, was used to classify participants living within a 100m distance from a freeway or 50m from a major road as exposed. The mean level of exposure to outdoor air pollution in long-term was calculated as a function of the regional background

pollution, pollution from urban sources (urban background), and pollution from nearby sources (nearby streets/roads). Both regional background and urban background were estimated using the black smoke data obtained from the National Air Quality Monitoring Network. As for local sources, the authors used measurement data from two Dutch traffic studies. On the basis of the data, living within 100m of a freeway resulted in exposure to black smoke concentration of 4.4μg/m^3, and for people living within 50m of a major inner-city road they were estimated to be exposed to 13μg/m^3 of black smoke concentration. These estimates were assigned to each exposed address independent of the actual distance to the road. After adjusting for confounders such as smoking habit, exposure to passive smoking, occupation, and alcohol consumption, results showed a relative risk of 1.95 (95% CI 1.09-3.51) for cardiopulmonary mortality amongst those who were living close to major roads. No relationships were found between exposure to black smoke and respiratory diseases or lung cancer. This study used a different approach from the two American cohort studies mentioned previously, in which exposure to air pollutants were based on the proximity of the residences from any major freeways or urban roads. In contrast, the American studies used an ecological indicator of exposure and assumed the same level of exposure across the same geographical area.

While increased mortality as a response to particulate air pollution was observed in adults, studies have shown similar effects in infants in their postneonatal period which appeared to be specific to respiratory causes. In the Czech Republic, Bobak and Leon studied 2,500 infant deaths between 1989 and 1991 and the possible association with TSP exposure in a case-control study [Bobak and Leon 1999]. After adjusting for maternal socioeconomic status, birth weight, birth length, and gestational age, the authors found a strong effect of TSP on postneonatal mortality from respiratory causes with an odds ratio of 1.74 (95% CI 1.01-2.98) per 50μg/m^3 increase in the pollutant's concentration. The effects seen were independent of socioeconomic factors and were not mediated by birth weight or gestational age. Results of this study confirmed Bobak and Leon's earlier findings, in which a relative risk of postneonatal mortality of 2.41 (95% CI 1.10-5.28) was observed in neonates who were exposed to the highest quintile of TSP compared with those exposed to the lowest quintile [Bobak and Leon 1992]. Woodruff *et al* analysed the association between early

postneonatal mortality and PM_{10} levels in approximately 4 million infants born between 1989 and 1991 in the United States [Wooddruff *et al* 1997]. The subjects were formed into different categories of high, medium, and low according to their levels of exposure to ambient PM_{10}. The overall mortality rates per 1,000 births were 3.1 among infants with low PM_{10} exposures, 3.5 among infants with medium PM_{10} exposures, and 3.7 among infants with high exposures. The effects were then examined by logistic regression controlled for demographic and environmental factors. The odds ratio of total postneontal mortality for the high exposure versus low exposure groups was 1.1 (95% CI 1.04-1.16). In infants with normal birth weight, exposure to high levels of PM_{10} was associated with respiratory deaths (RR = 1.4; 95% CI 1.05-1.85) and sudden infant death syndrome (RR = 1.26; 95% CI 1.14-1.39). No statistically significant results were found in infants with low birth weight.

2.2.2 Increased cancer incidence and mortality

Evidence showing an increasing incidence of lung cancer in the United States and Western Europe has led researchers to examine the possible role of air pollution on cancer development. In industrialised urban areas, known human carcinogens such as benzo[a]pyrene can be found in the outdoor air attached onto the surfaces of carbonaceous particles of the respirable range. Combustion of fossil fuels also releases carcinogenic particles into the air - diesel exhausts have been classified as a probable human carcinogen by the IARC [IARC 1989]. Few studies have been carried out to answer the question as to whether particulate air pollution causes lung cancer. The methods used were usually population-based cohort study design or case-control study design. Nonetheless they have both produced consistent results, showing positive relationships between particulate air pollution and cancer.

In Italy, Barbone *et al* conducted a case-control study to examine the relationships between lung cancer mortality and exposure to particulate air pollution [Barbone *et al* 1995]. From 1979 to 1981 and from 1985 to 1986 the levels of exposure to TSP of 1,510 deceased individuals were studied, of which half died of lung cancer and the other half died from other causes. After controlling for age, smoking, and occupation, the odds ratios of lung cancer deaths were 1.5 (95% CI 1.0-2.2) for residents of the city area, 1.4 (95% CI 1.0-2.1) for residents of the industrial area, and 0.6 (95% CI 0.4-1.0) for residents of the rural area. In Poland, Jedrychowski *et al* studied 2,100

individuals and compared their exposures to TSP [Jedrychowski *et al* 1990]. After adjusting for age, smoking, and occupation, the odds ratio of developing lung cancer amongst men living in highly polluted areas was 1.5 (95% CI 1.1-2.0) compare with those living in areas with low pollution levels.

In the United States, Vena studied 1,100 individuals residing in different areas within the Erie County of New York between 1957 and 1965 [Vena 1982]. Mean TSP levels ranged from 80 to 200μg/m^3 across towns. Results showed that for men exposed more than 50yrs to high levels of particulate air pollution, the odds ratio of lung cancer development was 1.7 (95% CI 1.0-2.9) after adjusting for age, smoking, and occupation. In Canada, a study of 96 women showed when residing in large urban areas the odds ratio of developing lung cancer was 2.3 times higher than those residing in small town or the countryside [Holowaty *et al* 1991]. Using data extracted from the cohort of the AHSMOG study, Beeston *et al* calculated that for an increase of 24μg/m^3 in PM_{10} concentrations, the relative risk of developing lung cancer was 5.21 (95% CI 1.94-13.99) among men. In contrast no statistically significant associations were observed in women. The authors explained the differences seen could be due to gender differences in exposure. Sanasuttipun *et al* studied 1,400 cases of lung cancer and 1,800 controls from the regions of Connecticut and Utah / Idaho, United States, retrospectively [Sanasuttipun *et al* 2002]. Among the regions, Connecticut had a relatively lower annual TSP level. Adjustments were made for age, sex, and cigarette consumption in the analysis and the selection probabilities used in randomised recruitment were also accounted for. Results showed that the odds ratios of lung cancer per 10μg/m^3 increase in TSP was 2.4 (95% CI 2.0-3.0) for Connecticut, and 1.3 (95% CI 1.1-1.5) for Utah / Idaho. Connecticut showed higher odds of lung cancer despite its relatively lower level of annual TSP. The authors proposed that this could be due to differences in the physical and chemical compositions between the areas.

2.2.3 Effects on birth outcome

Studying the effects of air pollution on birth outcome has become an important emerging field in environmental epidemiology. Birth outcomes serve as indicators of the health of the newborns and infants, and complications such as low birth weight

and prematurity are known to influence the subsequent health status of the individual. These include increased mortality and morbidity in childhood and an elevated risk of hypertension, coronary heart disease, and non-insulin-dependent diabetes in adulthood [Barker 1995, Osmond and Baker 2000]. For foetuses, due to their developing organ systems, physiological immaturity, and high rates of cell proliferation are particularly vulnerable to environmental pollutants [Perera *et al* 1999, Sram 1999] – a concept being similar to the association between maternal active and passive smoking and impaired reproductive outcomes. In a population-based case-control study carried out in the United States, Rogers *et al* analysed the combine effect on very low birth weight (<1,500g) of SO_2 and TSP levels, using annual exposure estimates [Rogers *et al* 2000]. Results showed that for babies born to mothers who were exposed to concentrations of the combined pollutants above the 95% percentile of the exposure distribution (56.8μg/m^3), the relative risk of low birth rate was 2.88 (95% CI 1.16-7.13). Another study carried out in the United States has found similar result – the authors examined the association between PM_{10} and birth weight in northern Nevada between 1991 and 1999, and found that a 10μg/m^3 increase in mean PM_{10} concentrations during the third trimester of pregnancy was associated with a reduction in birth weight of 11g (95% CI 2.3-19.8) [Chen *et al* 2002]. A European study carried out in the Czech Republic examined the relationship between low birth rate, premature birth, and ambient TSP during each trimester in 108,000 singleton live births [Bobak 2000]. The effects of these adverse birth outcomes were marginally stronger for exposures during the first trimester. For a 50μg/m^3 increase in TSP, the odds ratios of low birth rate and prematurity were 1.15 (95% CI 1.07-1.24) and 1.18 (95% CI 1.05-1.31) respectively. In China, Wang *et al* examined the effects of TSP on birth weight in four highly polluted areas of Beijing [Wang et 1997]. A cohort of 75,000 newborns was followed from early pregnancy until delivery. Regression models adjusted for gestational age, residence, year of birth, maternal age, and infant gender found that the mean birth weight was reduced by 6.1g for each 100μg/m^3 increase in TSP. The relative risk of low birth rate in association with a 100μg/m^3 increase TSP was 1.10 (95% CI 1.05-1.14). In another study carried out in Asia, Ha and colleagues examined 277,000 full-term births for a 2-year period in Seoul, South Korea [Ha *et al* 2001]. Results showed an increased risk of 4% (RR = 1.04; 95% CI 1.00-1.08) for low birth rate, and a 6.09g (95% CI 3.85-8.27) reduction in birth weight

for a 14.3μg/m^3 increase in prenatal exposure to TSP. The authors proposed that the adverse outcome maybe attributable to the production of free radicals induced by PM_{10} which resulted in an inflammatory response and enhanced blood viscosity. In contrast both Landgren, who studied the effects of air pollution on delivery of 38,000 Swedish women in 1985-1990 [Landgren 1996], and Maisonet *et al*, who studied the effects of PM_{10} in live births born in six northeastern cities of the United States [Maisonet *et al* 2001] showed results with no indication of any positive associations between prenatal exposure to particulate air pollution and low birth weight.

2.2.4 Changes in respiratory symptoms in adults

Studies have revealed significant associations between prolonged exposures to ambient air pollution and increased prevalence or incidence of varies respiratory symptoms in adults. In the United States, Schwartz used data collected from the first US National Health and Nutrition Examination Survey (NHANES I) to investigate the health effects of long-term exposure to particulate air pollution [Schwartz 1993]. A total of 3,800 adults aged between 30 and 74yrs were recruited from 53 urban areas across the country where TSP data were available. The frequency and severity of respiratory symptoms were recorded by symptoms questionnaires as well as through diagnosis by physicians, and the data were modelled in logistic regression controlled for age, sex, ethnicity, and smoking. The average concentration of TSP during the study period was 85.5μg/m^3. For every 10μg/m^3 increase in annual TSP concentration it was found to be significantly associated with chronic bronchitis (OR = 1.07; 95% CI 1.02-1.12) and respiratory illnesses diagnosed by a physician (OR = 1.06; 95% CI 1.02-1.10). No associations were found between TSP and the prevalence of asthma or dyspnoea. When smokers were completely removed from the model, the odds ratio for chronic bronchitis was increased to 1.11 (95% CI 1.02-1.21). However, TSP was only marginally significant as a predictor for respiratory illnesses diagnosed by a physician (OR = 1.07; 95% CI 1.00-1.15).

Data extracted from the AHSMOG study has also shown positive associations between the development of chronic respiratory symptoms and long-term exposure to particulate air pollution. Results published in 1987 using a subset of 7,400 non-smoking participants aged >25yrs showed a 22% increased risk of developing chronic

obstructive pulmonary disease symptoms when exposed to TSP levels above 200μg/m^3 for 750hrs per year [Euler *et al* 1987]. Other results from the AHSMOG study had also been published. One included a subset of 1,800 participants resided in the vicinity of nine airports throughout California and found that long-term exposure to ambient concentrations of $PM_{2.5}$ in excess of 20μg/m^3 were associated with the development of chronic bronchitis symptoms [Abbey *et al* 1995a]. In addition, the mean concentration of $PM_{2.5}$ was also associated with the increasing severity of respiratory symptoms relating to chronic obstructive pulmonary disease, chronic bronchitis, and asthma. Another study involved a subset of 3,900 participants and the authors found that the relative risks associated with exposure to concentrations of PM_{10} that exceeded 100μg/m^3 for 1,000hrs per year were 1.17 (95% CI 1.02-1.33) for airway obstructive disease, 1.21 (95% CI 1.02-1.44) for productive cough, and 1.30 (95% CI 0.97-1.73) for asthma symptoms [Abbey *et al* 1995b]. The risk was further increased to 1.66 (95% CI 1.15-2.33) in individuals with airway obstructive disease as a child.

In Europe, Heinrich and colleagues carried out a cross-sectional survey in Germany to investigate the possible relationships between respiratory health and local traffic [Heinrich *et al* 2004]. A cohort of 6,900 participants aged between 18 and 79yrs from the German Health Survey 1998 took part in the study. Self-administered questionnaires were given to the cohort to collect information on traffic intensity within their areas of residence. In addition, the European Community Respiratory Health Survey (ECRHS) questionnaire was used for collecting data on respiratory health. Logistic regression model was used to assess the relationship between traffic exposure and various health outcomes. Of the total study population, 64.5% were residing in areas with low traffic, 11.6% in areas with moderate traffic, and 23.9% in areas with high traffic. After adjusting for age, gender, education, community size, and smoking, results showed that living on busy roads compared with low-trafficked areas was significantly associated with chronic bronchitis (OR = 1.36; 95% CI 1.01-1.83). In addition, increased odds of nocturnal cough (OR = 1.24; 95% CI 0.98-1.57) and wheeze (OR = 1.21; 95% CI 0.93-1.57) were also observed, although both figures were statistically insignificant. In Switzerland, the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) study investigated health effects of air

particulates in a cross-sectional survey involving a random sample of 9,600 adults between the age of 18 and 60yrs from 8 different areas representing a range of air pollution exposure, urbanisation, altitude, and meteorological conditions [Zemp *et al* 1999]. Respiratory health data were collected using the European Community Respiratory Health Survey (ECRHS) questionnaire as well as assessments through spirometry, bronchial challenge tests, and allergy tests. Logistic regression models controlled for potential confounders such as age, body mass index, gender, and parental asthma and atopy showed that the odds for a $10\mu g/m^3$ increase in the annual mean concentration of PM_{10} was 1.35 (95% CI 1.11-1.65) for chronic phlegm production, 1.27 (95% CI 1.08-1.50) for chronic cough, 1.33 (95% CI 1.14-1.55) for breathlessness, and 1.32 (95% CI 1.18-1.46) for dyspnoea on exertion. The study also showed that a $10\mu g/m^3$ difference in PM_{10} levels between different zones led to a 41% difference in the frequency of dyspnoea and a 31% difference in the prevalence of bronchitis. Lung functions were also shown to be worse in the most polluted regions in the study. Since the annual mean PM_{10} concentration in the study areas was $21.2\mu g/m^3$ (range $10.1\text{-}33.4\mu g/m^3$), thus this study provided evidence that long-term exposure to even moderate levels of air particulates was associated with higher prevalence of respiratory symptoms in adults.

2.2.5 Changes in respiratory symptoms and lung functions in children

The effects of particulate air pollution on children warrant a separate section of review from those of the adults. Exposure to air pollution in children is a special concern because their immune system and lungs are not fully developed when exposure begins, and thus they may have different responses than those seen in adults. Children are physically different from adults because the human lungs are not well formed at birth until approximately 6yrs of age, when full functionality develops [Schwartz 2004]. For example, the number of alveoli in the human lung increases from 24 million at birth to 257 million at age 4 [Dunnil 1962]. Moreover, their lung epithelium is not fully developed, resulting in greater permeability of the epithelial layer [Schwartz 2004]. Children also have a larger lung surface area per kilogram of body weight than adults, and under normal breathing they will breathe 50% more air per kilogram of body weight than adults [Schwartz 2004]. In addition, exposure to air pollutants is higher in children because they tend to spend more time outdoors,

particularly in the summer and in the late afternoon [EPA 1997], although this may vary between children and the country / area they reside. One hypothesis suggests that preadolescent children with decreased level of lung function growth may be more susceptible to respiratory infections and environmental pollutants in their childhood, and this may subsequently lead to the development of chronic airflow obstruction in adult life [Jedrychowski 1999].

In a case-control study conducted in New York, Lin *et al* studied 400 children aged 0-14yrs who were admitted to the hospital for asthma [Lin *et al* 2000]. The group was compared with 400 age-matched controls who were admitted for non-respiratory conditions. Exposure assessments were carried out by linking the children's residential addresses to traffic information regarding vehicle miles travelled on their streets. Results showed that after adjusting for age and poverty, children hospitalised for asthma were more likely to live on roads with the highest tertile of vehicle miles travelled within 200m of their residence (OR = 1.93; 95% CI 1.13-3.29) and were more likely to have trucks and trailers passing by within 200m of their residence compared to the controls (OR = 1.43; 95% CI 1.03-1.99). However, no associations were found between hospital admission and annual vehicle miles travelled within 500m, nor whether trucks or trailers passed by within 500m. These suggested that local traffic within proximity of the children's residences have larger impact on their respiratory health than those that are further away. A Dutch cross-sectional study examined whether motor vehicle exhaust fumes from nearby freeways had any effects on respiratory health of children [van Vilet *et al* 1996]. The study was conducted in six residential areas with a large number of homes located within 300m of a major freeway which carried 80,000 to 150,000 vehicles per day. A total of 1,500 children aged between 7 and 12yrs took part in the study and questionnaires on respiratory symptoms were completed by their parents. Chronic cough (OR = 1.64; 95% CI 0.98-2.74) and wheeze (OR = 2.00; 95% CI 0.99-4.03) were found to be related, but marginally failed to reach statistical significance, to children living within 100m of a freeway. When stratified by sex, the associations have become statistically significant in girls with an OR of 2.45 (95% CI 1.16-5.56) for chronic cough and 3.05 (95% CI 1.11-8.41) for wheeze. For boys, the effects on chronic cough (OR = 1.05, 95% CI 0.50-2.22) and wheeze (OR = 1.29, 95% CI 0.45-3.68) were reduced and remained statistically insi gnificant. Braun -Fahrlander and other members of the SCARPOL

team (Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution, Climate and Pollen) investigated the impact of long-term exposure to air pollution on 4,400 schoolchildren living in 10 different communities in Switzerland [Braun-Fahrlander *et al* 1997]. The team studied the levels of PM_{10} and other gaseous pollutants in each community and the reported respiratory symptoms rates from children. Results showed that between the least and most polluted communities the levels of PM_{10} were associated with chronic coughs (OR = 3.07; 95% CI 1.62-56.81), nocturnal dry cough (OR = 2.88; 95% CI 1.69-4.89), and bronchitis (OR = 2.17; 95% CI 1.21-4.89). However, no relationships were found between long-term exposure to air pollution and asthmatic or allergic symptoms and illnesses.

A large-scale multi-centre cross-sectional survey carried out in 24 communities in the United Sates and Canada examined the effects of exposure to acidic air pollution in children [Dockery *et al* 1996, Raizenne *et al* 1996]. Regions of the eastern United States and Southern Canada experienced the greatest levels of particles with strong acidity, sulphate, and particle mass concentrations during the spring and summer months [Spengler *et al* 1996]. A total of 13,300 white children aged 8-12yrs were recruited from 24 communities which varied in acid aerosols levels. Information on respiratory symptoms were collected via questionnaires and lung function tests were also performed. After adjusting for confounders such as sex, history of allergies, parental asthma, parental education, and exposure to passive smoking, logistic regression models found positive associations between levels of fine particulates with strong acidity and bronchitis (OR = 1.65; 95% CI 1.12-2.42). In addition, results also shown that a 52nmol/m^3 difference in annual mean particles with strong acidity was associated with a 3.5% (95% CI 2.0-4.9) decrement in forced vital capacity (FVC) and a 3.1% (95% CI 1.6-4.6) decrement in forced expiratory volume in 1 second (FEV_1). FVC measures the total amount of air that can be forcibly blown out after full inspiration, and in contrast FEV_1 only measures the amount of air that can be forcibly blown out in one second. These tests are considered as the primary indicators of lung functions. Despite the relationships found between ambient particles and declined lung functions, the authors found no associations between exposure and wheeze, cough, and phlegm.

A prospective cohort study involving 1,700 children showed relationships between reduced lung growth in children and particulate air pollution [Gauderman *et al* 2004]. The study known as the Children's Health Study, followed the cohort of 10-yr old children from 12 southern California communities from 1993 to 2001, by then all had reached the age of 18. Details on lung functions and other baseline characteristics were collected through annual questionnaires and spirometric testing of the children. Levels of PM_{10} and both mass and chemical makeup of $PM_{2.5}$ were monitored by air-pollution-monitoring stations established in the 12 studied communities. Results generated by regression models adjusted for height, body-mass index, race, asthma, smoking habit, passive smoking, and respiratory illness on the day of the test, showed that lung development from the ages of 10 to 18yrs was reduced in children exposed to higher levels of ambient air pollution. For example, comparing the average growth of FEV_1 in children from the least and the most polluted communities, there was a 79.7ml difference (95% CI 6.4-153.0) for $PM_{2.5}$ and an 87.9ml difference (95% CI 29.4-146.4) for elemental carbon particles. However, no association was found between lung development and PM_{10}. In addition, during the last year of follow-up the authors have selected a subgroup of children with clinically significant deficit in attained FEV_1 to determine whether this was associated with exposure to air pollution. Such condition was defined as an attained FEV_1 below 80% of the predicted value, which is a criterion commonly used in clinical settings to identify persons who are at risk of adverse respiratory conditions. Across the 12 communities, clinically low FEV_1 was positively correlated with the levels of PM_{10} ($P<0.01$), $PM_{2.5}$ ($P<0.01$), and elemental carbon particles ($p<0.01$). For example, the estimated proportion of children with low FEV_1 was 1.6% at the lowest level of exposure and 7.9% at the highest level of exposure to $PM_{2.5}$. The authors continued to comment that those with clinically significant deficits in lung development in the study were unlikely to reverse as they complete the transition into adulthood. This was based on the fact that lung development are more or less completed in humans at the age of 18, and although boys will continue to develop until their early 20s, the much reduced rate of development will not lead to any significant changes in their conditions.

Decreased respiratory functions associated with long-term exposure to road traffic have been found in a cross-sectional study in Munich which examined 6,500 children aged 9-11yrs [Wjst *et al* 1993]. Density of motor traffic in the children's school

districts ranged from 7,000 to 125,000 cars per day. Respiratory symptoms collected by questionnaires and lung function tests results were analysed by regression models. Peak expiratory flow, which measures the speed of air moving out of the lungs at the beginning of the expiration, showed a significant decrease by 0.71% (95% CI 1.08%-0.33%) per increase of 25,000 cars per day passing through the school district on the main road. Forced Expiratory Flow 25-75%, which measures the average flow of air coming out of the lungs during the middle portion of the expiration, was decreased by 0.68% (95% CI 1.11%-0.25%). In addition, the prevalence of recurrent wheezing (OR = 1.08; 95% CI 1.01-1.16) and recurrent dyspnoea (OR = 1.10; 95% CI 1.00-1.20) with the same exposure were also increased. Since the unification of Germany in 1990 reduction in air pollution levels was seen in the former East Germany. Frye *et al* used this opportunity to demonstrate the benefits of such reduction in newer generations of children with improved lung functions [Frye *et al* 2002]. Three consecutive cross-sectional surveys were carried in 1992/1993, 1995/1996, and 1998/1999, in which lung function tests were performed in 2,500 children aged 11-14 from three communities in East Germany in each of the surveys. During the duration of the three surveys the annual mean of TSP declined from 79μg/m^3 to 25 μg/m^3, and the mean FVC of the three different generations of children increased from 1992/1993 to 1998/1999. The adjusted change of FVC was 4.7% (95% CI 0.2%-9.5%) per 50 μg/m^3 decrease in TSP. The significance of this study is not merely the demonstration of an association but that an intervention, i.e. the reduction of TSP produced improvements in health.

One thousand 9-year old children from two areas in Poland were recruited in a 2-year prospective cohort study to investigate the effects of black smoke and SO_2 on lung function growth [Jedrychowski 1999]. Daily concentrations of the pollutants of interest were obtained from the city network of 17 air monitoring stations. The children were assigned into either a high exposure group or a low exposure group depending on the levels of pollutants within the areas of their schools and residences. Lung function tests were performed on all children in 1995 and information on the children's household characteristics and respiratory health were collected from their parents. The same tests were performed 2 years later in 1997 and the results were compared. It was found that there were significant differences in lung function growth in children between the two groups, and larger increments for both FVC (0.517L v

0.497L in boys, 0.412L v 0.394L in girls) and FEV_1 (0.517L v 0.455L in boys, 0.434L v 0.394L in girls) were seen in children from the low exposure group regardless of gender. Results from a subset of children with slow lung function growth were also analysed. Slow lung function growth was defined by the authors as the lowest quintile of distribution of a given spirometric test. Using logistic regression models controlled for confounders such as environmental tobacco smoke, home heating, the presence of moulds in the household, and parental education, in boys the odds ratios were both 2.1 for the occurrence of slow lung function growth as measured by FVC (95% CI 1.27-3.46), and FEV_1 (95% CI 1.27-3.48). However, no significant effects were observed in girls. Similarly in Austria, 1,000 children in grades 2-3 were recruited from 8 areas in the region of lower Austria and were followed up between 1994 and 1997 [Horak Jr *et al* 2002]. Data on respiratory symptoms of the children were collected annually through questionnaires completed by their parents, and lung function tests were performed on the children twice a year. Collection of PM_{10} data was carried out using Harvard Impactors with an air flow of 4L/min set up at the children's schools. Pre-weighed Teflon filters were used to collect PM_{10} samples which were changed at 2-weekly intervals and reweighed. Results controlled for sex, atopy, passive smoking, height, initial height, and initial lung functions showed that an increase of summer PM_{10} by $10\mu g/m^3$ was associated with an 84ml/yr decrease in FEV_1 growth. In addition, mid-expiratory flow between 25 and 75% of the forced vital capacity (MEF_{25-75}), which is a lung function proxy for the development of small airways, showed a decrement of 329ml/s/yr for an increase of summer PM_{10} by $10\mu g/m^3$.

2.3 Mechanisms of adverse health effects caused by air particulates

While the health effects of respirable air particulates have been recognised little is known about the exact mechanism of damage. Most of the studies that examined the effects of particles on biological systems were often laboratory-based and carried out in cell lines or animal models. Currently the research is still in its early stages but several possible mechanisms have been suggested.

2.3.1 Effects on the cardiovascular system

Blood circulation in the body relies on correctly functioning control mechanisms. Cardiac death is the consequence of a complex interaction between the autonomic

nervous system, the current state of the myocardium, and the constant endogenous and exogenous stimuli the myocardium experienced which may predispose it to an adverse cardiac outcome. Usually the presence of a single condition is not sufficient to trigger cardiac events but sometimes a biological or psychological stress can induce a cascade of event leading to cardiac complications and even cardiac death [Zareba *et al* 2001]. Air pollution may be a stress factor sufficient to trigger this chain of events, especially in compromised individuals such as the elderly and patients with pre-existing cardiorespiratory conditions. The epidemiological evidence associated with increased cardiovascular morbidity and mortality with air pollution indicated several possible mechanisms by which air pollution may affect cardiovascular health. This includes neural mechanisms related to the response of the autonomic nervous system and changes in cardiac vulnerability.

Changes in the autonomic nervous system

The autonomic nervous system has important influences on cardiac health and disease, and one of the ways to assess this is by measuring heart rate variability (HRV). Heart rate variability refers to the beat-to-beat alterations in heart rate. Studies have shown that reduced HRV predicts sudden death in patients with myocardial infarction, and it also appears to be a marker of fatal ventricular arrhythmia [Kawachi *et al* 1995]. Several recent studies have shown relationships between increased levels of respirable air particulates and decreased HRV; Magari and colleagues found a small decrease in HRV when a group of 20 healthy individuals were exposed to respirable air particles [Magari *et al* 2002]. Such negative relationship has also been found in several other studies involved healthy elderly [Delvin *et al* 2003, Creason *et al* 2001, Gold *et al* 2000, Pope *et al* 1999a], and it was even stronger in those who were hypertensive [Liao *et al* 2004, Holguin *et al* 2003]. However, in an earlier study by Liao *et al* the effects were only observed in elderly people with pre-existing cardiovascular disease [Liao *et al* 1999]. In contrast to the negative associations found, Routledge and co-workers did not find any significant changes in HRV when healthy volunteers were exposed to carbon particles in a double-blinded human challenge study [Routledge *et al* 2003]. It may be possible that the effects seen with ambient air pollution is contributed by the reactive species on the particle surface rather than the particle itself. Changes in heart rate during an air pollution episode can also serve as a biomarker for altered autonomic activity. According to the

Framingham Study that spanned across 36 years involving 5,000 participants, elevated heart rate was a strong predictor of death and fatal heart disease amongst those with hypertension [Gillman *et al* 1993]. However the evidence of associations between exposure to air particulates and increased heart rate lacked consistency. For example, a significant increase in heart rate in response to increased ambient particulate levels was measured in a group of elderly in the Utah Valley, United States [Pope *et al* 1999b], and a smaller increase in the MONICA study carried out in Augsburg, Germany with young healthy volunteers [Peters *et al* 1999]. In contrast, decreased heart rate in response to higher concentrations of ambient particles were reported in both human [Ibald-Mulli *et al* 2004] and animal studies [Nadziejko *et al* 2002a, Nadziejko *et al* 2002b, Cheng *et al* 2003]. In addition to HRV and heart rate, blood pressure is also known to be a physiological parameter that can be used to assess the autonomic controls of the heart. However, studies on blood pressure had again generated mixed results; while blood pressure was found to be positively associated with air particulates concentration in two separate human studies [Linn *et al* 1999, Ibald-Mulli *et al* 2001], other studies with humans [Ibald-Mulli *et al* 2004] and animal models [Cheng *et al* 2003] generated opposite results.

Increase in myocardial vulnerability

The myocardium is under constant influence of both internal and external stimuli, and susceptibility to an adverse cardiac event varies between individuals depending upon their myocardial vulnerability, which may predispose them to conditions such as arrhythmias and ischemias. Measurements using electrocardiograms (ECG) of T-wave alternans and ST-segment changes, which are markers of electrical instability and myocardial ischemia respectively, as well as measuring the frequency and complexity of ventricular arrhythmias are some of the ways to determine the risk of cardiac death. Using these detection methods it has been found that different levels of myocardial vulnerability were induced when animal models were exposed to particulates [Lovett *et al* 1999] and oil fly ash [Watkinson *et al* 1998, Wellenius et 2003], which is a known a contributor to $PM_{2.5}$. In a study of patients with cardiac defibrillator implants, data on frequency of defibrillator discharges were used as an indictor of significant cardiac arrhythmias. Associations were found between air particulates level and increased defibrillator discharges [Peters *et al* 2000]. In another study led by the same researcher, increased risk of myocardial infarction onset was

associated with increased air particulates levels 2hrs prior to the attack [Peters 2001 *et al*].

2.3.2 Changes in blood rheology and coagulability

One hypothesised pathway was suggested by Seaton and co-workers that fine particulates may provoke alveolar inflammation, resulting in the release of potentially harmful cytokines [Seaton *et al* 1995]. Fibrinogen and C-reactive proteins (CRP) are part of the acute phase response mediated by the cytokines released during inflammatory reactions, and they can be used as indicators of tissue damage and inflammation. Increased levels of any proteins involved in the clotting cascade may trigger systemic increases in blood coagulability. In fact, increased fibrinogen levels and neutrophil counts were found to be associated with coronary heart disease and myocardial infarction [Dinerman *et al* 1990, Jousilahti *et al* 2001, Luc *et al* 2003, Lawlor *et al* 2005]. In addition, elevation of fibrinogen levels, which is a sign of inflammation, was found to be associated neutrophil activation [Rubel *et al* 2001].

Peters *et al* reported an increase in blood viscosity, as measured by fibrinogen and plasma proteins, in healthy volunteers when exposure to TSP was increased [Peters *et al* 1997b]. In addition to increased fibrinogen, Schwartz also found an increased platelet and white cell counts in respond to increased particle concentrations [Schwartz 2001]. Similar results were found in several other human studies using diesel exhaust fumes [Salvi *et al* 1999] and concentrated air particulates [Ghio *et al* 2000, Huang *et al* 2003], as well as in animal models when exposed to oil fly ash [Gardner *et al* 2000] and concentrated air particulates [Gordon *et al* 1998, Lei *et al* 2004]. However, one study showed an increase in only neutrophils but not fibrinogen when exposing animal models to ultrafine particles [Gilmour *et al* 2004]. Interestingly, Seaton *et al* who proposed the hypothesis of altered blood coagulability by air particles, obtained results that did not support their original hypothesis [Seaton *et al* 1999]. They found that the fibrinogen and platelet levels in the study subjects had actually fallen with increased air particulate concentrations, despite the levels of CRP were increased. Copolla *et al* had also found negative associations between both fibrinogen and platelet levels and gasoline exhaust fumes [Coppola *et al* 1989], whilst others found no changes at all [Hazell *et al* 1999, Clarke *et al* 2000, Nadziejko *et al* 2002]. Nevertheless, Seaton proposed a new hypothesis that the actions of particles on

the pulmonary endothelium was capable of altering the adhesive properties of the passing red cells and make them more likely to adhere to systemic capillaries. Hence the fallen fibrinogen level and platelet counts may indicate that they were being consumed for the coagulation of blood, which would increase the risk of ischaemic damage in individuals with compromised cardiovascular health. Further research is needed to support this hypothesis.

2.3.3 The role of oxidative stress

One of the potential mechanisms of cardiorespiratory injury caused by air particulates is through oxidative stress, which occurs when cells have lost control of their regulatory systems and results in a highly oxidised cellular environment. The oxidative capacity of these particles is primarily dependent upon their transition metal contents, which typically include iron, vanadium, chromium, manganese, cobalt, nickel, copper, zinc, and titanium [Prahalad *et al* 1999, Clarke *et al* 2000]. Some of these metals are capable of generating reactive oxygen species (ROS) [Stohs and Bagchi 1995]. ROS such as superoxide radicals, hydrogen peroxide, nitric oxide, and hydroxyl radicals are by-products of normal metabolic processes in cells. They are classified into two categories: free radicals and non-radical derivatives. Being chemically unstable, free radicals will quickly react with other molecules or radicals to achieve a stable configuration - this makes them more reactive than the non-radical derivatives. ROS can be found in several cells including macrophages and vascular smooth muscle cells. At low concentrations they act as physiological mediators of cellular responses, whereas higher concentrations may cause cell damage. ROS can exert oxidative stress on the cellular system, which can in turn trigger the release of redox sensitive transcription factors such as nuclear factor kappa B (NF-κB) [MacNee and Donaldson 2003] and activator protein 1 (AP-1) [Donaldson and MacNee 2001]. Oxidative stress will result in the depletion of reduced glutathione (GSH) in exchange of a rise in oxidized glutathione (GSSG), which leads to a drop in the intracellular GSH/GSSG ratio [Rahman *et al* 1999]. Oxidative stress can be considered as a biological emergency that would trigger a range of cellular responses. This can vary from protective to harmful effects depending on the level of oxidative stress. Li *et al* proposed that at lower levels of oxidative stress, antioxidant enzymes would be released in an attempt to restore the oxidant/antioxidant balance [Li *et al* 2003]. At an

intermediate level, induction of inflammatory response would occur through NF-κB and AP-1 activation and leads to the release of cytokines. At high level of oxidative stress, the completely overwhelmed cellular regulatory system would result in cell apoptosis. Oxidative injury to the pulmonary epithelium is prevented by a thin layer of fluid known as the respiratory tract lining fluid (RTLF). It is known that during the aging process there will be changes in the functions of leukocytes and reduction in antioxidant defences [MacNee and Donaldson 2003], thus their ability to handle oxidative stress from air particulates is reduced. If the hypothesis is true, then any lowering of the antioxidant defence mechanisms in the elderly may predispose them to harmful inflammatory responses.

There is much evidence published to support the theory that particles are capable of creating oxidative stress and triggers inflammatory processes. For example, instillation of urban PM_{10} samples into rat lungs produced inflammation as measured by bronchoalveolar lavage levels of neutrophils, and this was accompanied by a reduced level of GSH and an increased level of GSSG [Li *et al* 1996]. When rat heart microvessel endothelial cells were exposed to organic extracts of diesel exhaust particles and urban fine particles, mRNA levels of antioxidant enzymes were found to be positively associated with the dosage [Hirano *et al* 2003]. Carter *et al* showed that cells treated *in vitro* with PM_{10} activated both NF-κB and AP-1 which are important in controlling the expression of pro-inflammatory mediators [Carter *et al* 1997]. Finally the most direct evidence was the generation of hydrogen peroxide detected *in vivo* over the lungs of rats exposed to concentrated ambient particles [Gurgueira *et al* 2002].

2.3.4 Inhibition of phagocytosis and reduced clearance rate

Phagocytosis is the ingestion and destruction by individual cells of foreign particles. One of the phagocytic cells is the macrophage, which are large white cells that engulf and digest microorganisms and other antigenic particles. Macrophages are initially produced in the bone marrow as monocytes and they circulate in the blood for 24hrs before settling in tissues where they develop into macrophages. Specialised macrophages found in the lungs are known as alveolar macrophages. Macrophages are versatile and play many roles. As scavengers, they remove microbes, worn-out cells and other debris by engulfing and breaking them down into substances for

excretion or reutilisation. They also function as antigen-presenting cells for T cells activation. As secretory cells, macrophages are vital to the regulation of immune responses and the development of inflammation. Alveolar macrophages in the alveolar space are among the first cells to respond to the inhaled particles. They play a key role in the clearance of particles in the lung by phagocytosis. However, when deposition rate of inhaled particles is greater than clearance rate, macrophages can become overloaded and their ability to clear particles will be impaired or even inhibited. This will result in particles being deposited unphagocytosed in the lungs, which may lead to exacerbation of cardiorespiratory conditions by triggering inflammations of the epithelial cells and releasing harmful cytokines. Particles may also gain access to the pulmonary interstitium to create further damage.

Morrow proposed that clearance mechanisms would be affected as soon as the phagocytosed particle burden reached 6% of the internal volume of the alveolar macrophages, and would completely cease when it reached 60% [Morrow 1988]. In support of Morrow's theory, laboratory experiments showed that cytoskeletons of alveolar macrophages were affected when the particle burden reached 7-8% [Dorries and Valberg 1992], and almost a complete inhibition was observed when the phagocytic load occupied 60% of the total internal cell volume in vitro [Lenhert 1990, Oberdoster *et al* 1992]. The ability of particles to inhibit phagocytosis by alveolar macrophages depends not only on the number of particles present but also depends upon the size of the particles, with the optimum size around 1.5-3μm [Holma 1967]. Using titanium dioxide particles, Renwick and colleagues showed that ultrafine particles have greater abilities to inhibit phagocytosis than fine particles [Renwick *et al* 2001].

2.3.5 Effect of particle size

Scientists are increasingly focused onto the part ultrafine particles play in causing adverse health effects, as evidence to date suggested that they may be able to create more harm than their coarse and fine counterparts. The deposition of inhaled particles in the respiratory tract is influenced by their physical properties such as size and shape, and is also determined by the efficiency of the host's dust clearance defence mechanisms. As discussed in chapter 1, coarse particles are primarily deposited in the upper respiratory tract where they will be cleared away by the mucociliary clearance

mechanism of the body. Finer particles however are able to penetrate deep into the lungs into the terminal bronchioles and alveoli. Within the alveoli, soluble particles such as sulphates are dissolved into the lung lining fluid and their various constituents, whereas insoluble particles such as carbon may remain longer and may overcome the natural defence mechanism. Particles can also be translocated from the lungs into the circulation and be deposited in other organs. In a study carried out by Nemmar and colleagues, healthy volunteers were asked to inhale radioactive labelled ultrafine carbon particles [Nemmar *et al* 2002]. While radioactivity was detected in the lungs, it was also detected in the liver and the bladder at a later time. In addition, blood was drawn at regular intervals and at 1 minute radioactivity was already detected in the blood, reached a maximum between 10 and 20 minutes, and remained at this level up to 60 minutes. Another study using animal model led by the same researcher yielded similar results [Nemmar *et al* 2001]. Although the exact mechanism is yet to be established, its rapidity suggested that phagocytosis by macrophages and endocytosis by epithelial and endothelial cells were unlikely.

The main characteristic of ultrafine particles is their very large surface area and particle number per unit mass. For example, to obtain $10\mu g/m^3$ of $2\mu m$ diameter fine particles would require 1.2 particles per ml of air and the total surface area of particles would be $24\mu m^2/ml$. However, to obtain the same airborne mass concentration with particles of $0.02\mu m$ in diameter would require 2.4 million particles and the total surface area would be $3{,}016\mu m^2/ml$ [Kelly FJ, unpublished data]. It is highly likely that the lung would respond quite differently to 2.4 million particles with a large total surface area than to a relatively smaller number of larger particles with significantly smaller total surface area. Studies comparing healthy individuals with those suffering from asthma and chronic obstructive pulmonary disease (COPD) showed an increased deposition of inhaled ultrafine particles in their respiratory tracts [Anderson *et al* 1990, Brown *et al* 2002, Chalupa *et al* 2003]. This indicated that people with such underlying medical conditions have a higher deposition rate and deposition dosage of particles in their body for a given exposure, which may in addition to their depleted antioxidant defences contribute to their increased susceptibility to the health effects of air pollution.

2.4 Concluding remarks

Evidence from epidemiological studies has demonstrated the negative health effects of respirable air particulates on human health in both the short-term and long-term such as increased number of deaths and cancer incidence, exacerbation of cardiorespiratory symptoms in chronically ill individuals, increased incidence of respiratory tract irritations, decreased lung functions, as well as adverse birth outcome. While the effects found were often small they were nevertheless statistically significant. In the case of large-scale longitudinal studies and time-series studies, the odds/risks were estimated from large sample sizes often involving the whole population of one or more major cities. It is important to realise that when applying the small level of odds/risks in a huge population, the health burden of respirable air particulates is still substantial.

Currently the mechanisms of damage caused by respirable air particulates are still largely unknown. In fact, the study of air pollution on health as a branch of environmental epidemiology is still a relatively new research topic compared with other areas of medical sciences. Development in technology as well as research methods in the past few decades have improved our understanding about air particulates and its relationship to health in human beings. Therefore in the foreseeable future we should be able to answer questions that are not fully understood nowadays with regard the health effects and biological mechanisms of air particulates.

CHAPTER 3 – METHODOLOGY
SECTION 1
EXPOSURE COMPARISON STUDY

Traffic concentrations may give rise to microenvironments in which the levels of respirable air particulates may be higher than that measured from a fixed central site. Thus in theory, anyone residing within close proximity to heavy traffic will be exposed to higher levels of respirable particulate air pollution, compared with those residing in an urban area but distant from major traffic flow. This was investigated by measuring the levels of respirable particles in the environment and by examining markers of exposure in a group of healthy volunteers who reside in various trafficked and non-trafficked areas in the city of Cardiff.

3.1.1 Selection of study area

Like most developed cities in the UK, the city of Cardiff has a mixture of residential areas located in built-up areas close to the city centre with frequent traffic congestion, as well as areas in the suburbs where traffic density is minimal. In this study individual streets were selected based on their traffic flow densities and the number of houses present, and they were subsequently allocated into either the exposed or control group. A street was defined as exposed if it was a major A or B road with high traffic flow. On the other hand, a street was defined as control if it was a minor road or a cul-de-sac with low traffic volume, and that it was at least 750m away from the city centre and any major urban roads defined as exposed. In addition, both exposed and control streets must have a sufficient number of houses along it. These definitions are summarised in table 3.1.

Exposed	Control
Major A or B road	Minor roads, cul-de-sacs
High traffic flow	Low traffic flow
Have sufficient number of houses present	Have sufficient number of houses present
/	At least 750m away from the city centre and any major urban roads defined as exposed

Table 3.1: Selection criteria of the exposed and control areas.

Exposed areas

Although traffic flow data were not routinely collected in Cardiff at the time when the study commenced, traffic flow data were available in a small number of streets and such information was obtained from the Cardiff Council. Based on the traffic flow information 10 streets with sufficient number of houses along them were chosen from the list and classified as exposed areas. Extra streets were chosen based on long-term local knowledge of traffic queues and flow in certain areas of Cardiff city, where traffic volumes were high with residential areas within close distances.

Control areas

When choosing control areas for the study, the fact that no traffic data were available had again led to the use of long-term local knowledge. Several control areas were chosen based on the fact that they were both considerably far away from the city centre within an isolated residential area or community, and that the roads that lead to those areas were mainly consisted of small roads and cul-de-sacs. Careful considerations were also taken to avoid selecting streets from the control areas which had the possibility of being used as short-cuts by road users to gain access into another area rather than the local community itself. A whole area rather than individual streets were chosen for the controls because streets in the suburbs were often small with only a few houses. Groups of neighbouring streets from within an isolated area were chosen and referred by the name of that area instead of individual street names. Table 3.2 shows all the streets and areas that were chosen for the study. Those that are highlighted in red are areas which traffic flow data were available from the Cardiff Council. A map showing the locations of the studied areas can be found in pg370.

Exposed areas		Control areas
Cowbridge Road East	Cathedral Road	Fairwater
Cowbridge Road West	Manor Way	Llanedeyrn
Fidlas Road	Park Road	Llanishen
Llandaff Road	Pencisely Road	Marshfield
Mackintosh Place	Richmond Road	Michaelston-Super-Ely
Moorland Road	Tudor Street	St Mellons
Ninian Road	Western Avenue	
Penwyallt Road	Whitchurch Road	
The Philog		
Ty-Glas Road		

Table 3.2: List of streets/areas included in the study. Those with traffic flow data are highlighted in red.

3.1.2 Selection criteria of the participating subjects

Although the main objective of the study was to examine uptake rather than the effects of air particulates, it was thought that the use of only healthy individuals would reduce the variability between subjects in terms of daily activities and other unforeseen characteristics that may confound the results. The health status of each potential participant was determined by whether or not they had a history of cardiovascular disease or chronic obstructive pulmonary disease. Only one permanent resident was recruited from each participating household located in one of the target streets. In order to be chosen subjects were restricted to the male sex and aged 50 to 70 years of age, again for the purpose of reducing variability within the sampled population. Smoking, exposure to environmental tobacco smoke, and occupational exposure to air particulates and chemicals are considered as confounding factors that could lead to the overestimation of exposure to traffic-generated particulate matters. Therefore, all participating subjects must be non-smokers for at least 5 years with no frequent exposure to air particulates and chemicals, such as individuals who are employed in the transport or engineering businesses. In addition, the participating household must be a smoke-free home. All the selection criteria are summarised in table 3.3.

Selection Criteria
• Male
• 50-70yrs of age
• Permanent resident of the sampled house
• Non-smoker in the past 5yrs
• Reside in a non-smoking household
• No occupational exposure to air particles / chemicals
• No history of cardiovascular disease
• No history of chronic obstructive pulmonary disease

Table 3.3: Selection criteria of study subjects, Exposure Comparison Study.

3.1.3 Ethical approval

Prior to the commencing of recruitment it was essential that ethical approval was obtained from an appropriate governing body. An application together with an outline of the study proposal were sent to the Bro Taf Local Research Ethics Committee. Approval was granted subjected to the stipulation that all participants were provided with details of the study and be given opportunity to ask questions. In addition, the participants were required to sign a consent form which indicated that they fully understood what might involve in the study and that they were willing to take part voluntarily.

3.1.4 Recruitment of participating subjects

Recruitment of study subjects was carried out by sending letters addressed to the residents of each residential address along the 24 streets/areas of interest. All residential addresses were obtained through Royal Mail address finder, which were then extracted to a Microsoft Access® database. A universal letter template was used, and with the help of the mail merge function in Microsoft Word® thousands of letters addressed to different households were printed. In order to examine the effectiveness of such recruitment method, the first batch of letters were only sent to 3 streets from the exposed group, namely Mackintosh Place, Ninian Road, and Ty-Glas Road. Included in the mail was a brief covering letter providing basic information of the proposed study, as well as a short questionnaire with simple yes/no answers for the residents to express any likely interest in participation and to provide information

regarding their eligibility (appendix 1). A freepost return envelope was included in the letter for sending back the completed questionnaire. Those who were eligible and indicated possible interest in taking part were contacted via the phone, where they were asked further questions regarding their eligibilities. In addition, they were also given further information about the study and were given the opportunity to ask questions. Finally, interviews at the participating households were arranged with residents who were willing to take part in the study.

3.1.5 The interview

On the interview day the participants were visited by the researcher and the levels of both indoor and outdoor PM_5 concentrations were measured, and biological samples including hair and urine were collected. In addition, a customised questionnaire administered by the researcher was used to obtain information regarding the subjects' previous day's activities, travelling history in the past month, and the architectural design of the house. A copy of the questionnaire can be found in appendix 2. The participants were also given the opportunity to ask questions, and they were asked to sign a consent form stating their willingness to participate in the study voluntarily. A copy of the consent form is listed in appendix 3.

3.1.6 Measuring the levels of indoor and outdoor air particulates

Equipment

In this study one of the main objectives was to obtain information on the ambient levels of air particulates in different exposure areas. This monitoring work was carried out using a Quartz Crystal Microbalance (QCM) Mass Monitor produced by Booker Systems Ltd, UK (figure 3.1). It was connected to a cyclone head with a cut-off size of 5μm and had been calibrated by the manufacturer before the study commenced. This battery-powered equipment was capable of determining the amount of PM_5 collected on a second-by-second basis with a capacity of up to 4hrs. The QCM utilises a crystal as a sensitive microbalance, which has a precisely defined natural frequency at which it oscillates. When PM_5 particles extracted from the air are deposited onto the crystal via a small electrostatic precipitator, the mass load on its surface decreases its natural frequency. Thus, the particulate mass collected on the crystal can be determined by measuring the change in the natural frequency of the crystal. As the

QCM measures absolute mass, no correction factors for the particle shape or optical properties were required.

Figure 3.1: A Quartz Crystal Microbalance (QCM) Mass Monitor produced by Sensors Inc. under the licence of Booker Systems Ltd.
(Source: www.news.thomasnet.com)

Measuring indoor PM_5 levels

Levels of PM_5 were measured in each participating household during the interview. The duration of sampling was determined by the time needed to conduct the interview, but nevertheless set to be at least 20mins at anytime between 9am and 6pm, Monday to Friday. The measurements were taken by the QCM from the centre of the room that was facing towards the main road where possible. In the case where access to that room was restricted an alternative spot closest to it was used instead. Residents were asked not to purposely open or close any windows or doors during sampling so that the monitoring work was performed in a stable state for that house, with conditions unchanged during the monitoring period. It is well known that a number of indoor sources such as gas appliances would contribute toward the particle concentrations in an indoor environment. Therefore the researcher would ask the participants if such activities were performed within 2 hours prior to sampling, and an alternative sampling date would be arranged if so.

Measuring outdoor PM_5 levels

Outdoor measurements of PM_5 were conducted immediately after the interview when indoor PM_5 levels were recorded. Measurements were carried out using the QCM outside the participating households. The equipment was placed on the pavement of

the road of interest no further than 2m away from the traffic. Additional outdoor PM_5 measurements that followed the same sampling procedures were also made on separate occasions.

3.1.7 Collecting environmental samples

Equipment

In addition to the quantitative measurements of PM_5 levels in the environment, air particulate samples were also collected for the analysis of trace elements. This was carried out by a high volume air-sampler (JD Technical, UK) attached to a PM_{10} selective inlet head in the form of a horizontal elutriator (C30 Classifier, Negretti, UK) as shown in figure 3.2. Air at a rate of 30L/min was drawn by the pump through the inlet head, where particles less than 10μm were separated and collected onto a 47mm polycarbonate membrane filter (Millipore, UK).

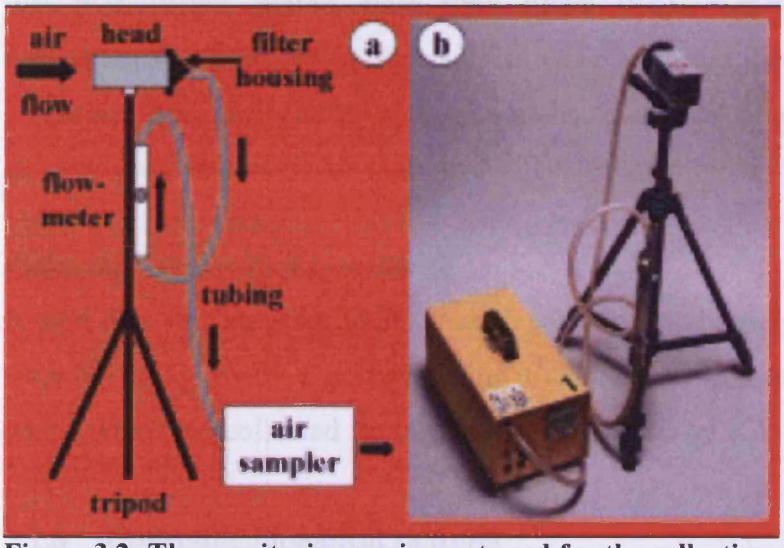


Figure 3.2: The monitoring equipment used for the collection of PM_{10}.
(a) Schematic representation of the equipment.
(b) Actual equipment.
(Courtesy of Dr T Jones, Cardiff University)

Collecting environmental PM_{10} samples

The samplings took place outside the houses of a sub-group of participants. The device was setup in the selected households with the pumps located inside the house, both for drawing power from the mains, and for safety reasons because they were not waterproof. The elutriator were connected to the pump via a rubber tube and placed outside the house facing the front towards the main road. A camera stand was used to support the elutriator and the tube so that the air samples were taken from

approximately 1m from the ground. Due to security reasons, the elutriator were only placed within the premises of the participants and thus the distance from the main road varied between samples. The sampling period was 24hrs, on any day between Monday and Friday. When collection was completed these filters were analysed by inductively coupled plasma mass spectrometry (ICP-MS) for the presence of any trace elements that may be attached on the particle surface. The analyses were carried out by Dr Tim Jones of the School of Earth, Ocean, and Planetary Sciences, Cardiff University.

Collecting environmental PAH samples

Additional PM_{10} samples were collected for the analysis of PAH attached on the surfaces of air particulates. The procedures and equipment used were identical to those used for the collection of PM_{10} for trace element analysis. The only exception was that Teflon coated glass fibre filters (SKC, USA) were used instead of polycarbonate filters. Once the samples were collected they were kept in cold dark conditions until analysis by high-pressure liquid chromatography (HPLC), carried out by Dr. Alun Hutchings of the Therapeutics and Toxicology Centre, Llandough Hospital.

Collecting indoor dust samples

A petri dish was also placed inside each participating households to collect dust. They were left inside rooms that were facing toward the main road for a period of 6months, which were then collected for trace element analysis by ICP-MS.

3.1.8 Collecting biological samples

In addition to recording data on indoor and outdoor PM_5 concentrations, biological samples were also collected during the interview that would allow comparisons between the levels of various exposure makers of respirable air particulates found in different exposure groups. The participants were asked to donate hair, urine, and blood samples on two occasions which were 6 months apart.

Hair samples

Hair samples were collected for the analysis of trace elements by neutron activation analysis (NAA), which was carried out in collaboration with the Medical Physics group of the University of Surrey, making use of the University of London reactor

centre. In order to maintain consistency, each time approximately 20-30 hair strands were cut off from the nape of the participants' necks which were 2-3mm from the scalp. The samples were then collected into resealable plastic bags for storage. Prior to NAA the collected samples were treated in accordance with the International Atomic Energy Agency (IAEA) recommended protocol [IAEA 1992]. The samples were washed in acetone and thrice in double deionised water followed by a second acetone wash. They were then agitated in acetone for a period of 10mins and were allowed to air-dry overnight at room temperature in a clean laminar flow unit. Once dried the samples were then loaded into pre-weighted pre-washed polyethylene capsules for weighting and transport. Due to the relatively slow speed of growth of the human hair, any markers found inside the hair would serve as indicators of long-term exposure to particulate air pollution. Because of this, hair samples were only collected from participants who had been residing in their residences for at least 20 days in the month prior to the interview, and the others were collected at a later date when such criterion was fulfilled.

Urine samples

Urine samples were also collected during the interview. Standard universal bottles for the collection of urine samples were sent to the participants in advance. They were asked to prepare the sample the night before the scheduled interview in order to assess exposure during the day. In the interview the participants were asked to provide information of their activities on the previous day, and they were asked to produce a replacement sample some other time if any unusual activities such as prolonged travel in motor vehicles were reported. Once collected the samples were freeze-stored until analysis by HPLC and ICP-MS for the detection of 1-hydroxpyrene and platinum respectively. Urine samples that were analysed by HPLC were carried out by Dr. Wolfgang Will of the Medizinisches Labor Bremen, Germany, and all samples analysed by ICP-MS were carried out by Dr. Steve Smith, Dept of Medical Biochemistry, University Hospital of Wales.

Blood samples

The participants were also asked to attend the Phlebotomy clinic at the University Hospital of Wales for a qualified phlebotomist to extract a small amount of blood for trace element analysis by ICP-MS, which was carried out by Dr. Steve Smith of the

Dept of Medical Biochemistry, University Hospital of Wales. Any exposure markers found in the blood would indicate the amount of exposure to air particulates in a long term. Because it was uncertain as to how long the markers would remain in the system before being excreted, therefore the participants were advised not to provide a blood sample immediately if they had been away from their residences overnight for more than 10 days in the last month prior to the interview. To ensure smooth operations as well as to facilitate the process, each participant was given a card attached with labels that contained their initials, date of birth, and unique ID number. They were asked to present this card to the phlebotomist, who then attached the labels onto the samples drawn from the participants, thus minimising the chances of mislabelling and mis-sorting. These cards were later returned to the researcher and any discrepancies found between the records and the actual number of blood samples received were followed-up. A flow chart that summarises the recruitment process of participants and the sampling procedures of the Exposure Comparison Study is shown in figure 3.3.

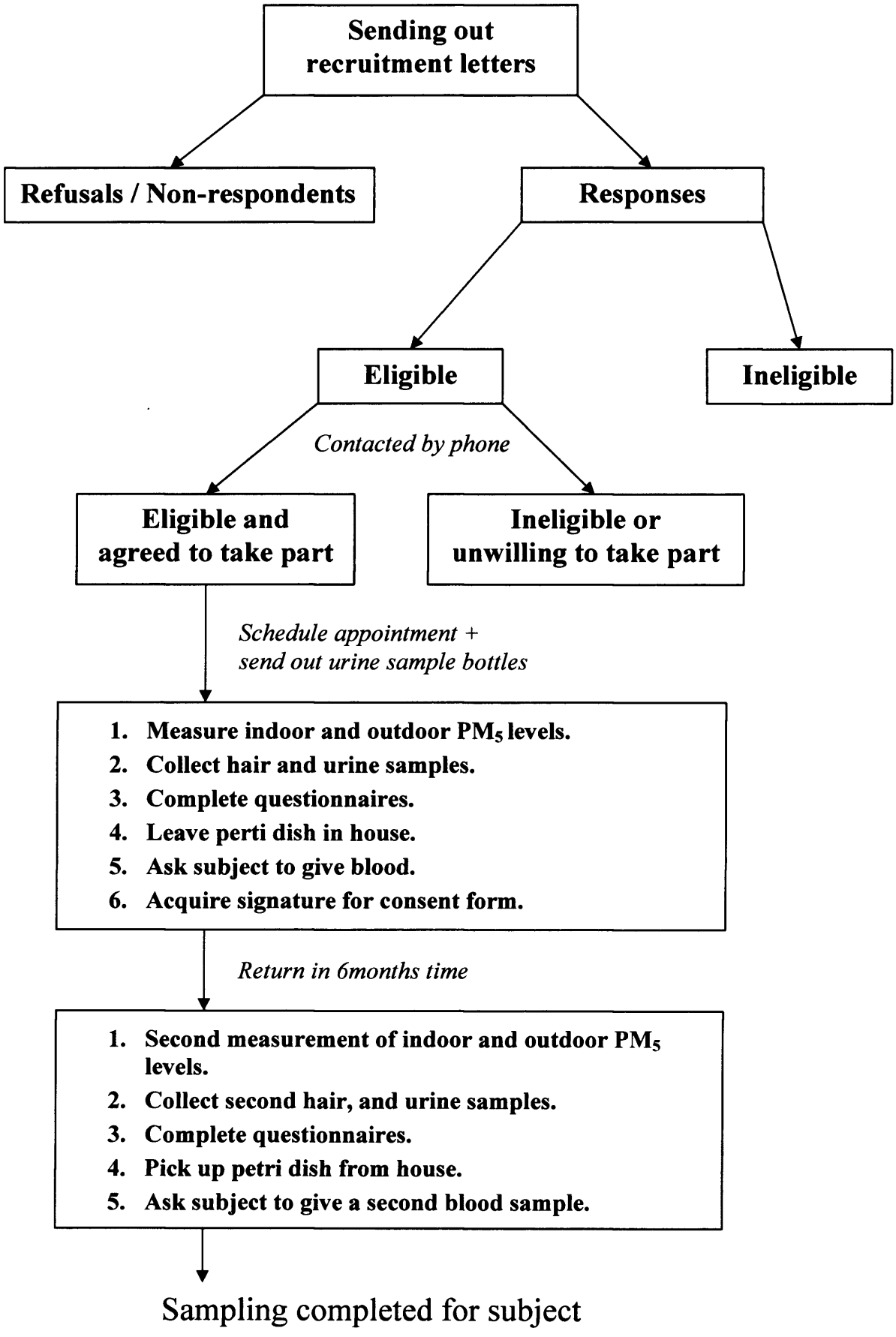


Figure 3.3: Flow chart of recruitment and sampling procedures, Exposure Comparison Study.

SECTION 2
SYMPTOMS COMPARISON STUDY

Results from time-series studies carried out in the past showed that short-term increase in the levels of ambient air particles led to the premature deaths of compromised individuals with chronic underlying medical conditions. While majority of studies investigated the short-term rise in mortality caused by excursions of ambient particle levels, relatively few of them focused on symptoms change. Since short-term increases in PM_{10} levels are associated with elevated death rates, it is therefore likely that such increase can also lead to the exacerbation of less severe symptoms. The objective of this questionnaire-based study is to investigate how sudden changes in the levels of PM_{10}, as measured from stationary central monitoring stations in South Wales, affect disease symptoms in compromised individuals. Disease-specific questionnaires were used to detect changes in symptoms, medication use, and the psychological well-being between different episodes of particulate air pollution.

3.2.1 Selection of study area

At the time of the study, within the region of South Wales there were a total of 6 stationary monitoring stations that collect data on PM_{10} concentrations continuously over 24hrs. Real time levels of PM_{10} recorded in these sites were accessible via databases on the Internet at http://www.welshairquality.co.uk. These stations are located in Cardiff (two stations: Cardiff Centre and Cardiff Briardene), Cwmbran, Narberth, Neath Port Talbot, and Swansea. Together with other monitoring sites set up in other locations of Wales, they are known as the Welsh Automatic Urban Pollution Monitoring network. Data from all but two stations were used in the study – Cardiff Centre was excluded due to large-scale construction works being carried out within close distance to the site at that time; and Narberth was excluded because it was located in a rural area with very few residential areas nearby. Further details regarding the site information of Cardiff Briardene, Cwmbran, Neath Port Talbot, and Swansea can be found in appendix 4. With PM_{10} data readily available from the selected sites, recruitment was therefore focused on those areas.

3.2.2 Selection criteria of the participating subjects

The research method used in the study was case-crossover study design, in which only case subjects were studied and each subject acted as his or her own control. The disease status of each participant was self-reported and according to the information provided they were then allocated into one of the three appropriate disease groups including asthma, respiratory disease excluding asthma, and cardiovascular disease group. In addition to their underlying conditions, each individual must also fulfil all of the following selection criteria:

Selection Criteria

- Aged 50-70yrs for respiratory and cardiovascular disease groups
- Aged 18-70yrs for asthma group
- Non-smoker in the past 5yrs
- Reside in a non-smoking household
- No occupational exposure to air particles / chemicals
- Residing within 10miles from their local stationary air monitoring stations

3.2.3 Ethical Approval

Applications along with copies of the research outline and questionnaires were sent to the Swansea Local Research Ethics Committee and the Gwent Local Research Ethics Committee. Ethical approvals for the study were granted by the panel.

3.2.4 Recruitment of participating subjects

The recruitment of study subjects was carried out via cardiology and respiratory hospital outpatient clinics located in South Wales, namely Cardiff, Swansea, Newport, and Neath Port Talbot. All medical consultants were contacted by mail for permissions to recruit volunteers from their clinics (appendix 5). Patients visiting those clinics were given an information sheet with brief information of the study and how they could help (appendix 6). They were asked to complete a "reply card" to indicate their possible interest in participating in the study together with their name, phone number, date of birth, and their consultant's name. Upon completion the cards were then collected by the clinic staff and sent back to the researcher every fortnight. A preliminary screen was carried out on all the cards and those who were eligible

were contacted via the phone. During the telephone conversation the researcher obtained details on the patient's medical conditions, as well as other information regarding their eligibility. In addition, the patients were also given the opportunity to ask questions and provide further information which they think were relevant to the study. All eligible individuals who wished to take part were assigned a unique identifying number and they were asked to sign and return a consent form (appendix 7) which were sent out following the phone call.

3.2.5 Questionnaire design

Three sets of disease-specific questionnaires were designed for the study and they were the Asthma Symptoms Questionnaire, the Heart Symptoms Questionnaire, and the Respiratory Symptoms Questionnaire. A copy of the questionnaires can be found in appendix 8.1, 8.2, and 8.3. These questionnaires were based on validated instruments including the Asthma Quality of Life Questionnaire, the Kansas City Cardiomyopathy Questionnaire, the MacNew Heart Disease Health-Related Quality of Life Questionnaire, the Seattle Angina Questionnaire, and the St George's Respiratory Questionnaire. Permission to use them had been granted from the authors. All disease-specific questionnaires include items that can be categorised, which focus on disease symptoms, medication use, and emotional well-being. In addition "check questions" were also included to identify the existence of any factors that may confound the results. The questions within each questionnaire were then randomised.

3.2.6 Data collection

Throughout the study period levels of PM_{10} in South Wales were monitored daily through databases via the Internet. Each individual were asked to complete a disease-specific questionnaire on 4 occasions in which two of these were subsequent to episodes of high pollution and two subsequent to normal pollution episode, which are defined as below:

- High pollution episode – Any 4hrs with a PM_{10} concentration above $50\mu g/m^3$ within a 16-hour period between 6am and 10pm.

- Normal pollution episode – 24hr mean with a PM_{10} concentration below $25\mu g/m^3$, with no readings above $30\mu g/m^3$.

The questionnaires collected symptoms data from the participants throughout a 7-day period following an air pollution episode that matched the pre-set criteria. Such period was referred as "the week of interest" in the questionnaire. There were no specific rules as to how widely spread between each questionnaire has to be sent out, but there must be at least a 3-week gap between each questionnaire. The definitions of these pollution episodes were judged based on real PM_{10} data observed in Cardiff between 2000 and 2003. The defined level of normal pollution episodes resembled the average PM_{10} concentrations seen in Cardiff, and is thus the representation of the levels of particulate pollution each individual would normally experience.

3.2.7 Dispatching the questionnaires

The question as to when to dispatch the questionnaires was regarded as crucial in the study. A questionnaire that arrives either too late or too early may have affects on its accuracy. Eventually, it was scheduled to be sent out on the fourth day after the pollution episode of interest has occurred, which also provided sufficient amount of time for the preparation of questionnaires. At last, these questionnaires were dispatched via Royal Mail 2nd class delivery with an estimated arrival time of 2 working days. According to the plan, the questionnaires will arrive around the sixth day of the week of interest and can be filled in within 1-2 days (figure 3.4).

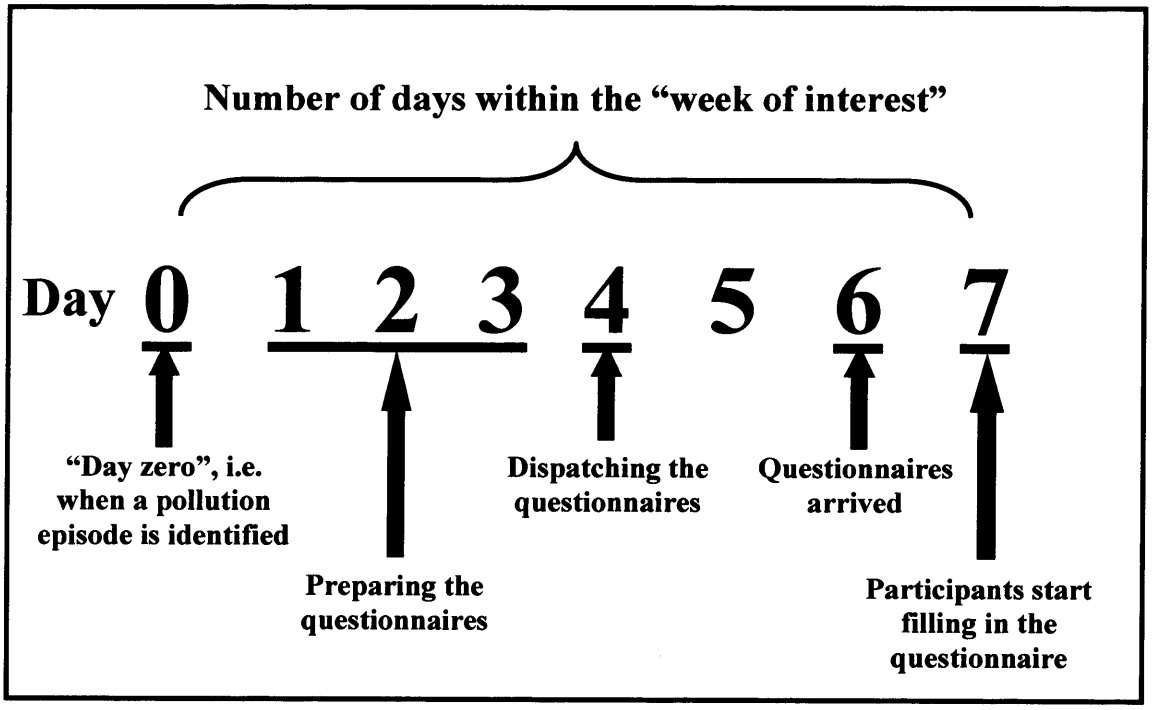


Figure 3.4: Flow chart showing the scheduled timing of dispatching the questionnaires.

3.2.8 Checking the returned questionnaires

Participants were encouraged to fill in the questionnaires promptly on the last day of the week of interest and to return the completed questionnaires at their earliest convenience. All returned questionnaires were checked and any incomplete questionnaires were subsequently filled in by contacting the participants on the phone. Within the questionnaires there were some "check questions" that concerned about various confounding factors that may lead to the under- or overestimation of the effects of PM_{10} on symptoms. The completed questionnaire would be automatically voided if the participants have experienced any of the followings during the week of interest:

- Had a chest infection.
- Had been exposed to other people's tobacco smoke for a prolong period.
- Had been away from their residences overnight for more than 3 days.

In addition, a questionnaire would also be invalidated if any unusual changes in PM_{10} levels were observed during the week of interest. For example, a sudden increase in PM_{10} occurred after questionnaires were sent out during the week of interest of a normal pollution episode. A flow chart that summarises the recruitment process of participants and the sampling procedures of the Symptoms Comparison Study is shown in figure 3.5.

3.2.9 Method of analysis

Each answer given by the participants in the completed questionnaires corresponded to a symptoms score. This symptoms score was used to examine the influence of air pollution at high levels relative to episodes of normal air pollution levels. Furthermore, certain responses which were believed to be more indicative of more severe asthma, respiratory, and cardiovascular disease symptoms were analysed as a separate category.

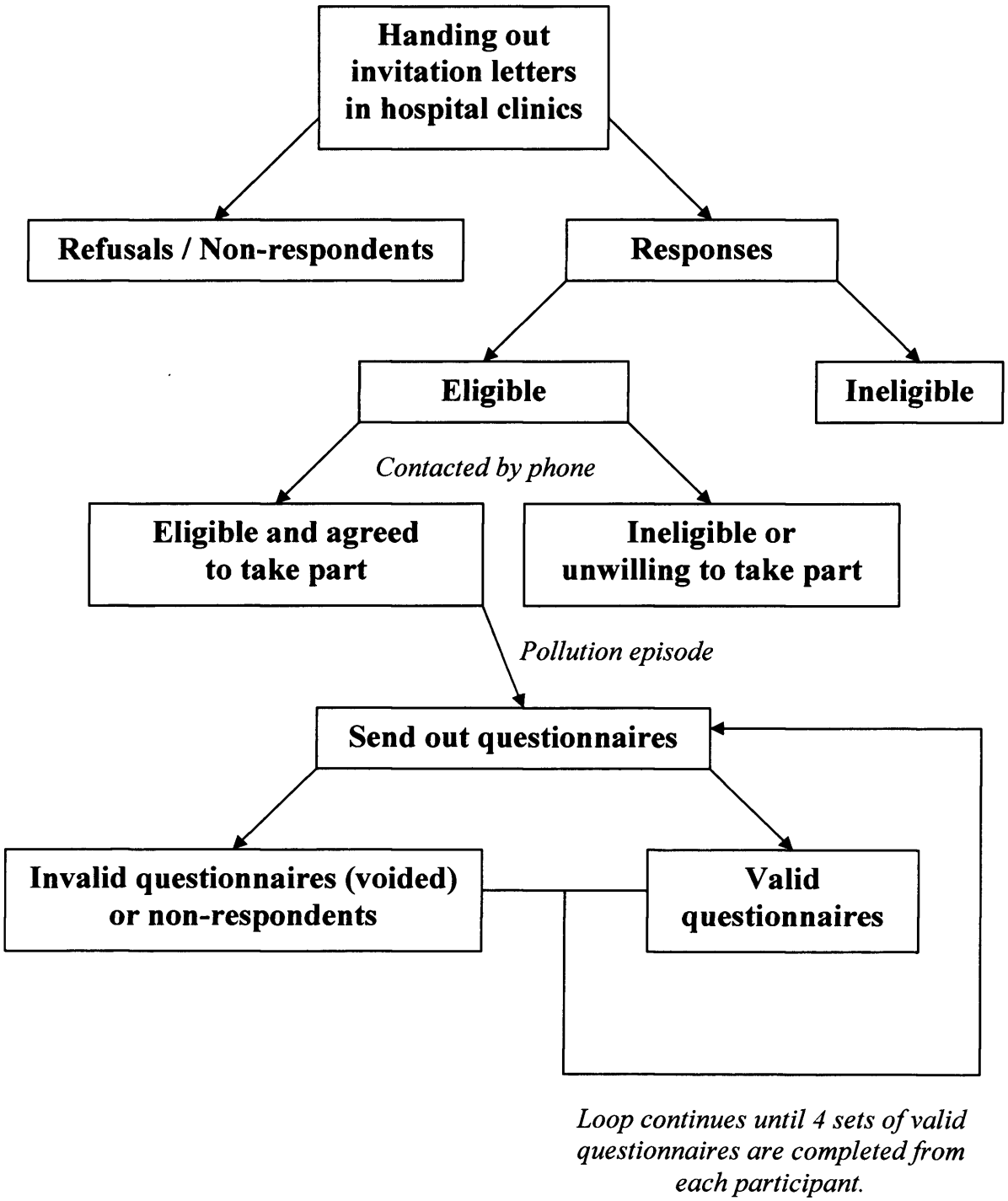


Figure 3.5: Flow chart of recruitment and sampling procedures, Symptoms Comparison Study.

CHAPTER 4 – RESULTS
SECTION 1
EXPOSURE COMPARISON STUDY

Compared with other large cities in the UK such as London and Birmingham, the absolute levels of PM_{10} as measured by stationary air quality monitoring stations are relatively low in Cardiff. However, there is a marked variation in traffic flow between the central urban areas and the sub-urban areas on the outskirt of the city. This section reports the levels of air particulates in microenvironments within Cardiff city with different traffic volumes, and also whether biomarkers of personal exposure to traffic particulates were elevated in more trafficked areas. Houses were chosen on streets with dense traffic flows and also in sub-urban areas where motor traffic was minimal. Outdoor and indoor measurements were made on the same occasion at each location and individual residents provided blood, urine, and hair samples for analysis of trace elements which may act as biomarkers of exposure to air particulates from motor vehicles.

4.1 Analysis of PM_5 air particulates in the environment

Recruitment

Recruitment first started in spring 2003, when approximately 500 letters were sent out to houses located in three exposed areas namely Mackintosh Place, Ninian Road and Ty-Glas Road. Recruitment was then expanded to other targeted areas. Over the study period recruitment was a continuous process, first concentrated on exposed areas then eventually switched to control areas when the numbers of participants in the exposed group reached 70. The last group of residents were recruited in spring 2005 as recruitment beyond that date would have left insufficient time for the analysis of biological samples and revisits 6 months later.

Outcome rates

Outcome rates of the study were presented as the response rate, which is expressed as a percentage and refers to the ratio of number of people who participated in the study divided by the number of eligible individuals ever contacted. Table 4.1 shows the breakdown of responses to the recruitment letters sent out. A total of 8,319 invitation

letters were sent out over the study period between 2003 and 2005, of which 4,043 were to the exposed areas and 4,276 to the control areas. Response received from the exposed area was slightly higher than those from the control areas. Ninety of the 250 responses received from residents residing in exposed areas were eligible for the study, and out of that 73 agreed to take part. In the control areas, 189 responses were received, of which 68 of them were eligible and eventually 50 took part in the study. The response rates were 81% and 74% for the exposed and control groups respectively.

Total number (n)	Exposed	Control
Letters sent out	4043	4276
Response received	250	189
Eligible response received	90	68
Respondents who agreed to take part	73	50

Table 4.1: Breakdown of responses to recruitment letters, exposed v control.

4.1.1 Ambient air particulate levels in the environment

Sampling durations were 20 minutes each time and were carried out between 9am and 6pm Monday to Friday. In order to get an overall picture of the PM_5 concentrations throughout the year, samplings took place in all seasons and under different weather conditions. Each time, outdoor levels of PM_5 were measured immediately after indoor measurements made during the interviews with the participants were completed. Additional outdoor measurements took place at random times again between 9am and 6pm Monday to Friday to collect extra PM_5 data that helped to determine the typical ambient particulate levels of the targeted streets.

Levels of PM_5 in the environment

Throughout the study a total of 373 ambient PM_5 measurements have been made in all areas. At least 10 random measurements were made in each target street, with the highest number of measurements made in the control area Michaelston-Super-Ely (29

times) and the lowest number in the exposed area Tudor Street (10 times). Figure 4.1 shows boxplots of the distribution of PM_5 levels in each studied street and figure 4.2 defines the structure of a boxplot. Table 4.2 shows the descriptive statistics of the measured PM_5 concentrations. The mean levels of PM_5 concentrations of the exposed streets ranged from 15.4μg/m^3 to 21.1μg/m^3, with Cowbridge Road West having the highest mean PM_5 concentration (21.1μg/m^3), followed by Cowbridge Road East (20.9μg/m^3) and Western Avenue (20.1μg/m^3). On the other hand, Mackintosh Place has the lowest mean PM_5 concentration (15.4μg/m^3), followed by Pencisely Road (15.7μg/m^3) and Ty-Glas Road (15.8μg/m^3). Amongst the control areas, Llanishen has the highest mean PM_5 concentration (13.2μg/m^3) and Marshfield has the lowest (10.4μg/m^3). The standard error of mean (SE) for each individual street was also examined and was expressed as a percentage of the mean [(SE / mean) x 100%], known as "SE%". The larger the SE% the more imprecise was the estimate of the mean. Results showed that Cowbridge Road West has the highest SE% (10.9%) and the lowest was Richmond Road (4.4%). In the control areas the SE% was highest in Marshfield (12.0%) and lowest in Llanishen (6.1%).

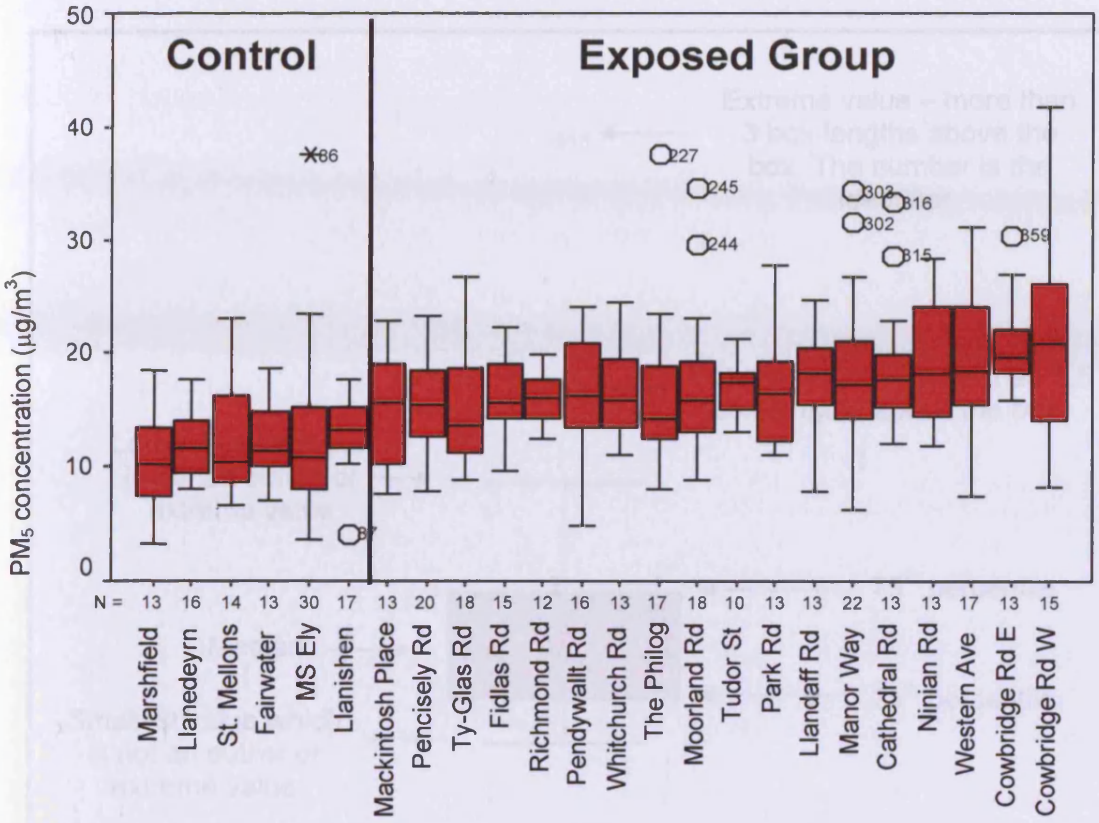


Figure 4.1: Distributions of ambient PM_5 levels in individual streets by exposure group, arranged in ascending order from the left by their mean PM_5 concentrations.

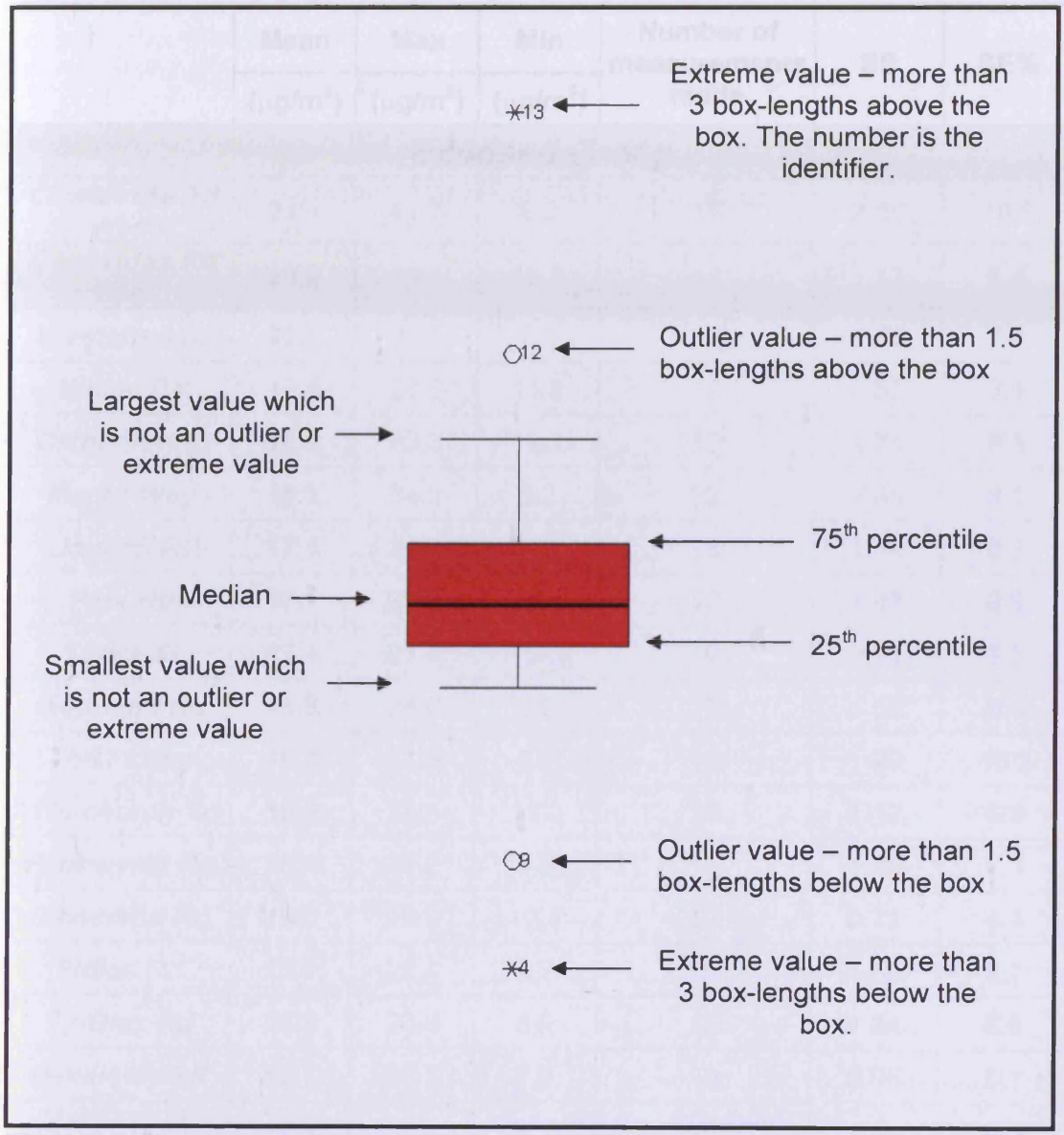


Figure 4.2: Structure of a boxplot.

	Mean ($\mu g/m^3$)	Max ($\mu g/m^3$)	Min ($\mu g/m^3$)	Number of measurements made	SE	SE%
Exposed Group						
Cowbridge Rd West	21.1	41.7	8.2	15	2.30	10.9
Cowbridge Rd East	20.9	30.4	15.9	13	1.13	5.4
Western Ave	20.1	31.1	7.4	17	1.58	7.9
Ninian Rd	19.4	28.3	11.9	13	1.57	8.1
Cathedral Rd	18.8	33.3	12.1	13	1.74	9.2
Manor Way	18.1	34.3	6.2	22	1.46	8.1
Llandaff Rd	17.4	24.7	7.8	13	1.44	8.3
Park Rd	17.1	27.8	11.1	13	1.47	8.6
Tudor St	17.1	21.4	13.0	10	0.91	5.3
Moorland Rd	16.8	34.6	8.9	18	1.58	9.4
The Philog	16.6	37.5	8.0	17	1.70	10.3
Whitchurch Rd	16.6	24.5	11.0	13	1.12	6.8
Pendwyallt Rd	16.4	24.2	4.9	16	1.36	8.3
Richmond Rd	16.0	20.0	12.5	12	0.71	4.4
Fidlas Rd	16.0	22.4	9.7	15	1.56	9.7
Ty-Glas Rd	15.8	26.6	8.9	18	1.34	8.5
Pencisely Rd	15.7	23.3	7.9	20	0.96	6.1
Mackintosh Place	15.4	23.0	7.7	13	1.38	9.0
Control Group						
Llanishen	13.2	17.8	4.1	17	0.80	6.1
Michaelston-Super-Ely	12.3	23.6	3.6	29	1.27	10.3
Fairwater	12.1	18.7	7.1	13	1.01	8.4
St Mellons	12.1	23.0	6.7	14	1.28	10.7
Llanedeyrn	11.9	17.8	8.0	16	0.72	6.1
Marshfield	10.4	18.5	3.2	13	1.25	12.0

Table 4.2: Environmental PM_5 measurements of all study areas.

Defining the control group

Initially, the allocation of participants into either the exposed or control group was dependent on the proximity of their houses to an urban road with high volumes of traffic. A total of six areas were selected for the study as controls, which consisted of minor roads and cul-de-sacs that were at least 750m away from the city centre or any urban roads with high volumes of traffic flow. According to the measurements made in the control areas, the difference between the means of the highest and lowest PM_5 concentrations was only 2.8μg/m^3. If it could be proved that the mean PM_5 levels observed in each area were not significantly different from each other, it was possible to combine the measurements made in all control areas and form into one large control group. Doing so would increase the statistical power of the information collected due to the increased number of measurements that can be included in the statistical analysis at one time. For this purpose, a statistical test called Analysis of Variance (ANOVA) was chosen. In brief, ANOVA is a statistical method for making simultaneous comparisons between the means of two or more groups. It produces a value that can be tested to determine whether the relation observed between the variables is statistically significant. However, since ANOVA assumes the data being analysed were normally distributed, therefore it is essential to check for the distribution and identify any abnormalities in the data set. This can be done by constructing boxplots, which allows the visual examination of the data set and the identification of any extreme values as demonstrated in figure 4.2. If any extreme values were present, it is necessary to consider whether or not to remove them before engaging in further analysis.

In this case, ANOVA tested the null hypothesis (H_o) that the mean PM_5 concentrations observed in the 6 different control areas were not different from each other. Results from the ANOVA test yielded a large p-value ($F = 0.48$; $p = 0.79$), meaning the differences observed were likely to be by chance and thus H_o was accepted. Boxplots (figure 4.3) also confirmed the distributions of the data and there were no extreme values present. With the help of boxplots and ANOVA test, the decision of combining all of the six control areas into one large control group was justified. The new control group now consisted of 102 measurements in total, with a mean and median of 11.8μg/m^3 and 11.5μg/m^3 respectively (table 4.3).

Defining the exposed group

In the study all eligible individuals who agreed to take part were allocated into the exposed group if they resided within 20m of an urban road with high traffic flow. The mean environmental PM_5 concentration of all the exposed areas was 17.5μg/m^3 with a median value of 16.7μg/m^3, which were both approximately 50% higher than the mean and median PM_5 levels observed in the control group (table 4.3). Apart from the presence of several outlying values toward the upper end, the distribution of the data was more or less normal, as shown in figure 4.3.

	Exposed	Control
N	271	102
Mean (μg/m^3)	17.5	11.8
Median (μg/m^3)	16.7	11.5
Minimum (μg/m^3)	4.9	3.2
Maximum (μg/m^3)	41.7	23.5
Percentiles 25th (μg/m^3)	13.3	8.9
75th (μg/m^3)	20.6	14.4

Table 4.3: Descriptive statistics of environmental PM_5 concentrations, exposed v control.

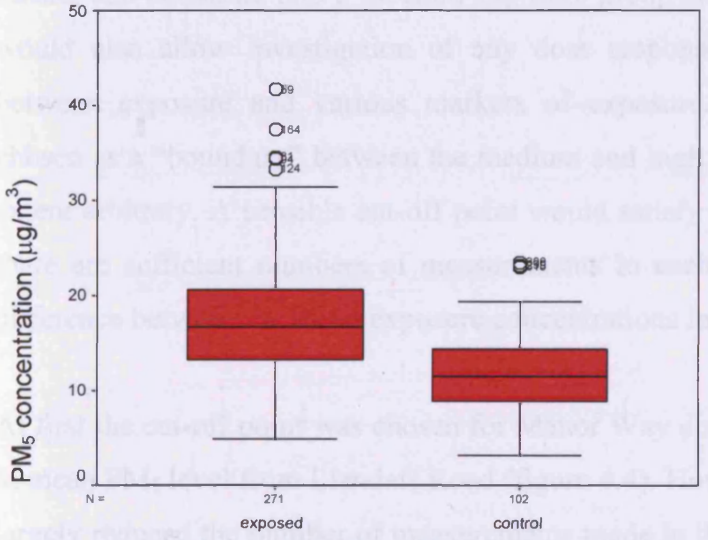


Figure 4.3: Concentrations of environmental PM_5, exposed v control.

Testing the difference in mean PM_5 levels between the exposed and control groups

The difference in means of the two groups were analysed by the Independent-Samples T-Test, which is a statistical method for comparing the means of two independent groups of samples. Results showed that the means of the two exposure groups were statistically different from each other ($t(372) = 8.40$; $p<0.01$). In addition, the differences in medians between the two exposure groups were also compared. For this purpose the non-parametric statistical test Mann-Whitney test was used, which examines the medians of two independent sets of samples. In this case, the H_0 is that both the samples from the exposed and control groups were drawn from a single population, and there is no difference between the medians of the two groups. Results showed that the difference observed was highly significant at the 1% significance level ($z = -8.45$; $p<0.01$), and thus the H_0 was rejected.

Redefining the exposed group

It was apparent after the outdoor PM_5 measurements were made that significant variations in terms of mean PM_5 concentrations between individual streets within the exposed group existed. For example, Cowbridge Road West has the highest mean PM_5 concentration recorded in the study and was 37% higher than the mean concentration of Mackintosh Place, which was the lowest amongst all the exposed streets. This observation indicated that the group defined as exposed may usefully be further sub-classified into a medium exposure group and a high exposure group. This would also allow investigation of any dose response relationship that may exist between exposure and various markers of exposure. The exposure concentration chosen as a "boundary" between the medium and high exposure group is to a certain extent arbitrary. A sensible cut-off point would satisfy the criteria of a) ensuring that there are sufficient numbers of measurements in each group and b) that there is a difference between the mean exposure concentrations in each group.

At first the cut-off point was chosen for Manor Way due to the more marked increase in mean PM_5 level from Llandaff Road (figure 4.4). However, when using this point it largely reduced the number of measurements made in the high exposure group – only 93 measurements in the high exposure group and 178 in the medium exposure group. As a result a second choice was sought and Moorland Road was considered as a more favourable alternative. This was because Moorland Road was situated close to the

centre point when all streets were arranged in an ascending order according to their mean PM_5 concentrations. Also it would increase the number of measurements in the high exposure group to 147 and reduce the size of the medium exposure group to 124. Moreover, the mean PM_5 concentrations were also compared; if the cut-off point was made at Manor Way the mean PM_5 levels would be 19.7μg/m^3 for the high exposure group and 16.4μg/m^3 for the medium exposure group. On the other hand, if the cut-off point was made at Moorland Road instead, the mean PM_5 concentrations would be 18.7μg/m^3 for the high exposure group and 16.1μg/m^3 for the medium exposure group. Since the differences between the means of PM_5 levels were small when the two cut-off points were compared, and the number of measurements would be more evenly distributed if the cut-off point was chosen at Moorland Road, therefore that was finally decided to be the point where the two groups would split. A summary of these figures is shown in table 4.4 below. According to figure 4.4, the medium exposure group consisted of streets from Mackintosh Place to The Philog inclusive, and the high exposure group consisted of all streets from Moorland Road onwards.

Cut-off point	Number of measurements		Mean PM_5 levels (μg/m^3)	
	High exposure	Medium exposure	High exposure	Medium exposure
Manor Way	93	178	19.7	16.4
Moorland Road	147	124	18.7	16.1

Table 4.4: Differences in the number of measurements and mean PM_5 levels of the two different cut-off points.

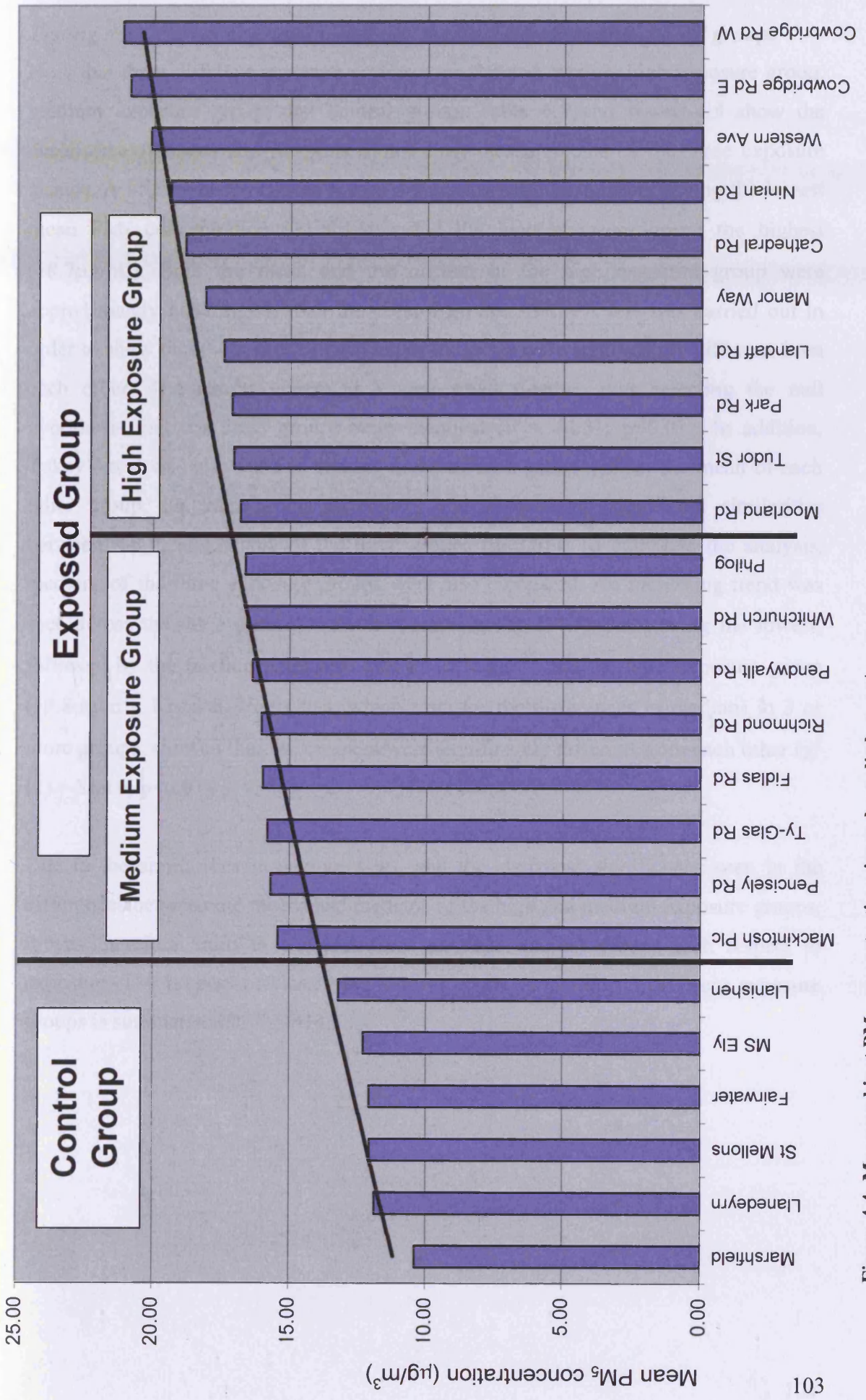


Figure 4.4: Mean ambient PM_5 concentrations in each studied street/area.

Testing the differences between high and medium exposure and control groups

Now that three different exposure groups were defined, namely high exposure group, medium exposure group, and control group. Table 4.5 and figure 4.5 show the descriptive statistics and boxplots of the PM_5 measurements of the three exposure groups. A linear trend was seen across the groups with the controls having the lowest mean PM_5 concentration ($11.8\mu g/m^3$) and the high exposure group the highest ($18.7\mu g/m^3$). Both the mean and the median of the high exposure group were approximately 60% higher than the control group. ANOVA test was carried out in order to show that the means of each exposure group were significantly different from each other. The results generated a very small p-value, thus rejecting the null hypothesis that the three groups were identical ($F = 44.51$; $p<0.01$). In addition, Tukey's test was also used to test the mean of each group against the mean of each other group, i.e. intra-group difference, and showed no significant similarities between the means of any of the three groups ($p<0.01$). To complete the analysis, medians of the three exposure groups were also compared. An increasing trend was seen across the three groups, with the control group ($11.5\mu g/m^3$) being the lowest, followed by the medium exposure group ($15.5\mu g/m^3$) and the high exposure group ($17.8\mu g/m^3$). Kruskal-Wallis test, which tests for the differences in medians in 3 or more groups, showed that the medians were significantly different from each other ($\chi^2(2) = 81.16$; $p<0.01$).

Due to the similarities in sample sizes, and the statistical significance seen in the differences between the means and medians of the high and medium exposure groups, it was therefore valid to consider them as three distinct groups with respect to exposure. The process of classifying various target streets into 3 different exposure groups is summarised in figure 4.6.

	High exposure	Medium exposure	Control
N	147	124	102
Mean ($\mu g/m^3$)	18.7	16.1	11.8
Median ($\mu g/m^3$)	17.8	15.5	11.5
Minimum ($\mu g/m^3$)	6.2	4.9	3.2
Maximum ($\mu g/m^3$)	41.7	37.5	23.5
Percentiles 25th ($\mu g/m^3$)	14.5	12.8	8.9
75th ($\mu g/m^3$)	21.6	19.2	14.4

Table 4.5: Descriptive statistics of environmental PM_5 concentrations, high exposure v medium exposure v control.

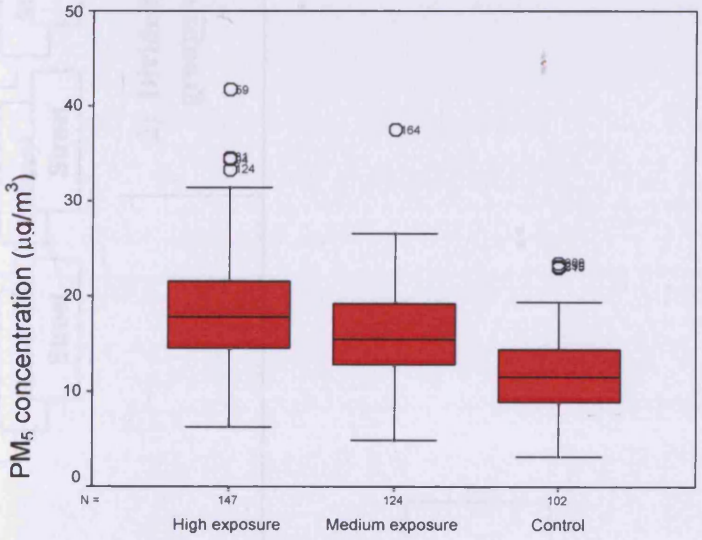


Figure 4.5: Concentrations of environmental PM_5, high exposure v medium exposure v control.

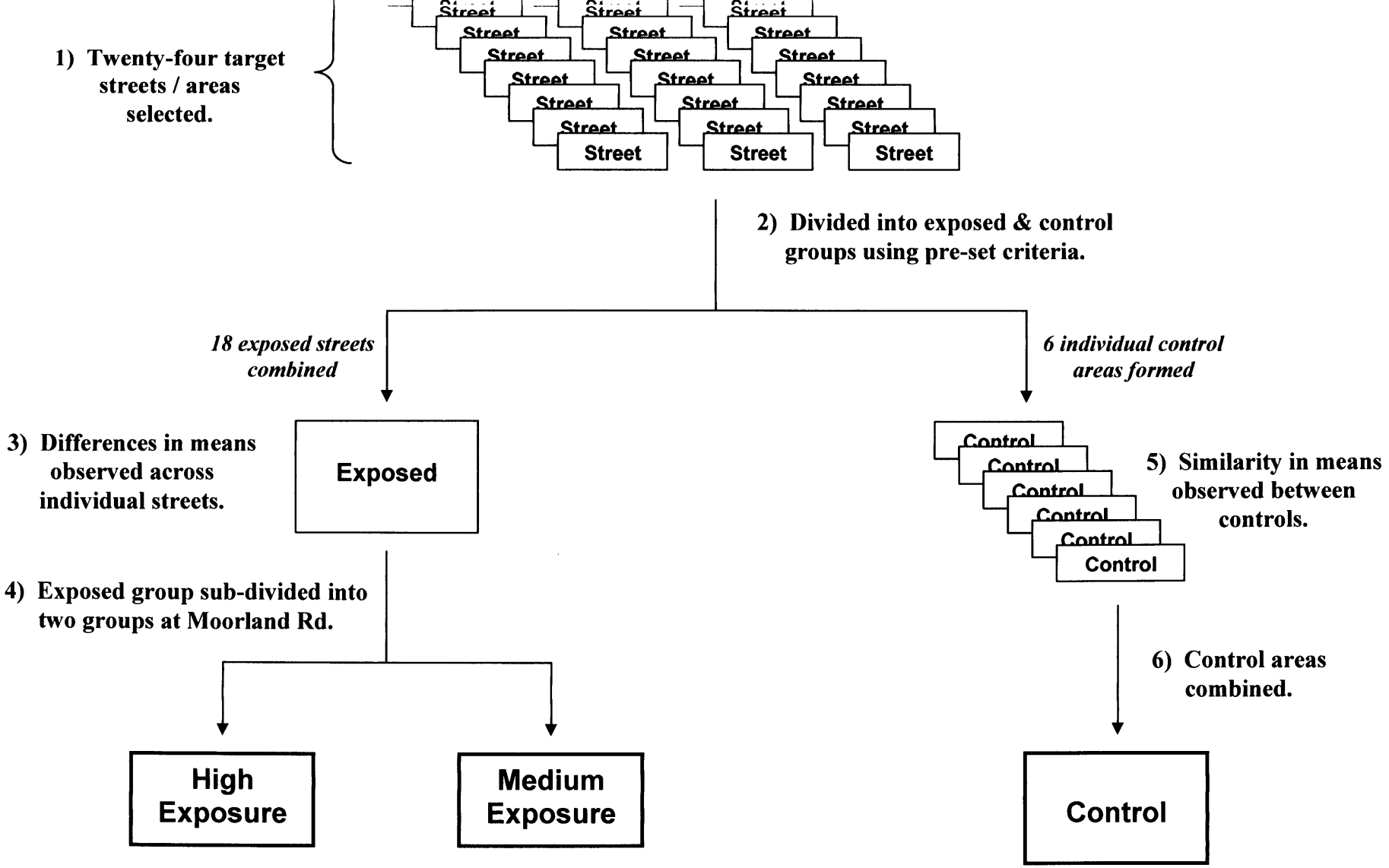


Figure 4.6: Classification of streets / areas into high exposure, medium exposure, and control groups

4.1.2 Indoor air particulate levels in the sampled households

In addition to the outdoor sampling work carried out, PM_5 measurements were also made in indoors on the same occasion as outdoors. Doing so would allow the comparisons between indoor air qualities in houses located in different exposure areas, as well as the examination of any correlations that may exist between indoor and outdoor PM_5 levels. Obviously the architectural design of the house will influence the indoor levels of particle concentrations, this will be dealt with in section 4.1.4. Throughout the study period each participating household was sampled twice 6 months apart for indoor PM_5 concentrations, the figures were then combined to form a mean PM_5 level that represents the house. A total of 73 houses were sampled in the exposed areas and 50 in the control areas. Due to the skewness of the data, medians instead of means of the two groups were compared. This was done by the non-parametric statistical methods Mann-Whitney and Kruskal-Wallis tests.

Differences in exposed and control groups

Houses in the exposed group (13.2μg/m^3) had a higher median indoor PM_5 concentration than the control group (9.4μg/m^3). The range of the values in both groups were high, especially in the exposed group where the maximum PM_5 concentration was more than six-fold higher than the minimum concentration recorded (32.2μg/m^3 v 5.0μg/m^3). Although one extreme value was present in the exposed group, its removal did not alter the medians significantly (figure 4.7). A summary of the statistics can be found in table 4.6. The median of the exposed group was 40% higher than the control group, and when the medians were tested by Mann-Whitney test it was found that the difference observed was statistically significant ($z = 8.64$; $p<0.01$).

	Exposed	Control
N	73	50
Median ($\mu g/m^3$)	13.2	9.4
Minimum ($\mu g/m^3$)	5.0	3.0
Maximum ($\mu g/m^3$)	32.2	21.8
Percentiles 25th ($\mu g/m^3$)	11.7	7.1
75th ($\mu g/m^3$)	16.2	12.1

Table 4.6: Descriptive statistics of indoor PM_5 concentrations, exposed v control.

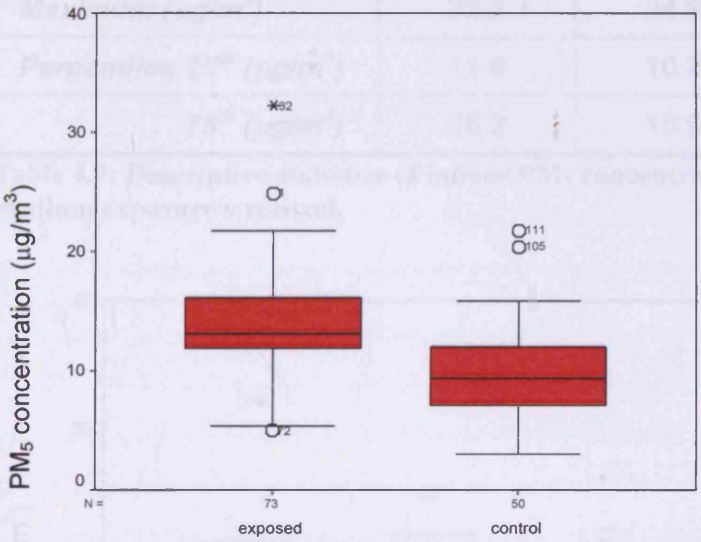


Figure 4.7: Boxplots of indoor PM_5 concentrations, exposed v control.

Differences in high exposure, medium exposure, and control groups

The exposed group was subdivided into high exposure group with 39 measurements, and medium exposure group with 34 measurements. The median indoor PM_5 concentrations were compared, and despite the division a decreasing trend can still be seen across the three exposure groups. Although both the high and medium exposure groups had medians that were higher than the control group, the difference between the high and medium exposure group was actually quite small (13.8µg/m^3 v 13.0µg/m^3). The median of the high exposure group was 47% higher than the control group. Table 4.7 and figure 4.8 show the statistics and distribution of the data of the different exposure groups. Kruskal-Wallis test was performed and showed that the

medians were significantly different from each other (χ^2 (2) = 78.49; p<0.01). In addition, differences between each group were also analysed by Mann-Whitney test including high exposure group v medium exposure group, high exposure group v control group, and medium exposure group v control group. All results were found to be statistically significant at the 1% level.

	High exposure	Medium exposure	Control
N	39	34	50
Median ($\mu g/m^3$)	13.8	13.0	9.4
Minimum ($\mu g/m^3$)	5.0	6.7	3.0
Maximum ($\mu g/m^3$)	32.2	24.9	21.8
Percentiles 25th ($\mu g/m^3$)	11.9	10.2	7.1
75th ($\mu g/m^3$)	16.2	15.9	12.1

Table 4.7: Descriptive statistics of indoor PM_5 concentrations, high exposure v medium exposure v control.

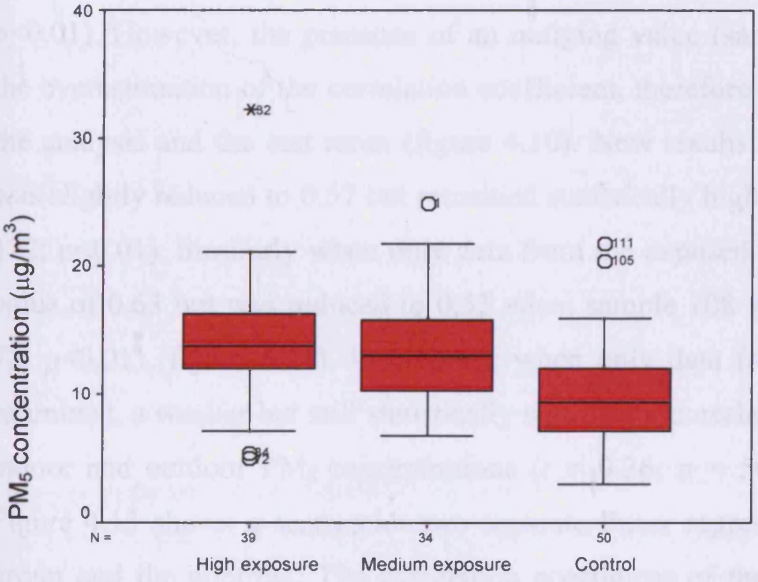


Figure 4.8: Boxplots of indoor PM_5 concentrations, high exposure v medium exposure v control.

4.1.3 Correlations between indoor and outdoor PM_5 concentrations

Correlations between indoor and outdoor PM_5 levels in different exposure areas were examined. In this section the Pearson (r) was used to measure the strength of the correlation coefficient between indoor and outdoor PM_5 levels. The correlation coefficient is defined as a statistic devised to measure the degree of a supposed linear association between two variables [Kinnear & Gray 2000]. The Pearson correlation can only be in a range from –1 to +1 inclusive, and the stronger the association, the greater the absolute value. A positive association is indicated by a positive r and a negative association by a negative r. A perfect correlation arises when the values of one variable can be exactly predicted from the other variable, then r takes a value of ±1. Oppositely, when there is no association between two variables whatsoever r will become zero.

Firstly all PM_5 data obtained through environmental surveys were included in the analysis, and the indoor and outdoor measurements were found to be moderately correlated as shown in figure 4.9. The correlation coefficient was 0.64 with a p-value of <0.01, meaning r was statistically significant at the 1% level ($r = 0.64$; $n = 123$; $p<0.01$). However, the presence of an outlying value (sample 108) may have led to the overestimation of the correlation coefficient, therefore the pair was removed from the analysis and the test reran (figure 4.10). New results showed that the value of r was slightly reduced to 0.57 but remained statistically highly significant ($r = 0.57$; $n = 122$; $p<0.01$). Similarly when only data from the exposed group were studied r had a value of 0.63 but was reduced to 0.53 when sample 108 was removed ($r = 0.53$; $n = 72$; $p<0.01$) (figure 4.11). In contrast, when only data from the control cases were examined, a weaker but still statistically significant correlation was observed between indoor and outdoor PM_5 concentrations ($r = 0.36$; $n = 50$; $p = 0.01$) (figure 4.12). Figure 4.13 shows a scatterplot two separate linear regression lines for the exposed group and the controls. The correlation coefficient of the exposed group was 47% higher than that of the controls.

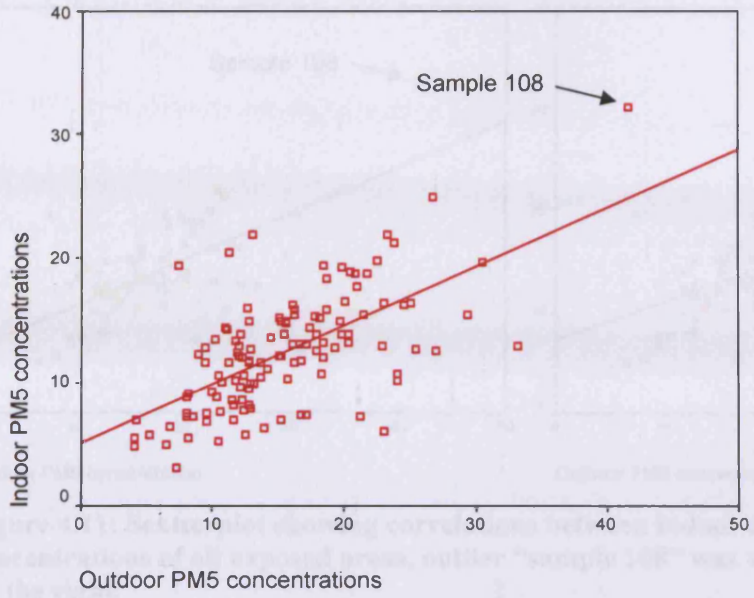


Figure 4.9: Scatterplot showing correlations between indoor and outdoor PM_5 concentrations of all areas.

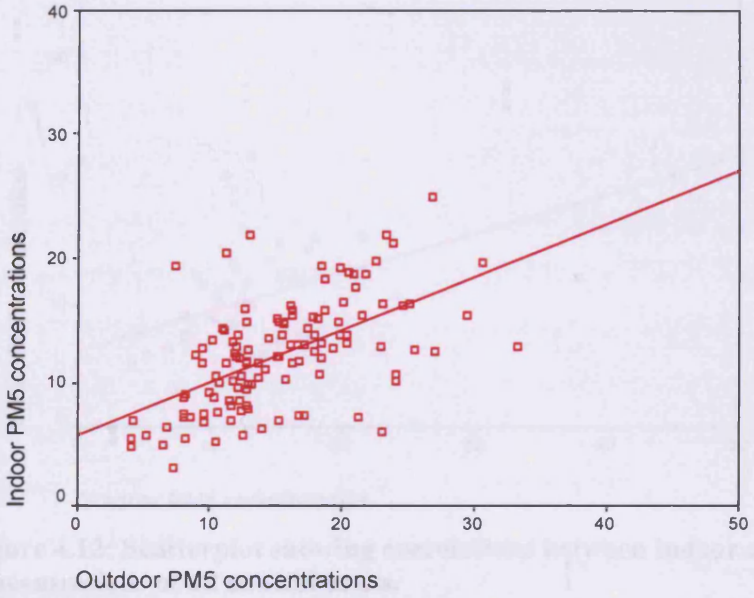


Figure 4.10: Scatterplot showing correlations between indoor and outdoor PM_5 concentrations of all areas, with outlier "sample 108" removed.

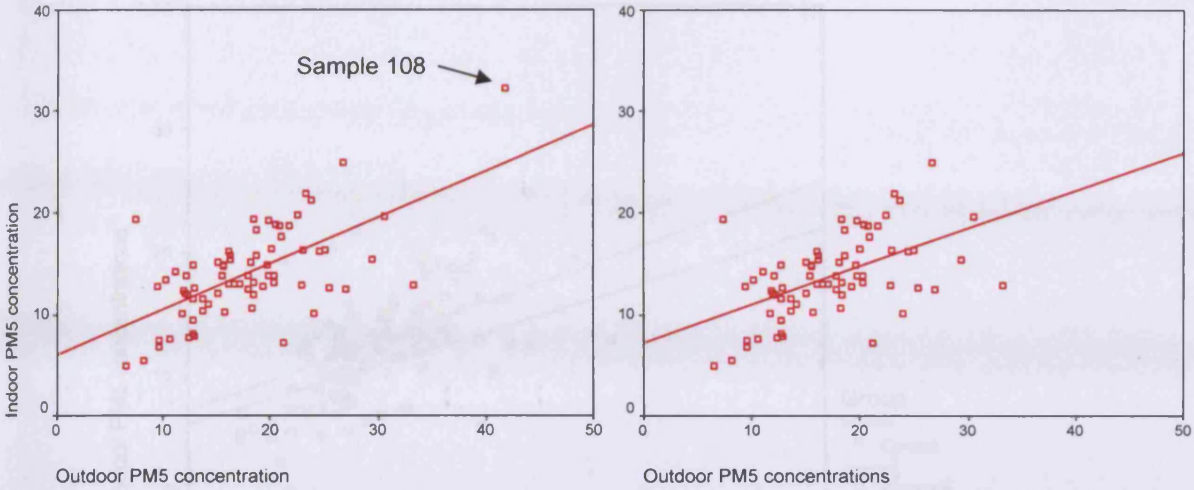


Figure 4.11: Scatterplot showing correlations between indoor and outdoor PM_5 concentrations of all exposed areas, outlier "sample 108" was removed from the figure on the right.

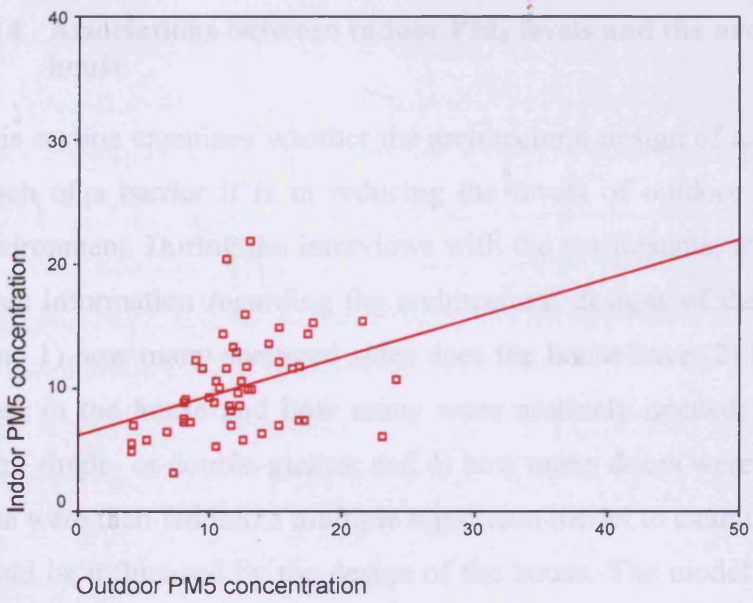


Figure 4.12: Scatterplot showing correlations between indoor and outdoor PM_5 concentrations of all control areas.

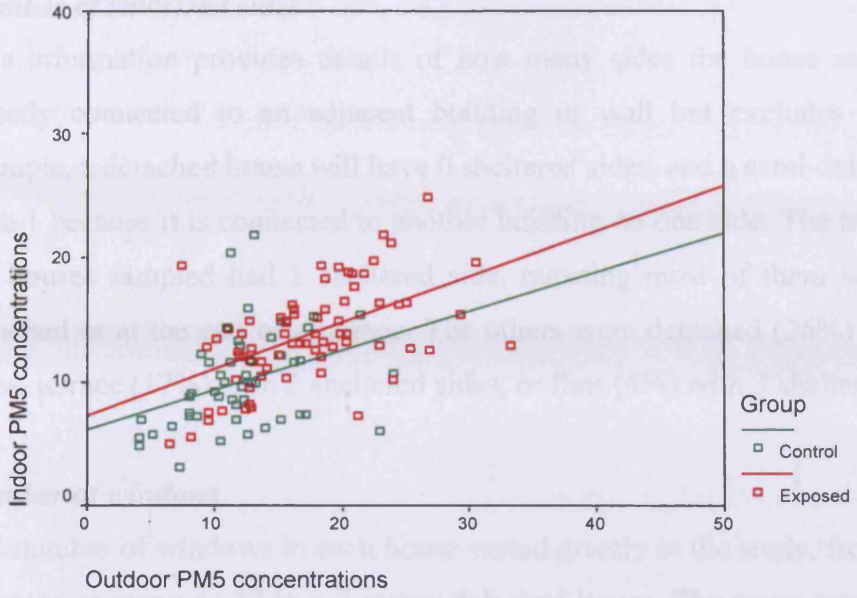


Figure 4.13: Scatterplot showing correlations between indoor and outdoor PM_5 concentrations separated into exposed and control areas.

4.14 Associations between indoor PM_5 levels and the architectural design of the house

This section examines whether the architectural design of a house can determine how much of a barrier it is in reducing the levels of outdoor PM_5 entering the indoor environment. During the interviews with the participants, they were asked to provide basic information regarding the architectural designs of the house. Details collected were 1) how many sheltered sides does the house have; 2) how many windows were there in the house and how many were routinely opened; 3) whether the windows were single- or double-glazed; and 4) how many doors were there in the house. These data were then fed into a multiple regression model to examine if levels of indoor PM_5 could be influenced by the design of the house. The model takes into account of the independent variables, in this case the design of the house, and estimates the coefficient of a linear equation that best predicts the value of the dependent variable, which in this case is the level of indoor PM_5. A total of 114 participants provided details of the house, in which 37 of them were from the high exposure group, 28 from the medium exposure group, and 49 from the control group. Seven refused to provide any details.

Number of sheltered sides

This information provides details of how many sides the house was sheltered, i.e. directly connected to an adjacent building or wall but excludes the ceiling. For example, a detached house will have 0 sheltered sides, and a semi-detached house will have 1 because it is connected to another building on one side. The majority (53%) of the houses sampled had 1 sheltered side, meaning most of them were either semi-detached or at the end of a terrace. The others were detached (26%) with 0 sheltered sides, terrace (17%) with 2 sheltered sides, or flats (4%) with 3 sheltered sides.

Number of windows

The number of windows in each house varied greatly in the study, from as few as 3 in a flat, to as many as 32 in a 3-storey detached house. The mean number of windows recorded was 14, with a 25^{th} and 75^{th} percentile of 9 and 18 respectively.

Number of routinely opened windows

Participants were asked about how many windows were routinely opened in their houses in daytime, during the period when the interviews were conducted. The same questions were asked once again in the second interview six months later. The answers were then combined to form a single value that represent the frequency of windows being opened in the house and expressed as a percentage. On average 28% of the windows were regularly opened, with a 25^{th} and 75^{th} percentile of 11% and 36% respectively. In addition, 17% of the households never had windows opened routinely, and 5% had always opened all their windows on a daily basis.

Glazing

Most of the houses sampled had double-glazing (84%) and the rest with single-glazing. In houses where a mixture of both was present, the type of glazing installed was determined by their proportions and were allocated into the group that was larger.

Number of external doors

Information of the number of external doors that opens to the outside was collected. Those that opened to the garage and garage doors were excluded, and a set of patio doors was counted as one. Approximately 61% of the houses had 3 to 4 external doors, and 33% had 1 to 2. A small proportion (6%) had no external doors because

their main front doors were opened to a public hallway within a building that led to another main door to the outside.

The multiple regression model

Before the variables could be fed into the regression model they must be checked for normality. This applies to all continuous variables including the percentage of windows that were routinely opened in the house, and the indoor and outdoor PM_5 levels of each house. Using P-P plots the distributions of these variables were examined, in which the points would cluster around a straight line if normal distributions were observed. Any skewness present in the data can be fixed by taking the $\log_{10}$ of the values, although this method does not fully eliminate the problem. Figures 4.14 – 4.16 show the P-P plots of all the continuous variables in the model before and after adjustments made by taking $\log_{10}$. It appeared that the distributions of the three variables were all skewed, as shown on the P-P plots on the left of the figures. Both variables "% of windows routinely opened" and "outdoor PM_5 levels" partially restored normality after adjustment by taking $\log_{10}$. In contrast, the variable "indoor PM_5" appeared to be less skewed before adjustment and was therefore unchanged.

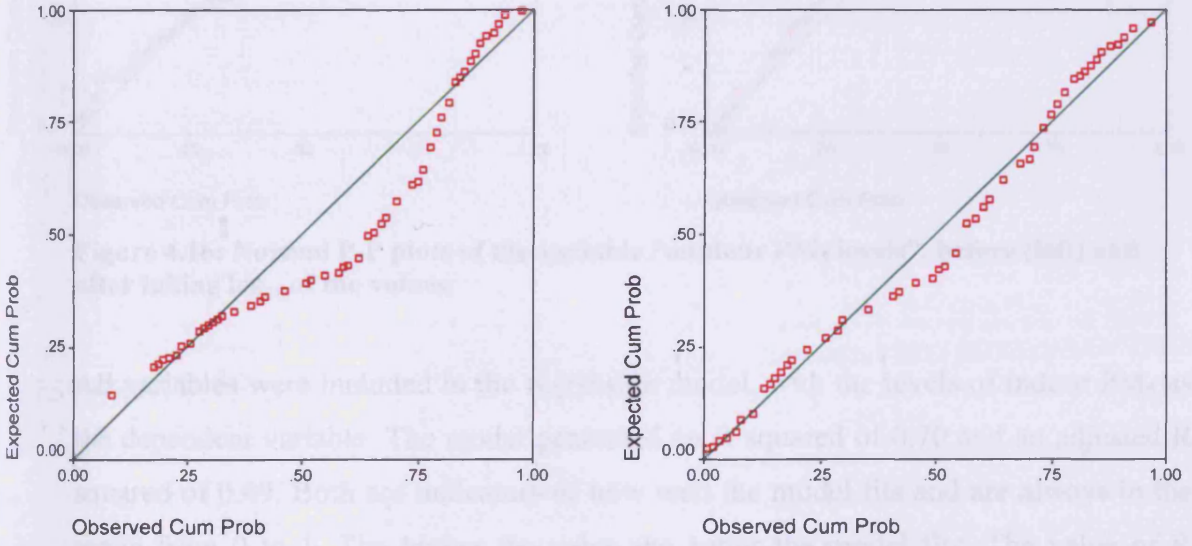


Figure 4.14: Normal P-P plots of the variable "% of windows routinely opened", before (left) and after taking $\log_{10}$ of the values.

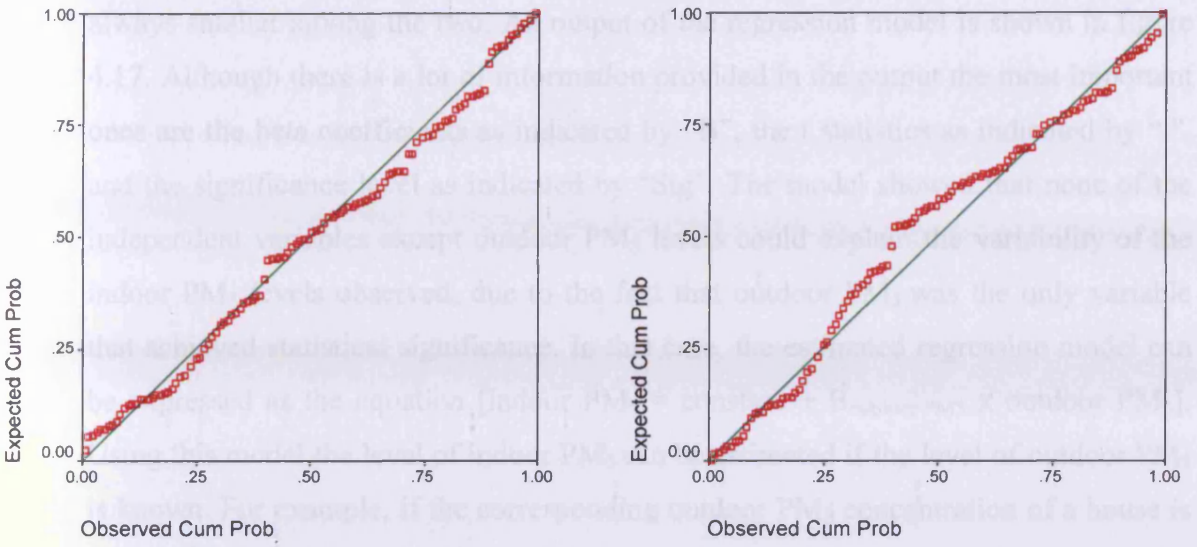


Figure 4.15: Normal P-P plots of the variable "indoor PM_5 levels", before (left) and after taking $\log_{10}$ of the values.

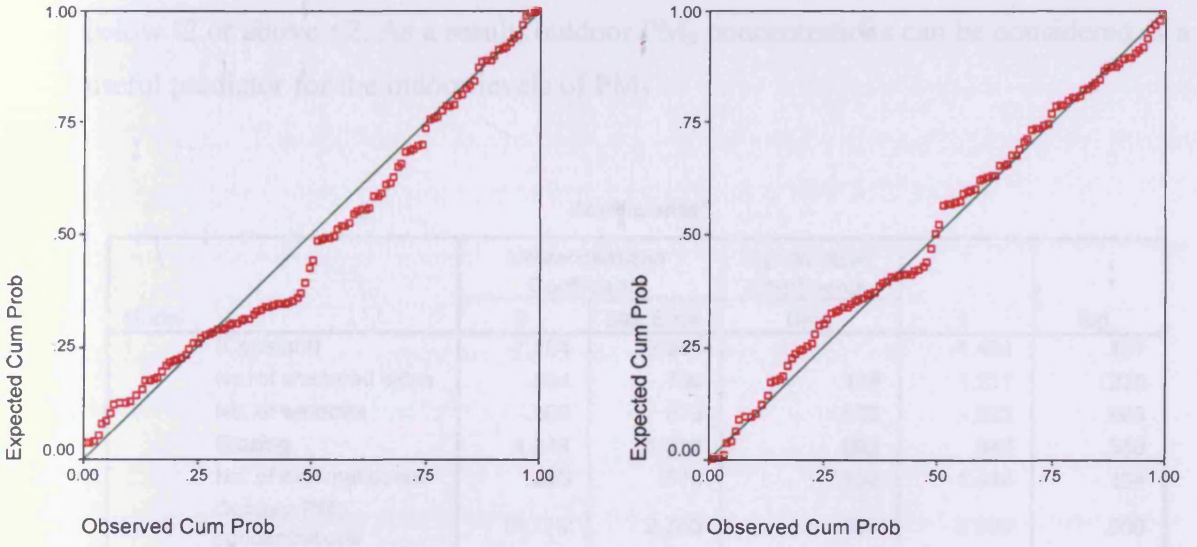


Figure 4.16: Normal P-P plots of the variable "outdoor PM_5 levels", before (left) and after taking $\log_{10}$ of the values.

All variables were included in the regression model, with the levels of indoor PM_5 as the dependent variable. The model generated an R squared of 0.70 and an adjusted R squared of 0.49. Both are indicators of how well the model fits and are always in the range from 0 to 1. The higher the value the better the model fits. The value of R squared represents the proportion of variation in the dependent variable explained by the model, and tends to optimistically estimate how well the model fits. In contrast, the adjusted R square will correct the R squared so that it will more closely reflect the goodness of fit of the model. This explains why the value of adjusted R squared is

always smaller among the two. An output of the regression model is shown in figure 4.17. Although there is a lot of information provided in the output the most important ones are the beta coefficients as indicated by "B", the t statistics as indicated by "t", and the significance level as indicated by "Sig". The model showed that none of the independent variables except outdoor PM_5 levels could explain the variability of the indoor PM_5 levels observed, due to the fact that outdoor PM_5 was the only variable that achieved statistical significance. In this case, the estimated regression model can be expressed as the equation [indoor PM_5 = constant + $B_{\text{outdoor PM5}}$ x outdoor PM_5]. Using this model the level of indoor PM_5 can be estimated if the level of outdoor PM_5 is known. For example, if the corresponding outdoor PM_5 concentration of a house is $20\mu g/m^3$, using the regression model the predicted indoor PM_5 would therefore be [-7.704 + log15.179 x 20] = $15.92\mu g/m^3$. The t statistics helps to determine the relative importance of each variable in the model, and useful predictors are usually below -2 or above +2. As a result, outdoor PM_5 concentrations can be considered as a useful predictor for the indoor levels of PM_5.

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-7.704	5.384		-1.431	.157
	No. of sheltered sides	.884	.730	.138	1.211	.230
	No. of windows	-.002	.078	-.002	-.022	.983
	Glazing	1.243	1.320	.092	.942	.350
	No. of external doors	.823	.570	.153	1.444	.154
	Outdoor PM5 concentrations	15.179	2.760	.607	5.500	.000
	% of windows routinely opened	-1.078	1.708	-.063	-.631	.530
	Exposure group	-1.088	1.143	-.111	-.952	.345

a. Dependent Variable: Indoor PM5 concentrations

Figure 4.17: Output of multiple regression model.

4.1.5 Trace elements in outdoor ambient air samples

Apart from monitoring the concentrations of air particulates in the environment, PM_{10} samples were also collected to examine the elemental contents of the particles in the air. A total of 19 outdoor ambient air samples were taken within a 6-week period. Nine of the samples were from exposed areas and 10 were from control areas. Presence of trace elements in these environmental samples collected on polycarbonate filters were detected by neutron activation analysis. A set of control blanks were also analysed and the mean concentrations of each trace element found on these filters were deducted from the results obtained from the environmental samples. Seventeen different elements including sodium (Na), magnesium (Mg), aluminium (Al), sulphur (S), chlorine (Cl), potassium (K), calcium (Ca), titanium (Ti), vanadium (V), cobalt (Co), manganese (Mn), copper (Cu), bromine (Br), antimony (Sb), tin (Sn), iodine (I), and holmium (Ho) were quantified, with V, Cu, Br, and Sb as the main elements of interest. When comparing the levels of trace elements between different exposure groups, the use of medians were thought to be more appropriate due to the skewness of the data. The difference in medians was examined by the non-parametric Mann-Whitney test. When the concentrations of some elements in a sample fell under the minimum detection limits, they were treated as zero. Ideally the value of the minimum detection limit should be quoted instead, but due to the fact that the detection limits of certain elements were unknown, thus zero was used throughout the results section to maintain consistency. Furthermore, since median was calculated instead of mean, the decision of whether to use zero or the value of the minimum detection limit would have no effects on the results at all. On the other hand, any extreme values present in the data were still being included in the analysis.

Vanadium (V)

Table 4.8 shows the descriptive statistics of vanadium concentrations in ambient air samples. One sample from the exposed group contained undetectable amount of vanadium and there were no outlying values in the dataset (figure 4.18). Median concentration of vanadium found in the exposed areas was almost half of the level seen in the control areas. The median concentration for exposed area was 0.07ng per m^3 of air sampled and 0.12ng/m^3 for control areas. Mann-Whitney test showed that the different medians observed in the two exposure groups was statistically significant ($z = 2.25$; $p = 0.03$).

	Exposed	Control
N	9	10
Median (ng/m^3)	0.07	0.12
Minimum (ng/m^3)	0.00	0.06
Maximum (ng/m^3)	0.14	0.21
Percentiles 25th (ng/m^3)	0.03	0.07
75th (ng/m^3)	0.11	0.15

Table 4.8: Vanadium concentrations in ambient air samples, exposed v control.

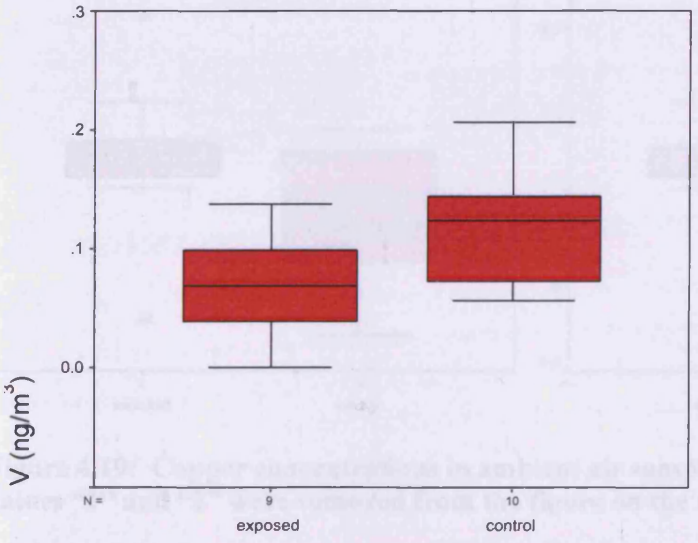


Figure 4.18: Vanadium concentrations in ambient air samples, exposed v control.

Copper (Cu)

Table 4.8 shows the descriptive statistics of copper concentrations in ambient air samples. All samples contained detectable amount of copper. Although two extreme values were found in the exposed group, their existence had no significant effects in the median (figure 4.19). The exposed group has a higher median copper concentration than the control group by 41% (1.21ng/m^3 v 0.86ng/m^3). Mann-Whitney test showed that it was not statistically different from the median of the control group ($z = 1.72$; $p = 0.1$).

	Exposed	Control
N	9	10
Median (ng/m^3)	1.21	0.86
Minimum (ng/m^3)	0.30	0.06
Maximum (ng/m^3)	2.06	1.41
Percentiles 25th (ng/m^3)	1.10	0.55
75th (ng/m^3)	1.46	1.29

Table 4.9: Copper concentrations in ambient air samples, exposed v control.

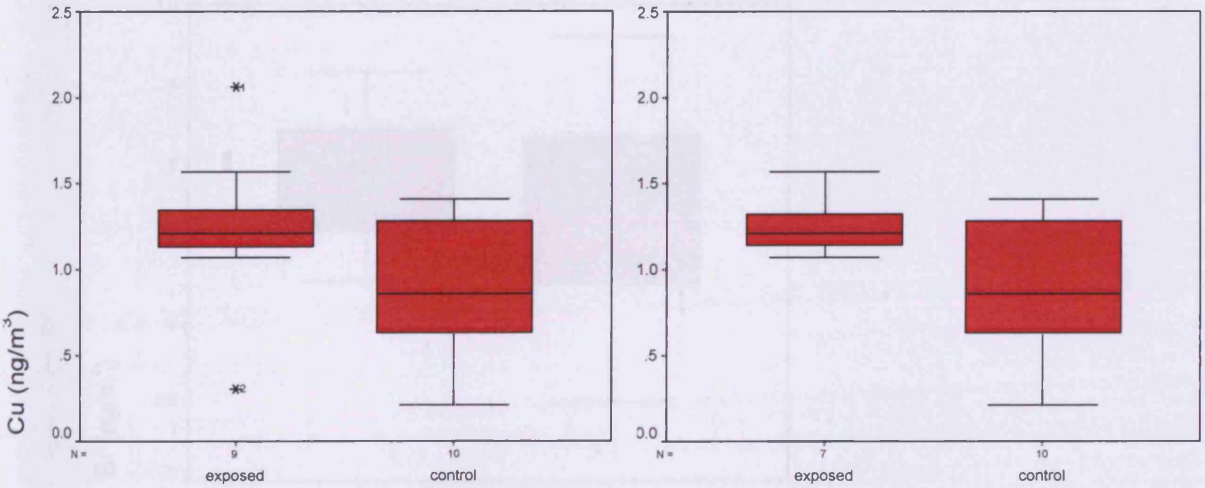


Figure 4.19: Copper concentrations in ambient air samples, exposed v control. Extreme values "1" and "2" were removed from the figure on the right.

Bromine (Br)

Table 4.10 shows the descriptive statistics of bromine concentrations in ambient air samples. Bromine was not detected in one of the control samples and there were no extreme values present in the data. The median bromine concentration of the exposed group was 0.47ng/m^3, which was approximately 19% lower than the control group (0.58ng/m^3) as shown in figure 4.20. There was no significant difference between the medians of the exposed and control areas as shown by Mann-Whitney test (z = 0.41, p = 0.72).

	Exposed	Control
N	9	10
Median (ng/m^3)	0.47	0.58
Minimum (ng/m^3)	0.30	0.00
Maximum (ng/m^3)	0.83	0.92
Percentiles 25th (ng/m^3)	0.41	0.26
75th (ng/m^3)	0.74	0.67

Table 4.10: Bromine concentrations in ambient air samples, exposed v control.

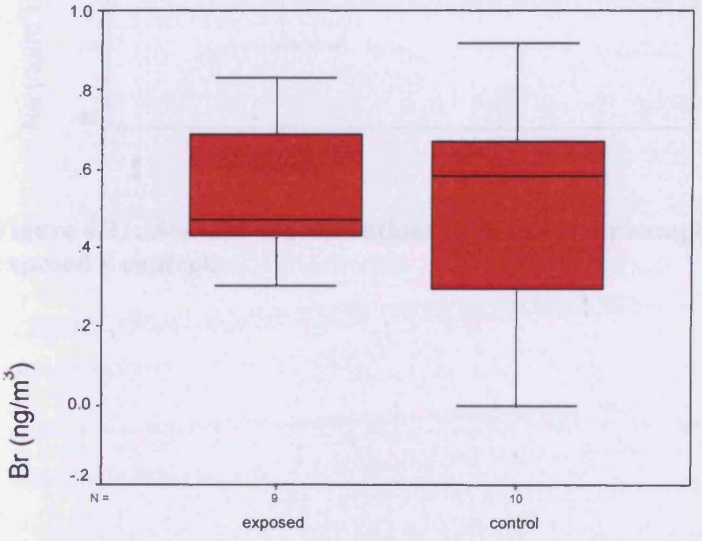


Figure 4.20: Bromine concentrations in ambient air samples, exposed v control.

Antimony (Sb)

Insufficient amount of data were available for the analysis of antimony in the ambient air samples.

Others

Amongst all other elements analysed, only sodium ($z = 2.29$; $p = 0.02$) and chlorine ($z = 2.21$; $p = 0.03$) achieved statistical significance when tested by Mann-Whitney test. Boxplots of sodium and chlorine concentrations are shown in figures 4.21 and 4.22. Both elemental concentrations observed have medians significantly higher in the exposed group than the control group. For sodium, the median of the exposed and control groups were 50.8ng/m^3 and 17.3ng/m^3 respectively; for chlorine, the median of the exposed and control groups were 24.6ng/m^3 and 10.3ng/m^3 respectively.

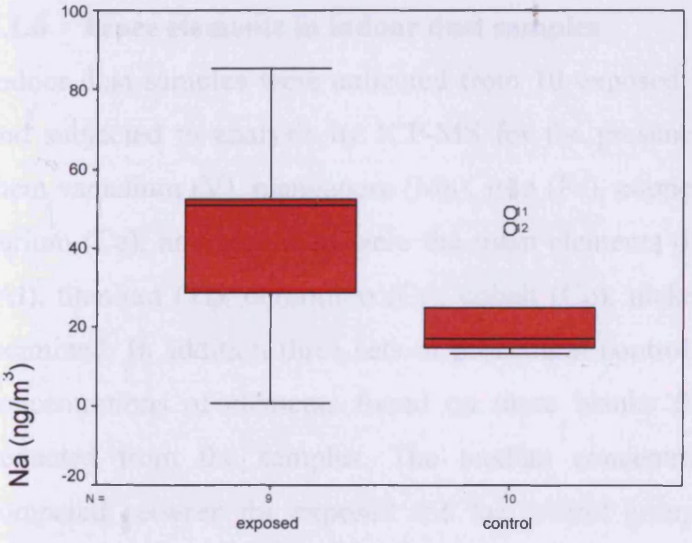


Figure 4.21: Sodium concentrations in ambient air samples, exposed v control.

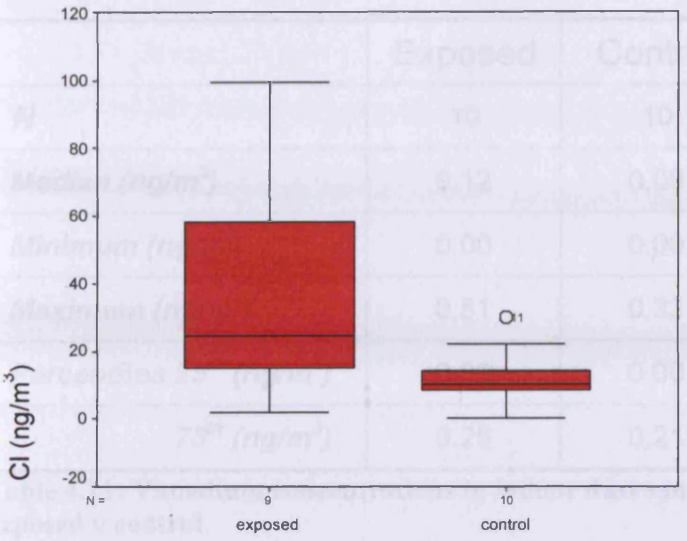


Figure 4.22: Chlorine concentrations in ambient air samples, exposed v control.

4.1.6 Trace elements in indoor dust samples

Indoor dust samples were collected from 10 exposed houses and 10 control houses, and subjected to analysis by ICP-MS for the presence of trace elements. Amongst them vanadium (V), manganese (Mn), iron (Fe), copper (Cu), zinc (Zn), barium (Ba), cerium (Ce), and lead (Pb) were the main elements of interest, although aluminium (Al), titanium (Ti), chromium (Cr), cobalt (Co), nickel (Ni), and tin (Sn) were also examined. In addition three sets of procedural control blanks were included and the concentrations of elements found on these blanks filters were then averaged and deducted from the samples. The median concentrations of each element were compared between the exposed and the control groups. Any undetectable elements that fell below the minimum detection limits were regarded as zero when analysing the data, and any extreme values present were also included in the analysis.

Vanadium (V)

Table 4.11 shows the descriptive statistics of vanadium concentrations in indoor dust samples. There were a total of 4 samples from the exposed group and 3 samples from the control group that fell below the minimum detection limit. No extreme values were found (figure 4.23). Median concentration of vanadium from the exposed group was 33% higher than the control. The difference observed was tested by Mann-Whitney test but it failed to achieve statistical significance ($z = 1.14$; $p = 0.25$).

	Exposed	Control
N	10	10
Median (ng/m^3)	0.12	0.09
Minimum (ng/m^3)	0.00	0.00
Maximum (ng/m^3)	0.51	0.33
Percentiles 25th (ng/m^3)	0.00	0.00
75th (ng/m^3)	0.25	0.21

Table 4.11: Vanadium concentrations in indoor dust samples, exposed v control

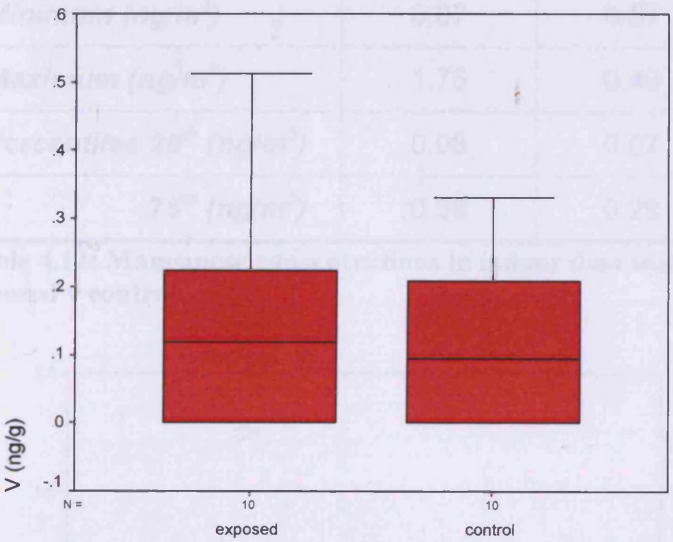


Figure 4.23: Boxplots of vanadium concentrations in indoor dust samples, exposed v control.

Manganese (Mn)

Table 4.12 shows the descriptive statistics of manganese concentrations in indoor dust samples. All 20 samples were above the detection limit and there were no extreme values present (figure 4.24). Median concentration of manganese in the exposed group was 56% higher than the control group. Mann-Whitney test was carried out to compare the medians observed and they were found to be statistically insignificant (z = 1.07; p = 0.29).

	Exposed	Control
N	10	10
Median (ng/m^3)	0.28	0.18
Minimum (ng/m^3)	0.07	0.07
Maximum (ng/m^3)	1.75	0.49
Percentiles 25th (ng/m^3)	0.08	0.07
75th (ng/m^3)	0.59	0.29

Table 4.12: Manganese concentrations in indoor dust samples, exposed v control.

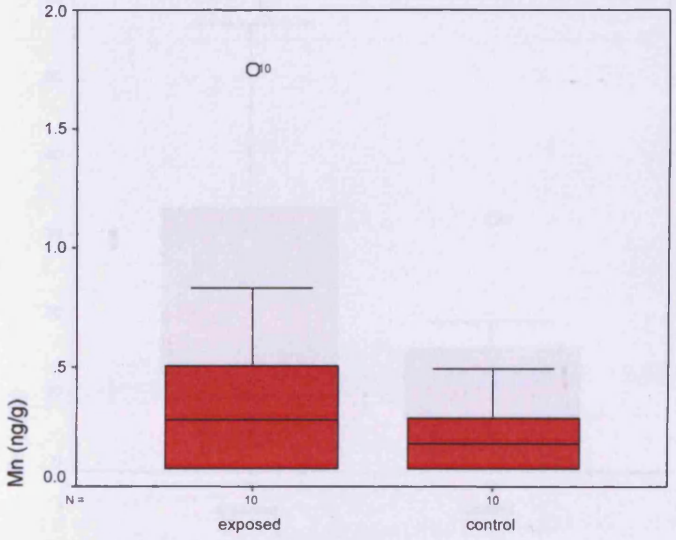


Figure 4.24: Boxplots of manganese concentrations in indoor dust samples, exposed v control.

Iron (Fe)

Table 4.13 shows the descriptive statistics of iron concentrations in indoor dust samples. All values were above the detection limit and extreme values were not present (figure 4.25). Median concentration of iron in the exposed group was markedly higher and nearly doubled the median concentration found in the controls. Mann-Whitney test was carried out and the difference observed did not reach statistical significance ($z = 1.63$; $p = 0.10$).

	Exposed	Control
N	10	10
Median (ng/m^3)	15.3	8.8
Minimum (ng/m^3)	3.0	2.8
Maximum (ng/m^3)	56.5	31.9
Percentiles 25th (ng/m^3)	11.1	6.3
75th (ng/m^3)	34.1	16.4

Table 4.13: Iron concentrations in indoor dust samples, exposed v control.

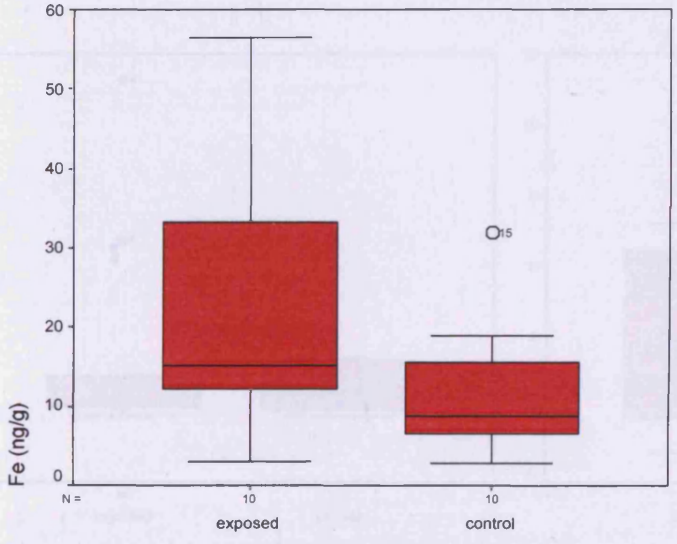


Figure 4.25: Boxplots of iron concentrations in indoor dust samples, exposed v control.

Copper (Cu)

Table 4.14 shows the descriptive statistics of copper concentrations in indoor dust samples. None of the samples contained copper that was below the minimum detection limit but there were two extreme values present (figure 4.26). The median concentration of copper was lower in the exposed group than the control group by 21%. However, the difference observed was found to be statistically insignificant by Mann-Whitney test ($z = 0.23$; $p = 0.82$). Note that the range between the 25th and 75th percentiles was unusually large.

	Exposed	Control
N	10	10
Median (ng/m^3)	5.5	7.0
Minimum (ng/m^3)	0.8	0.7
Maximum (ng/m^3)	55.6	10.2
Percentiles 25th (ng/m^3)	2.0	1.7
75th (ng/m^3)	12.8	10.0

Table 4.14: Copper concentrations in indoor dust samples, exposed v control.

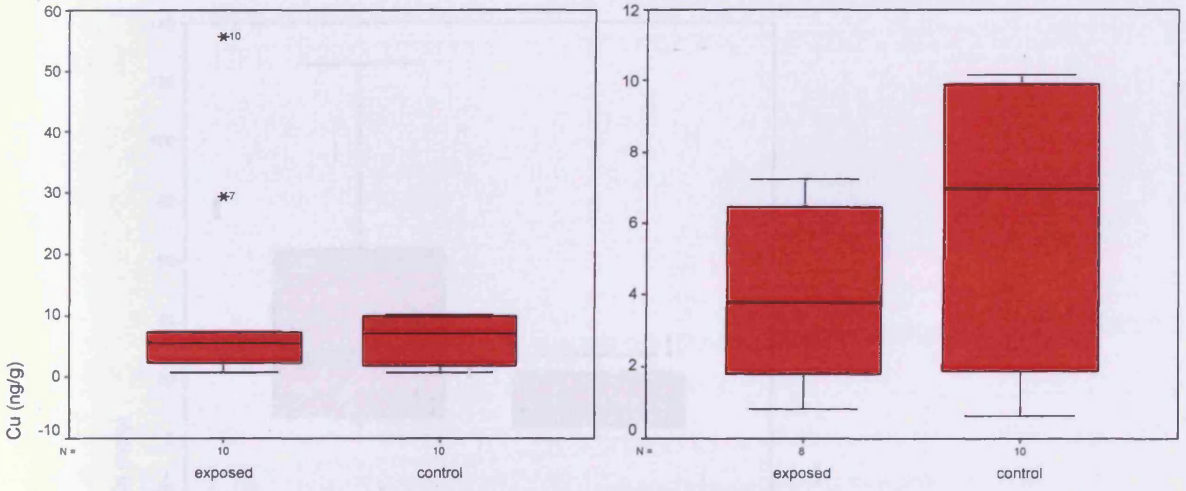


Figure 4.26: Boxplots of copper concentrations in indoor dust samples, exposed v control. Extreme values "7" and "10" were removed from the figure on the right.

Zinc (Zn)

Table 4.15 shows the descriptive statistics of zinc concentrations in indoor dust samples. One sample from the exposed group contained undetectable amount of zinc and was therefore treated as 0 in the analysis. No extreme values were present in either group (figure 4.27). Median concentration of zinc found in the exposed group was significantly higher than the control group more than two-fold. The observed difference in medians was test by Mann-Whitney test and was found to be statistically insignificant ($z = 1.29$; $p = 0.20$).

	Exposed	Control
N	10	10
Median (ng/m^3)	26.1	9.8
Minimum (ng/m^3)	0.0	0.2
Maximum (ng/m^3)	125.9	28.4
Percentiles 25th (ng/m^3)	6.7	4.4
75th (ng/m^3)	66.7	23.7

Table 4.15: Zinc concentrations in indoor dust samples, exposed v control.

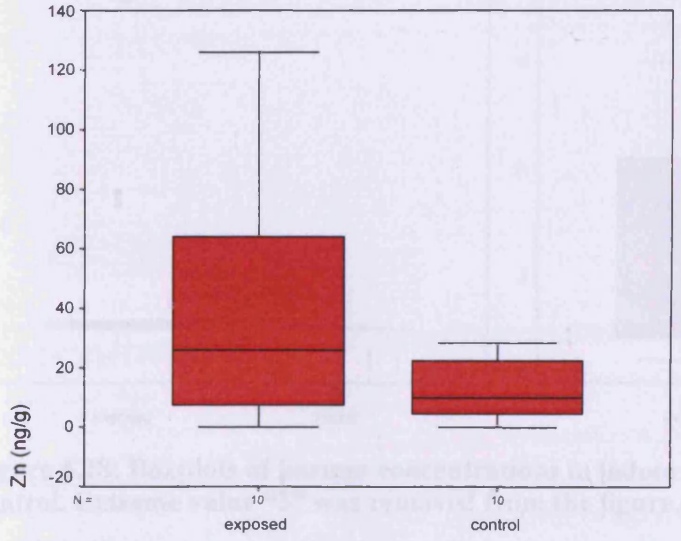


Figure 4.27: Boxplots of zinc concentrations in indoor dust samples, exposed v control.

Barium (Ba)

Table 4.16 shows the descriptive statistics of barium concentrations in indoor dust samples. All samples contained concentrations of barium that were above the detection limits but one extreme value was present in the exposed group (figure 4.28). The median concentration of barium in the exposed group was more than 2-fold higher than the controls. The observed difference was tested by Mann-Whitney test and was found to be statistically insignificant ($z = 1.97$; $p = 0.05$).

	Exposed	Control
N	10	10
Median (ng/m^3)	5.6	2.7
Minimum (ng/m^3)	1.1	0.6
Maximum (ng/m^3)	621.1	5.3
Percentiles 25th (ng/m^3)	2.1	1.2
75th (ng/m^3)	12.4	3.1

Table 4.16: Barium concentrations in indoor dust samples, exposed v control.

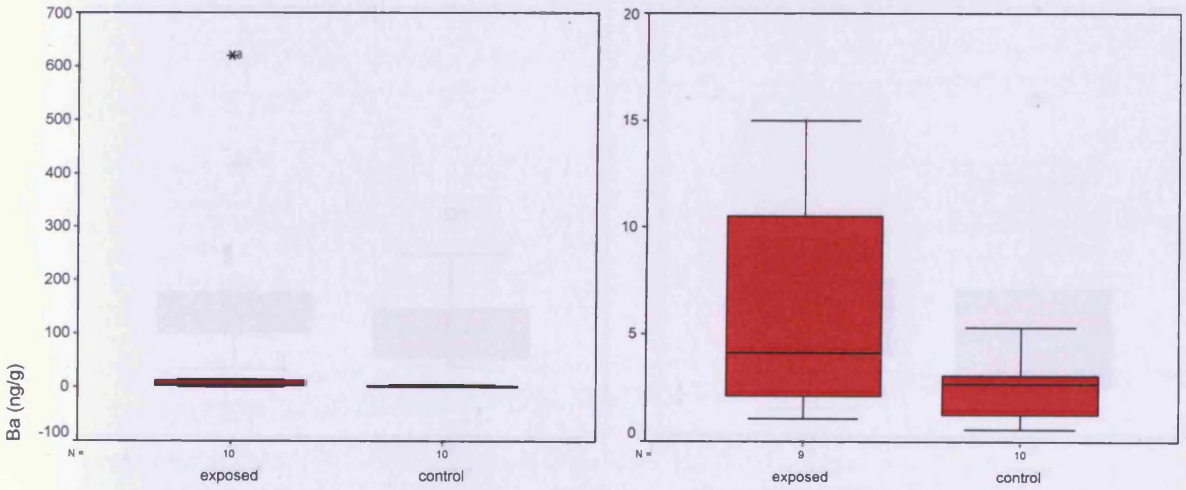


Figure 4.28: Boxplots of barium concentrations in indoor dust samples, exposed v control. Extreme value "3" was removed from the figure on the right.

Cerium (Ce)

Table 4.17 shows the descriptive statistics of cerium concentrations in indoor dust samples. All samples contain concentrations of cerium above the minimum detection limits but two extreme values were present in the exposed group (figure 4.29). Median cerium concentration in samples from the exposed group was 33% higher than those from the control group. The observed difference was tested by Mann-Whitney test but did not reach statistical significance ($z = 0.09$; $p = 0.36$).

	Exposed	Control
N	10	10
Median (ng/m^3)	0.12	0.09
Minimum (ng/m^3)	0.03	0.03
Maximum (ng/m^3)	0.61	0.31
Percentiles 25th (ng/m^3)	0.08	0.04
75th (ng/m^3)	0.23	0.15

Table 4.17: Cerium concentrations in indoor dust samples, exposed v control.

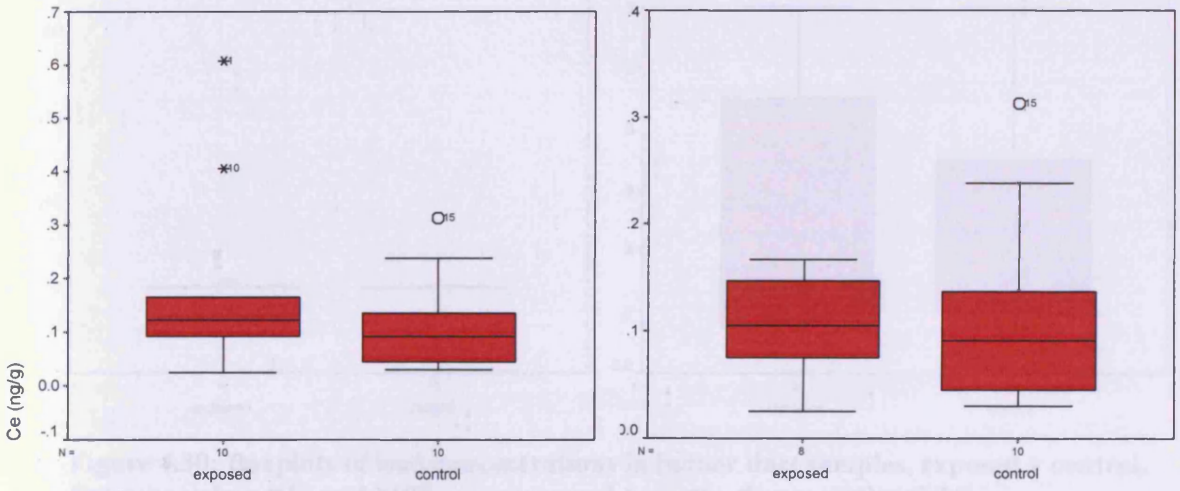


Figure 4.29: Boxplots of cerium concentrations in indoor dust samples, exposed v control. Extreme values "1" and "10" were removed from the figure on the right.

Lead (Pb)

Table 4.18 shows the descriptive statistics of lead concentrations in indoor dust samples. Lead was detected in all the samples but there were two extreme values in the exposed group (figure 4.30). The median lead concentration found in the exposed group was 3-fold higher than the controls. However, the observed difference did not reach statistical significance when tested by Mann-Whitney test ($z = 0.10$; $p = 0.36$).

	Exposed	Control
N	10	10
Median (ng/m^3)	0.60	0.20
Minimum (ng/m^3)	0.10	0.10
Maximum (ng/m^3)	367.10	1.20
Percentiles 25th (ng/m^3)	0.18	0.15
75th (ng/m^3)	2.48	0.75

Table 4.18: Lead concentrations in indoor dust samples, exposed v control.

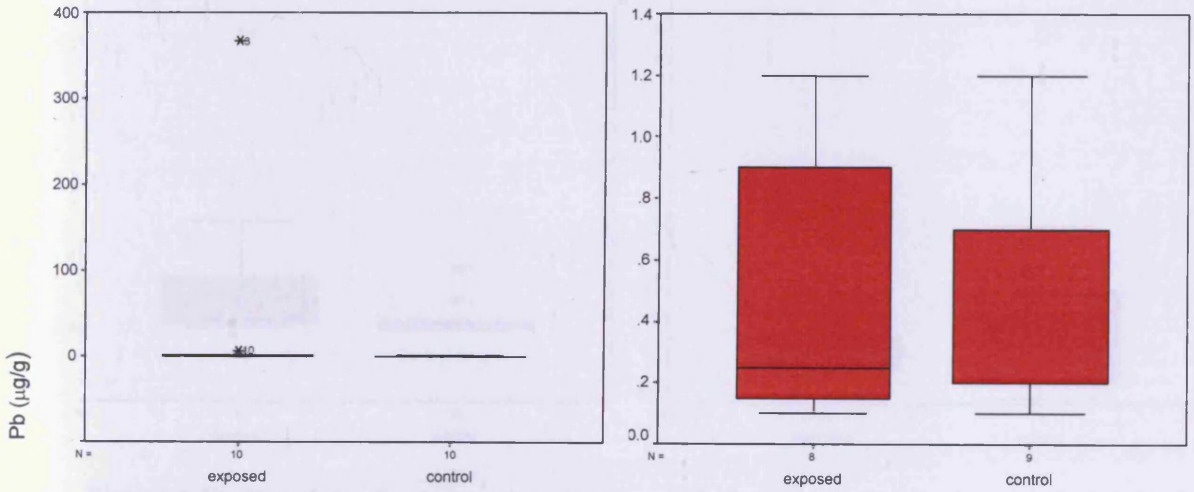


Figure 4.30: Boxplots of lead concentrations in indoor dust samples, exposed v control. Extreme values "3" and "10" were removed from the figure on the right.

Others

Median tests were also performed for the remaining elements includeing Al, Ti, Co, and Sn. Although the median concentrations of Al, Co, and Sn were higher in samples from the exposed group than the controls (figures 4.31 – 4.33), none of them have

reached statistical significance. Analysis was not carried out for Cr and Ni due to the absence of sufficient data that were above the minimum detection limits.

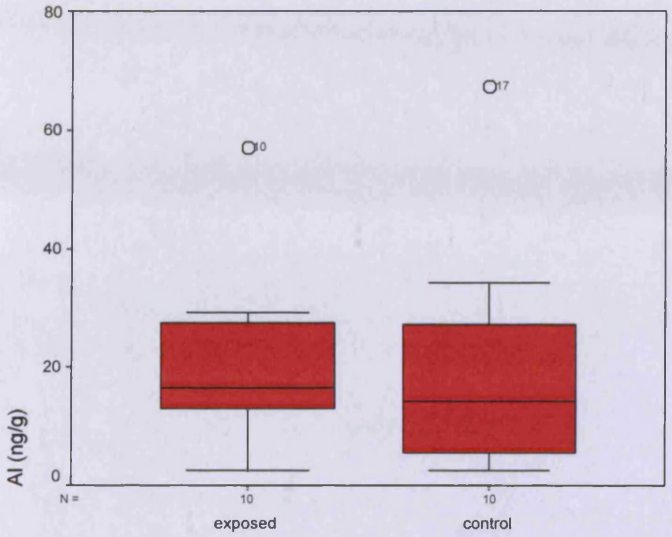


Figure 4.31: Boxplots of aluminium concentrations in indoor dust samples, exposed v control.

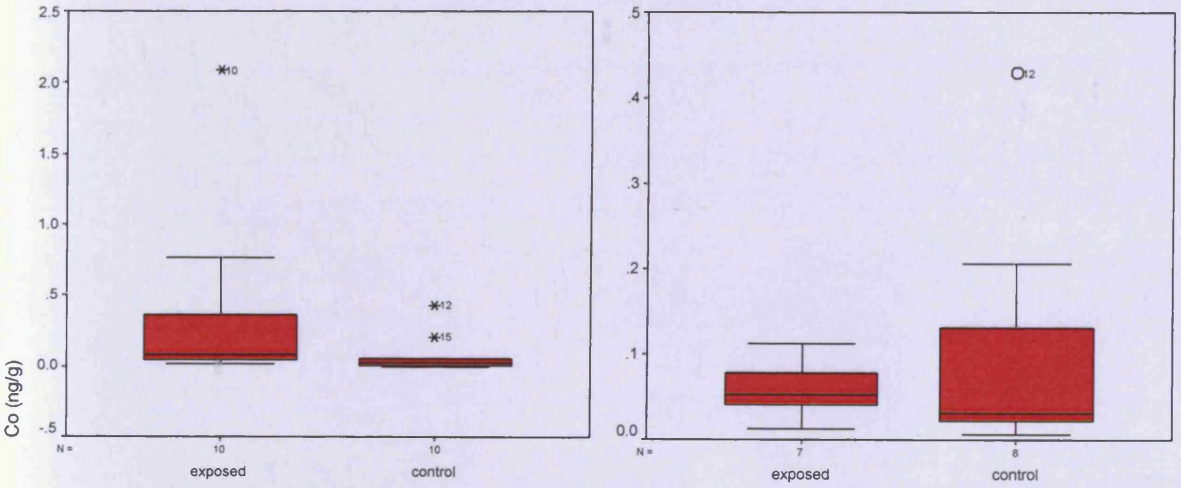


Figure 4.32: Boxplots of cobalt concentrations in indoor dust samples, exposed v control. Extreme values "3", "7", "10", "12"and "15" were removed from the figure on the right.

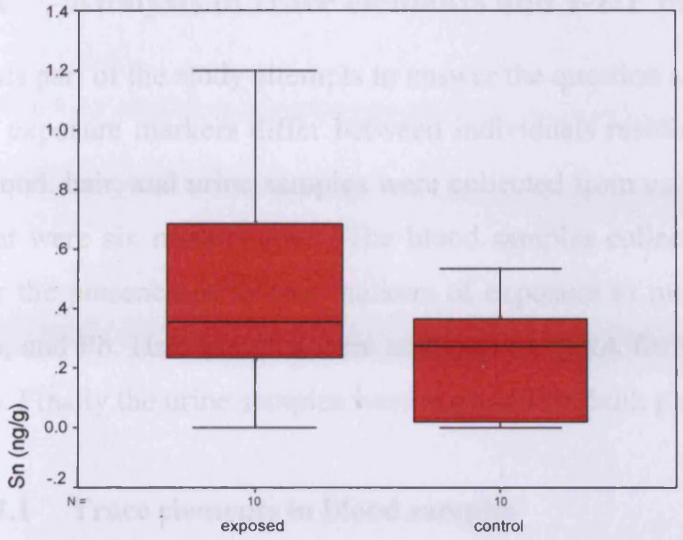


Figure 4.33: Boxplots of tin concentrations in indoor dust samples, exposed v control.

4.1.7 PAH concentrations in environmental air samples

A total of 9 environmental PAH samples were collected throughout the study, of which 5 were from exposed areas and 4 were from control areas. Fibreglass filters used for sampling were subjected to HPLC for the analysis of 16 PAH compounds including napthalene, acenapthylene, acenapthene, fluorene, anthracene, phenanthrene, fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, indeno[123cd]pyrene, benzo[ghi]perylene, and dibenz[ah]anthracene. The minimum detection limits for these compounds were approximately 5ng/ml, which is roughly equivalent to 15ng of PAH per filter, although there may be some slight variations depending upon the particular compound. Results of the analysis showed that all filters contained undetectable levels of PAH compounds.

4.2 Analysis of trace elements and 1-HP in biological samples

This part of the study attempts to answer the question as to whether the concentrations of exposure markers differ between individuals residing in different exposure areas. Blood, hair, and urine samples were collected from each participant on two occasions that were six months apart. The blood samples collected were analysed by ICP-MS for the presence of known markers of exposure to motor vehicles including Cu, Fe, Zn, and Pb. Hair samples were analysed by NAA for the presence of V, Cu, Br, and Sb. Finally the urine samples were analysed for both platinum (Pt) and 1-HP.

4.2.1 Trace elements in blood samples

Throughout the study period a total of 84 participants agreed to donate two blood samples that were 6 months apart, of which 53 were from the exposed group and 34 were from the control group. They were asked to attend the Phlebotomy clinic in the University Hospital of Wales where a qualified phlebotomist extracted a small amount of blood via a Vacutainer®. Samples of whole blood were then separated and serum was used for the analysis of Cu, Fe, Zn, and Pb by ICP-MS. The elemental concentrations of the two samples donated by each subject were then combined to give a mean concentration. Any elements that fell below the minimum detection limit within a sample were treated as zero, and all extreme values were included in the analysis. Mann-whitney and Kruskal-Wallis tests were used to find out whether or not the differences in medians were significant.

Differences in exposed and control groups

Copper (Cu)

Table 4.19 shows the descriptive statistics of copper concentrations in blood samples. All samples contained concentrations of copper that were above the minimum detection limit and there were no extreme values presented (figure 4.34). The medians of the exposed group and the control group were very similar (15.6μmol/L v 15.1μmol/L) with a difference of only 3%. Mann-Whitney test showed that the medians of the two groups were not significantly different from each other ($z = 1.63$; $p = 0.10$).

	Exposed	Control
N	53	34
Median (μmol/L)	15.6	15.1
Minimum (μmol/L)	12.8	11.3
Maximum (μmol/L)	21.4	19.5
Percentiles 25th (μmol/L)	14.4	13.4
75th (μmol/L)	17.8	16.7

Table 4.19: Copper concentrations in blood, exposed v control.

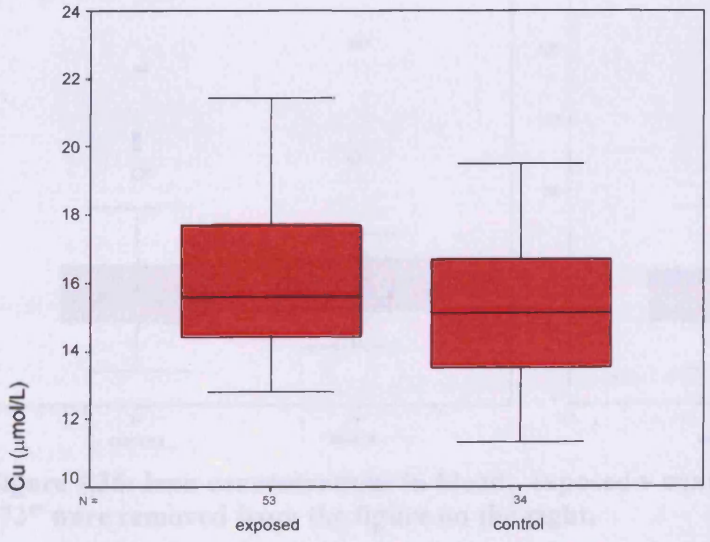


Figure 4.34: Copper concentrations in blood, exposed v control.

Iron (Fe)

Table 4.20 shows the descriptive statistics of iron concentrations in blood samples. Only 52 out of 53 blood samples in the exposed group were available for iron detection by ICP-MS. Both the exposed and control groups had one extreme value, and all samples had detectable levels of iron (figure 4.35). The medians of the exposed and control groups were very similar, with the controls having a slightly larger median than the exposed group by 2% (29.4μmol/L v 30.1μmol/L). The observed difference in the medians was found to be statistically insignificant by Mann-Whitney test ($z = 0.98$; $p = 0.33$).

	Exposed	Control
N	52	34
Median (μmol/L)	29.4	30.1
Minimum (μmol/L)	9.7	16.1
Maximum (μmol/L)	95.3	102.1
Percentiles 25th (μmol/L)	22.7	25.7
75th (μmol/L)	39.4	41.5

Table 4.20: Iron concentrations in blood, exposed v control.

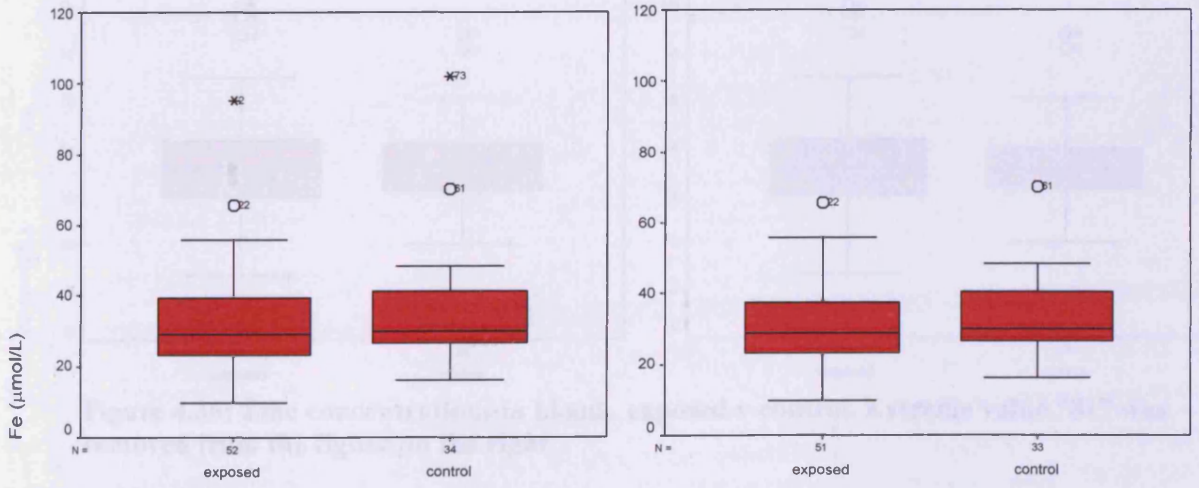


Figure 4.35: Iron concentrations in blood, exposed v control. Extreme values "2" and "73" were removed from the figure on the right.

Zinc (Zn)

Table 4.21 shows the descriptive statistics of zinc concentrations in blood samples. One extreme value was present in the control group and zinc was detected in all samples (figure 4.36). The median of zinc concentrations were very similar between the two groups with less than 1% difference. The exposed group has a median of 13.2µmol/L, and the control group 13.3µmol/L. Mann-Whitney test showed that the difference observed was statistically insignificant (z = 0.51; p = 0.61).

	Exposed	Control
N	53	34
Median (µmol/L)	13.2	13.3
Minimum (µmol/L)	8.7	10.0
Maximum (µmol/L)	20.8	22.3
Percentiles 25th (µmol/L)	11.7	12.2
75th (µmol/L)	14.5	14.3

Table 4.21: Zinc concentrations in blood, exposed v control.

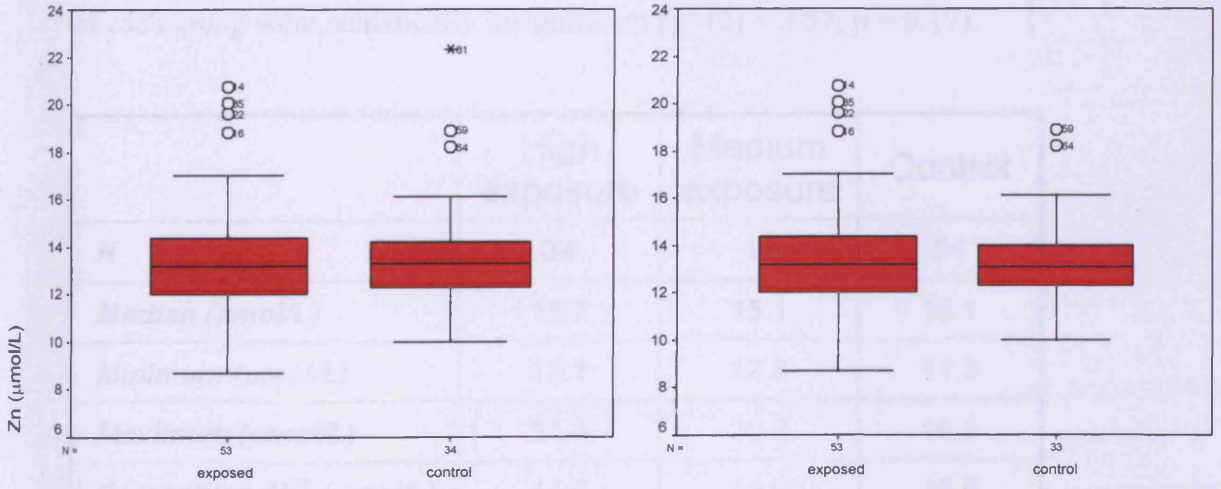


Figure 4.36: Zinc concentrations in blood, exposed v control. Extreme value "81" was removed from the figure on the right.

Lead (Pb)

None of the samples contained significant quantity of lead for detection by ICP-MS. The minimum detection limit for lead is approximately 0.1nmol/L.

Differences in high exposure, medium exposure, and control groups

The exposed group was subdivided into high exposure and medium exposure groups according to the criterion set before, so that any dose response relationships that exist can be identified. The total number of samples from the high exposure group was 34 and medium exposure group was 19. Because there were no changes to the control group hence the number remained the same at 34.

Copper (Cu)

Table 4.22 shows the descriptive statistics of copper concentrations in blood samples. The medians of the three different exposure groups were compared; the highest was in the high exposure group at 15.7μmol/L, followed by the medium exposure group and controls which were both at 15.1μmol/L. No extreme values were present that may affect the medians (figure 4.37), and all samples contained detectable amount of copper. Kruskal-Wallis test showed that the difference observed between the medians of each group were statistically insignificant (χ^2 (2) = 3.57; p = 0.17).

	High exposure	Medium exposure	Control
N	34	19	34
Median (μmol/L)	15.7	15.1	15.1
Minimum (μmol/L)	13.1	12.8	11.3
Maximum (μmol/L)	21.4	20.2	19.5
Percentiles 25th (μmol/L)	14.6	14.0	13.5
75th (μmol/L)	18.1	17.2	16.8

Table 4.22: Copper concentrations in blood, high exposure v medium exposure v control.

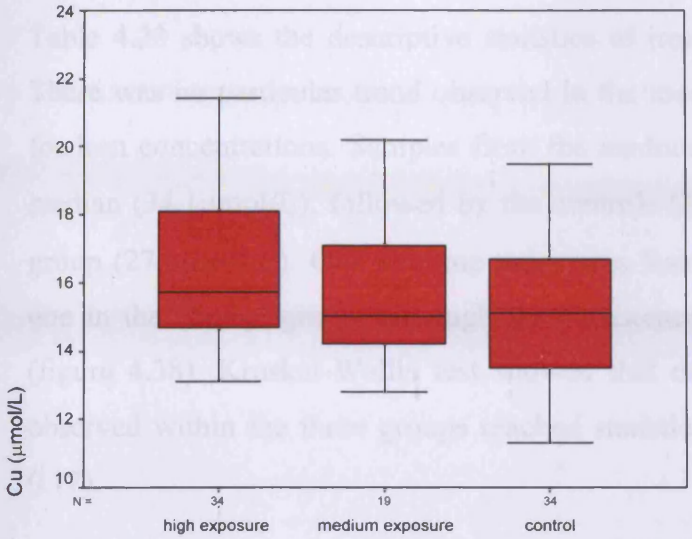


Figure 4.37: Copper concentrations in blood, high exposure v medium exposure v control.

Iron (Fe)

Table 4.23 shows the descriptive statistics of iron concentrations in blood samples. There was no particular trend observed in the medians of the three exposure groups for iron concentrations. Samples from the medium exposure group have the highest median (34.1μmol/L), followed by the controls (30.1μmol/L) and the high exposure group (27.1μmol/L). One extreme value was found in the high exposure group and one in the control group, although their existence had little effects on the medians (figure 4.38). Kruskal-Wallis test showed that none of the differences in medians observed within the three groups reached statistical significance (χ^2 (2) = 3.52; p = 0.17).

	High exposure	Medium exposure	Control
N	33	19	34
Median (μmol/L)	27.1	34.1	30.1
Minimum (μmol/L)	9.7	15.7	16.1
Maximum (μmol/L)	95.3	55.8	102.1
Percentiles 25th (μmol/L)	21.1	24.8	25.7
75th (μmol/L)	35.2	43.8	41.5

Table 4.23: Iron concentrations in blood, high exposure v medium exposure v control.

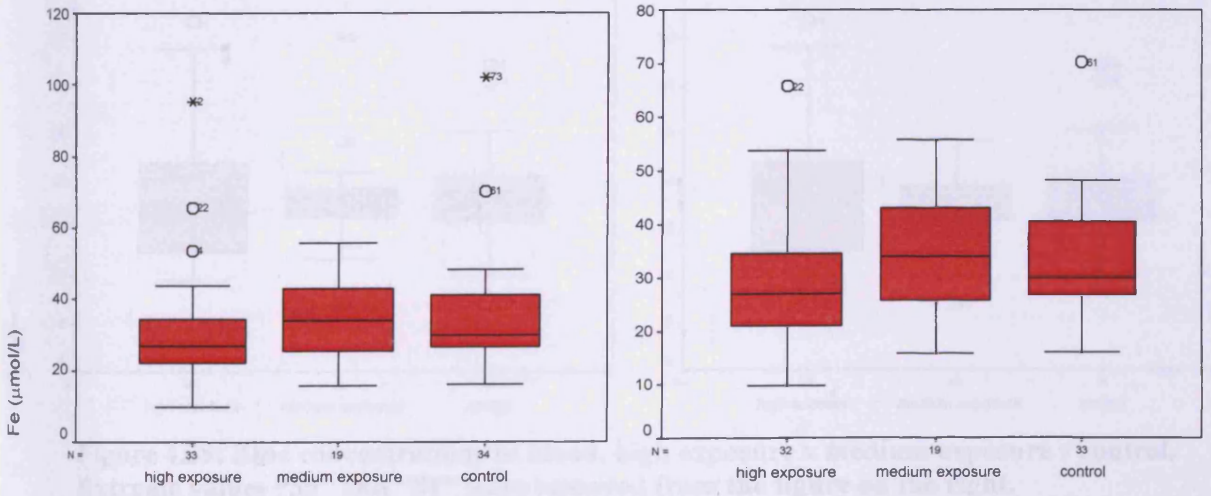


Figure 4.38: Iron concentrations in blood, high exposure v medium exposure v control. Extreme values "2" and "73" were removed from the figure on the right.

Zinc (Zn)

Table 4.24 shows the descriptive statistics of zinc concentrations in blood samples. Medians of zinc concentrations found across the three exposure groups did not vary greatly despite a slightly increasing trend seen from the high exposure group (13.0μmol/L), through the medium exposure group (13.2μmol/L), and to the control group (13.3μmol/L). There were two extreme values in the medium exposure group and the one in the control group (figure 4.39). Kruskal-Wallis test was performed and the differences in medians were found to be statistically insignificant (χ^2 (2) = 0.28; p = 0.87).

	High exposure	Medium exposure	Control
N	34	19	34
Median (μmol/L)	13.0	13.2	13.3
Minimum (μmol/L)	9.8	8.7	10.0
Maximum (μmol/L)	20.8	20.1	22.3
Percentiles 25th (μmol/L)	11.0	12.3	12.2
75th (μmol/L)	14.8	13.7	14.3

Table 4.24: Zinc concentrations in blood, high exposure v medium exposure v control.

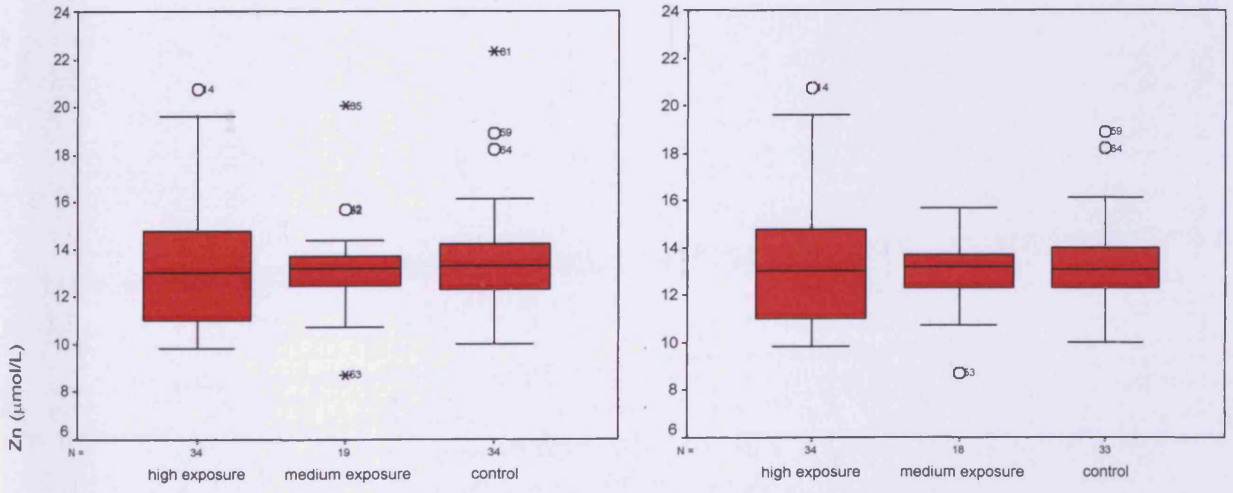


Figure 4.39: Zinc concentrations in blood, high exposure v medium exposure v control. Extreme values "35" and "81" were removed from the figure on the right.

Lead (Pb)

Statistical analysis was not carried out because the level of lead fell below the minimum detection limit in all samples.

4.2.2 Trace elements in hair samples

A total of 109 hair samples were collected from the participants, of which 67 were from the exposed group and 42 from the control group. Twelve participants were unable to provide sufficient amount of hair samples and were therefore excluded. A suite of trace elements were analysed by NAA including V, Mn, Cu, Br, and Sb which were markers of exposure to motor traffic, and also some other elements including Na, Mg, Al, S, Cl, K, Ca, Ti, Co, Sn, I, and Ho. A set of control blanks were also analysed and thus the total amount of elements present in the hair samples were equal to the results obtained minus the mean concentrations found in the blanks.

Differences in exposed and control groups

Trace elements concentrations in the hair samples were compared between the exposed and the control groups. Due to the fact that the distributions of the levels were skewed, medians were used in the calculations instead of the means. For elements that were below the minimum detection limits and were therefore undetectable, they were all treated as zero.

Vanadium (V)

Table 4.25 shows the descriptive statistics of vanadium concentrations in hair samples. Of the 109 hair samples collected, vanadium was detectable in 96 samples. The difference in the medians between the two groups was very small. In the exposed group the median concentration of vanadium was 0.09μg/g and in the control group 0.10μg/g. There were three extreme values found in the exposed group and two in the control group (figure 4.40). Mann-Whitney test was used to compare the medians of the two groups and found that they were not significantly different from each other (z = 0.29; p = 0.82).

	Exposed	Control
N	67	42
Median (μg/g)	0.09	0.10
Minimum (μg/g)	0.00	0.00
Maximum (μg/g)	1.00	0.99
Percentiles 25th (μg/g)	0.04	0.05
75th (μg/g)	0.17	0.21

Table 4.25: Vanadium concentrations in hair, exposed v control.

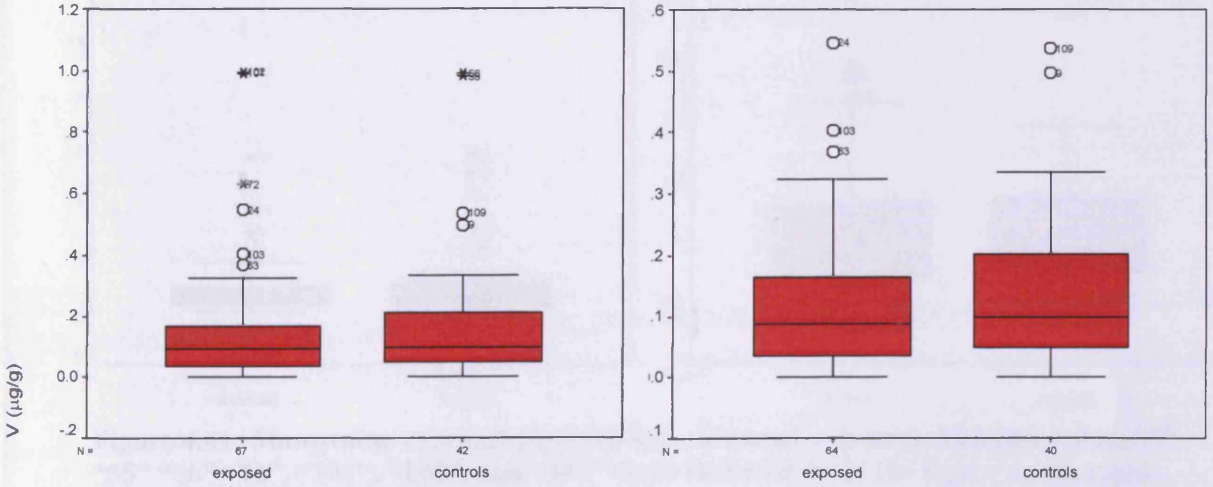


Figure 4.40: Vanadium concentrations in hair, exposed v control. Extreme values "55" "56" "72" "101" and "102" were removed from the figure on the right.

Manganese (Mn)

Table 4.26 shows the descriptive statistics of manganese concentrations in hair samples. There were a total of 18 samples with undetectable amount of manganese. A large number of extreme values were present in both the exposed and control groups (figure 4.41). The median concentration was higher in the exposed than the control group by approximately 35% (0.57μg/g v 0.42μg/g). The difference in medians was tested by Mann-Whitney test and was found to be statistically insignificant (z = 0.96; p = 0.34).

	Exposed	Control
N	67	42
Median (μg/g)	0.57	0.42
Minimum (μg/g)	0.00	0.00
Maximum (μg/g)	5.77	12.30
Percentiles 25th (μg/g)	0.27	0.30
75th (μg/g)	0.98	1.13

Table 4.26: Manganese concentrations in hair, exposed v control.

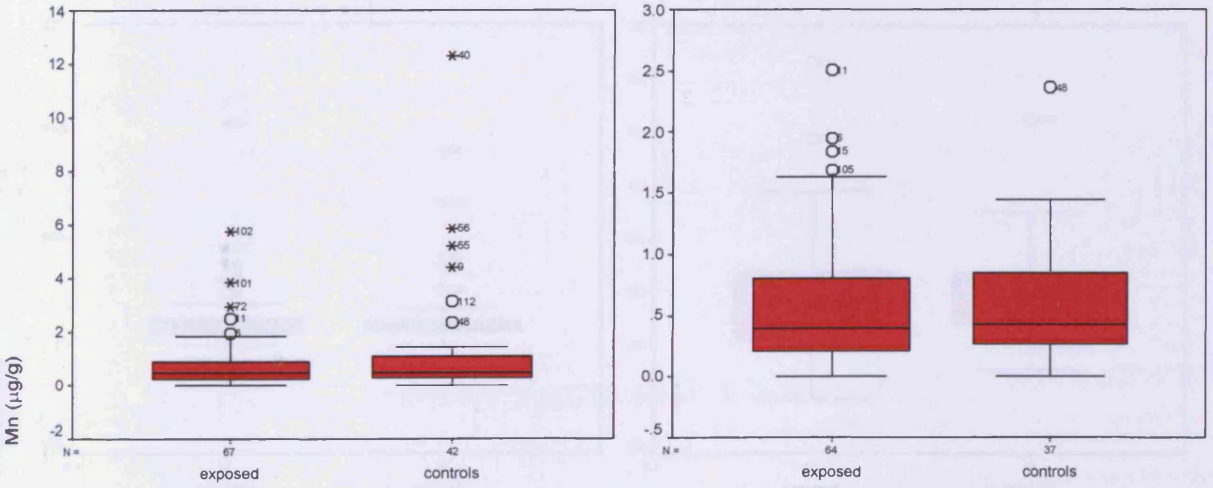


Figure 4.41: Manganese concentrations in hair, exposed v control. Extreme values "9" "55" "56" "72", "101", "102", and "112" were removed from the figure on the right.

Copper (Cu)

Table 4.27 shows the descriptive statistics of copper concentrations in hair samples. Eight of the 109 hair samples had copper levels that were below the minimum detection limit. A large number of extreme values were present in both the exposed and control groups (figure 4.42). The median of copper concentration was 18μg/g in the exposed group, and 19.1μg/g in the control group. Mann-Whitney test showed that the medians of the two groups were not significantly different from each other (z = 0.74; p = 0.46).

	Exposed	Control
N	67	42
Median (μg/g)	18.0	19.1
Minimum (μg/g)	0.0	0.0
Maximum (μg/g)	206.8	182.0
Percentiles 25th (μg/g)	11.0	14.3
75th (μg/g)	25.3	25.2

Table 4.27: Copper concentrations in hair, exposed v control.

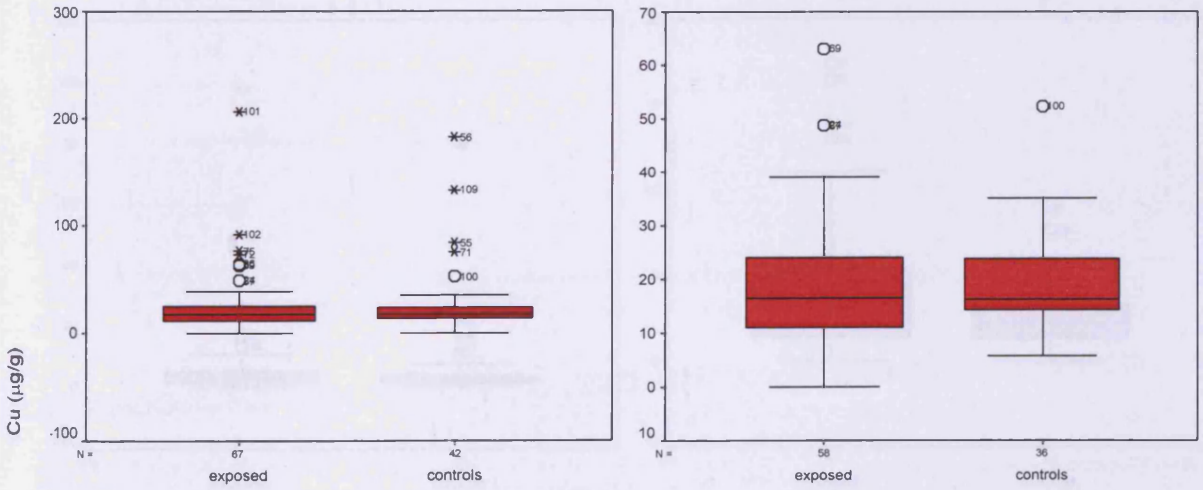


Figure 4.42: Copper concentrations in hair, exposed v control. Extreme values "21", "36", "37", "51", "55", "56", "71", "72", "75", "76", "86", "101", "102", "109" and "112" were removed from the figure on the right.

Bromine (Br)

Table 4.28 shows the descriptive statistics of bromine concentrations in hair samples. A total of 101 samples had detectable amount of bromine but the remaining 8 samples fell below the minimum detection limit. A larger number of extreme values were found in both exposure groups (figure 4.43). The median concentration of bromine was 50% higher in the exposed group than the controls. Results from Mann-Whitney test showed that the medians of the two groups were not significantly different from each other ($z = 1.27$; $p = 0.2$).

	Exposed	Control
N	67	42
Median (μg/g)	3.7	2.5
Minimum (μg/g)	0.0	0.0
Maximum (μg/g)	97.1	79.5
Percentiles 25th (μg/g)	1.4	1.4
75th (μg/g)	6.3	4.1

Table 4.28: Bromine concentrations in hair, exposed v control.

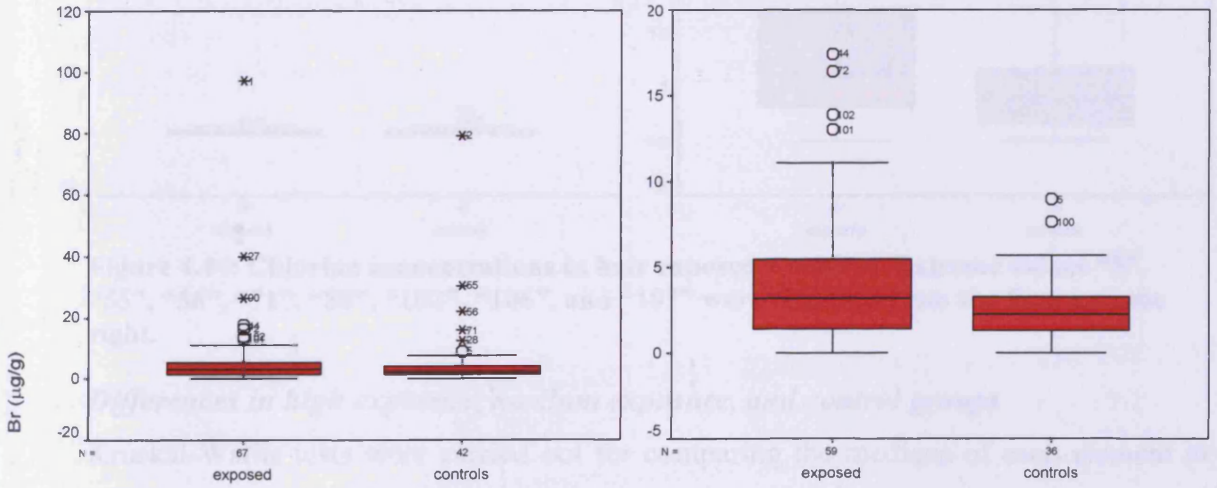


Figure 4.43: Bromine concentrations in hair, exposed v control. Extreme values "1", "2", "6", "27", "28", "55", "56", "71" and "90" were removed from the figure on the right.

Antimony (Sb)

Comparison between levels of antimony in the exposed and control groups was not possible because antimony was undetectable in 98% of the samples.

Others

Of the remaining elements namely Na, Mg, Al, S, Cl, K, Ca, Ti, Co, Mn, Sn, I, and Ho, insufficient data were available for the comparisons of K, Sn, and Ho due to the presence of a large amount of measurements below the minimum detection limits. Mann-Whitney test was run for each of the remaining elements and none of the results suggested significant difference between any of the groups (results not shown). Moreover, the median concentrations were always found to be higher in the control group than the exposed group – the only exception being Cl, in which the level found in the samples of the exposed group was higher than the controls (0.68mg/g v 0.52mg/g), as shown in figure 4.44.

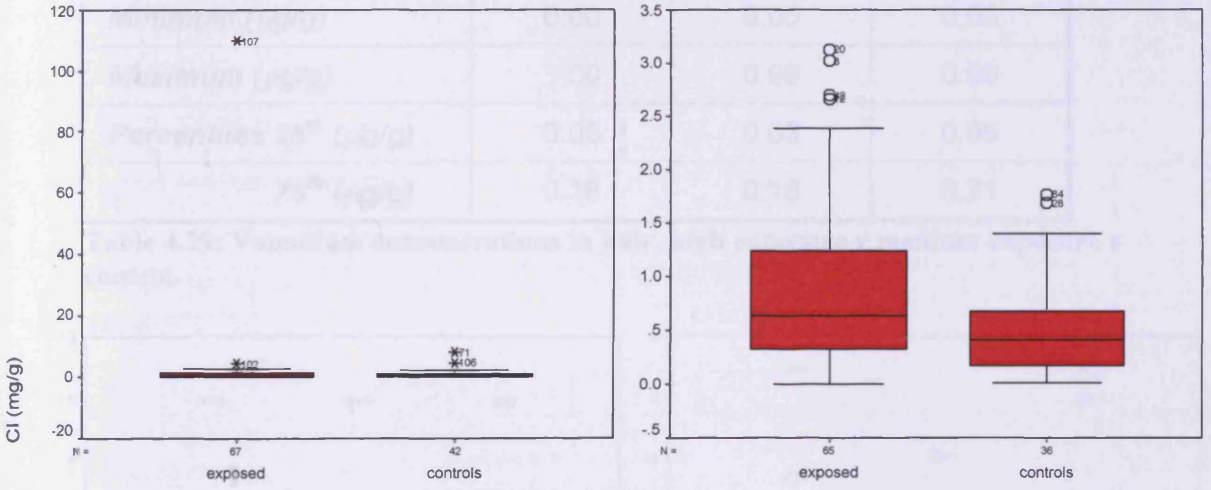


Figure 4.44: Chlorine concentrations in hair exposed v control. Extreme values "5", "55", "56", "71", "88", "102", "106", and "107" were removed from the figure on the right.

Differences in high exposure, medium exposure, and control groups

Kruskal-Wallis tests were carried out for comparing the medians of each element in the hair samples between the three different exposure groups. There were 35 samples from the high exposure group, 32 from the medium exposure group, and 42 from the control group. In addition, Mann-Whitney tests were also carried out to identify possible differences in medians between pairs of groups, i.e. high v medium, high v control, and medium v control.

Vanadium (V)

Table 4.29 shows the descriptive statistics of vanadium concentrations in hair samples. Extreme values were present in all groups but had no significant effects on the medians (figure 4.45). The median concentrations of vanadium were almost the same across the three exposure groups although the high exposure group had a slightly lower median. Kruskal-Wallis test was performed and showed that there were no significant differences in the medians across the three exposure groups (χ^2 (2) = 0.05; p = 0.97). Mann-Whitney tests also failed to detect any statistically significant differences between pairs of groups.

	High exposure	Medium exposure	Control
N	35	32	42
Median (μg/g)	0.09	0.10	0.10
Minimum (μg/g)	0.00	0.00	0.00
Maximum (μg/g)	1.00	0.99	0.99
Percentiles 25th (μg/g)	0.05	0.03	0.05
75th (μg/g)	0.18	0.16	0.21

Table 4.29: Vanadium concentrations in hair, high exposure v medium exposure v control.

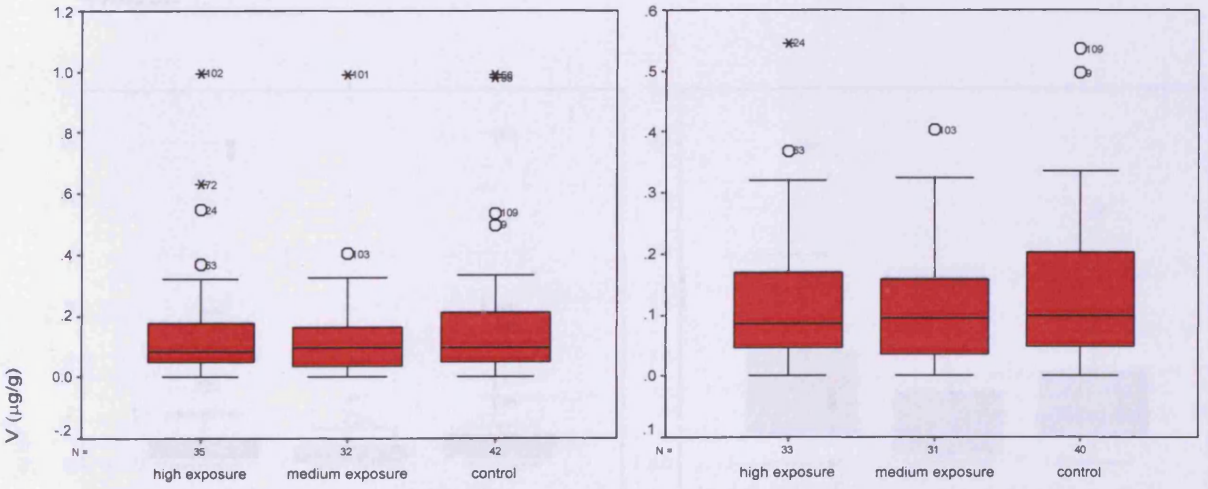


Figure 4.45 Vanadium concentrations in hair, high exposure v medium exposure v control. Extreme values "55", "56", "72", "101" and "102" were removed from the figure on the right.

Manganese (Mn)

Table 4.30 shows the descriptive statistics of manganese concentrations in hair samples. A number of extreme values were present in all three groups, but had no significant effects on the medians (figure 4.46). No particular trend in the median concentrations of manganese was seen across the different exposure groups. The high exposure group has a median of 0.56μg/g, medium exposure group 0.29μg/g, and control group 0.42μg/g. Kruskal-Wallis test was carried out and found no statistically significant difference between the three medians (χ^2 (2) = 4.90; p = 0.09). Mann-Whitney was also carried out to compare pairs of medians, but again yielded insignificant results.

	High exposure	Medium exposure	Control
N	35	32	42
Median (μg/g)	0.56	0.29	0.42
Minimum (μg/g)	0.00	0.00	0.00
Maximum (μg/g)	2.95	1.69	2.36
Percentiles 25th (μg/g)	0.29	0.08	0.26
75th (μg/g)	1.06	0.66	0.85

Table 4.30: Manganese concentrations in hair, high exposure v medium exposure v control.

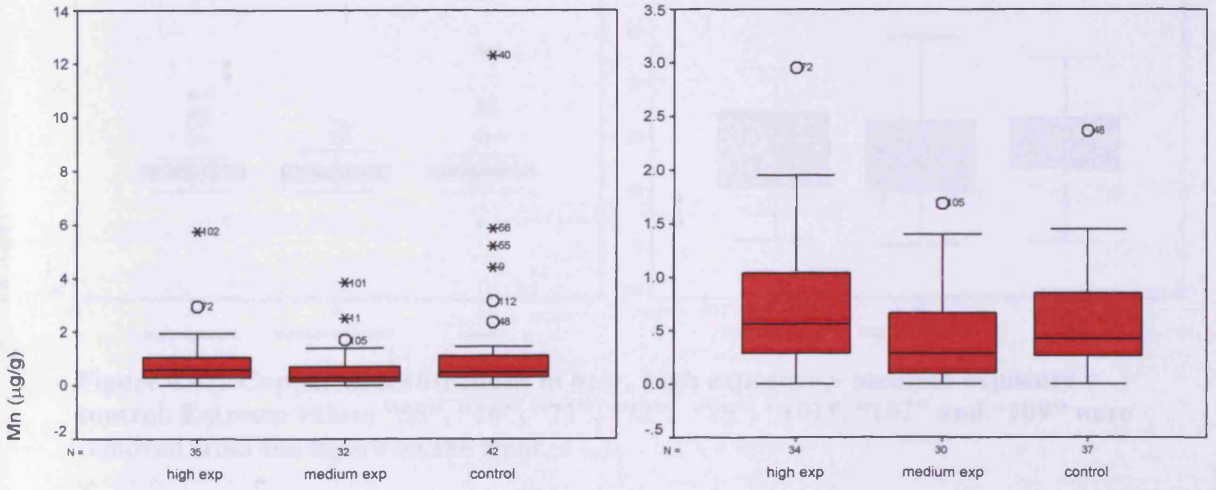


Figure 4.46: Manganese concentrations in hair, high exposure v medium exposure v control. Extreme values "9", "11", "40", "55", "56", "101", "102" and "112" were removed from the figure on the right.

Copper (Cu)

Table 4.31 shows the descriptive statistics of copper concentrations in hair samples. Large number of extreme values was present in all groups. The median copper concentration in the controls was highest amongst the three exposure groups (19.1μg/g), followed by high exposure (18.6μg/g) and medium exposure group (18μg/g). Kruskal-Wallis test showed that there were no significant differences between the medians across the three exposure groups (χ^2 (2) = 0.74; p = 0.69) nor did Mann-Whitney when comparing pairs of medians.

	High exposure	Medium exposure	Control
N	35	32	42
Median (μg/g)	18.6	18.0	19.1
Minimum (μg/g)	0.00	0.00	0.0
Maximum (μg/g)	91.6	206.8	182.0
Percentiles 25th (μg/g)	10.9	11.0	14.3
75th (μg/g)	26.0	24.3	25.2

Table 4.31: Copper concentrations in hair, high exposure v medium exposure v control.

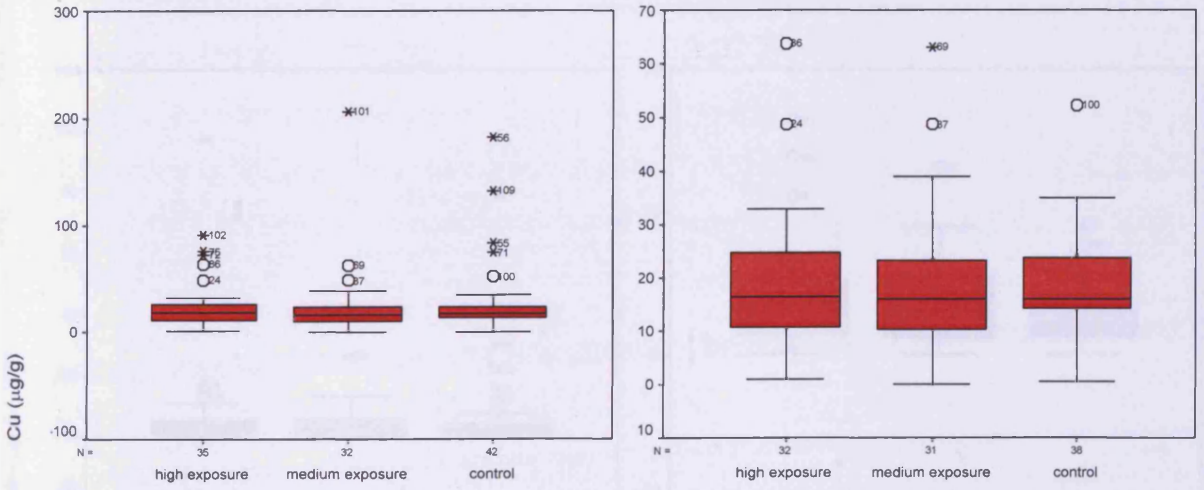


Figure 4.47: Copper concentrations in hair, high exposure v medium exposure v control. Extreme values "55", "56", "71", "72", "75", "101", "102" and "109" were removed from the figure on the right.

Bromine (Br)

Table 4.32 shows the descriptive statistics of bromine concentrations in hair samples. A large number of extreme values were present in all groups (figure 4.48). The medians of bromine concentrations showed a linear decreasing trend across the three exposure groups. The high exposure group has a median of 3.8μg/g, medium exposure group 3.1μg/g, and the control group 2.5μg/g. The differences in medians across different exposure groups failed to reach statistical significance when tested by Kruskal-Wallis test (χ^2 (2) = 1.53; p = 0.47) and Mann-Whitney test.

	High exposure	Medium exposure	Control
N	35	32	42
Median (μg/g)	3.8	3.1	2.5
Minimum (μg/g)	0.0	0.0	0.0
Maximum (μg/g)	97.1	39.9	79.5
Percentiles 25th (μg/g)	1.5	1.1	1.5
75th (μg/g)	5.5	6.1	4.1

Table 4.32: Bromine concentrations in hair, high exposure v medium exposure v control.

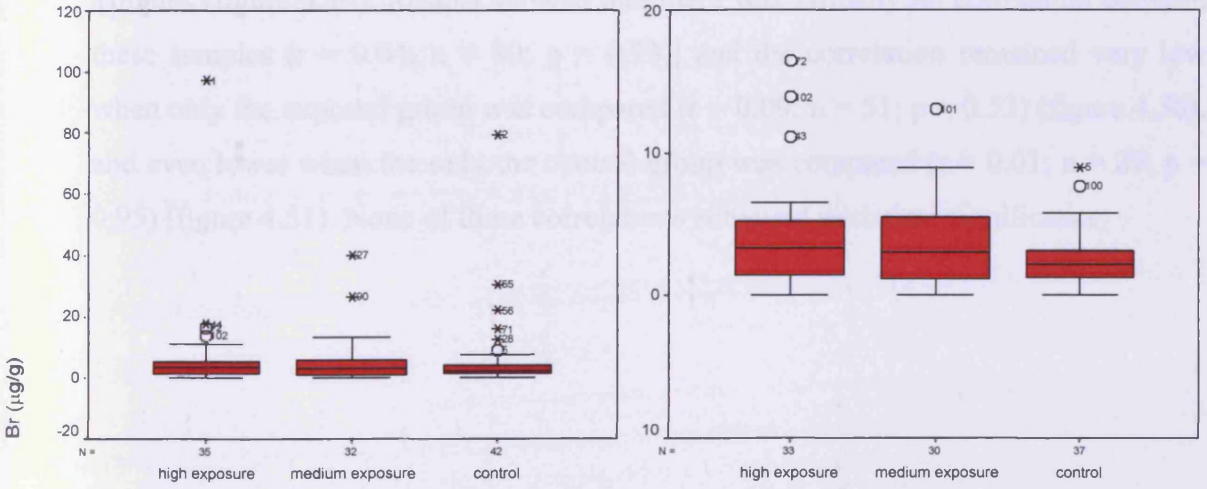


Figure 4.48: Bromine concentrations in hair, high exposure v medium exposure v control. Extreme values "1", "2", "27", "28", "44", "55", "56", "71"and "90" were removed from the figure on the right.

Antimony (Sb)

Tests were not carried out for antimony because there was insufficient amount of data available.

Others

Medians of the three exposure groups were also compared for Na, Mg, Al, S, Cl, Ca, Ti, Co, Mn. These data were tested by Kruskal-Wallis test and no statistically significant differences were found between the three exposure groups in any of these elements. Moreover, none of these elements have shown any linear trends across the different exposure groups (results not shown).

4.2.3 Correlation between trace elements concentrations in blood and hair samples

Trace elements that were recovered from hair samples were the result of depositions of these elements from the blood. Copper was the only element that was both analysed in hair and blood samples in the study, and the correlations between its concentrations were compared in 80 sets of samples.

Exposed and control groups

Correlations between copper concentrations in hair and blood were tested in all 80 samples (figure 4.49). Results showed that there was virtually no correlation between these samples ($r = 0.04$; $n = 80$; $p = 0.73$), and the correlation remained very low when only the exposed group was compared ($r = 0.09$; $n = 51$; $p = 0.53$) (figure 4.50), and even lower when the only the control group was compared ($r = 0.01$; $n = 29$; $p = 0.95$) (figure 4.51). None of these correlations achieved statistical significance.

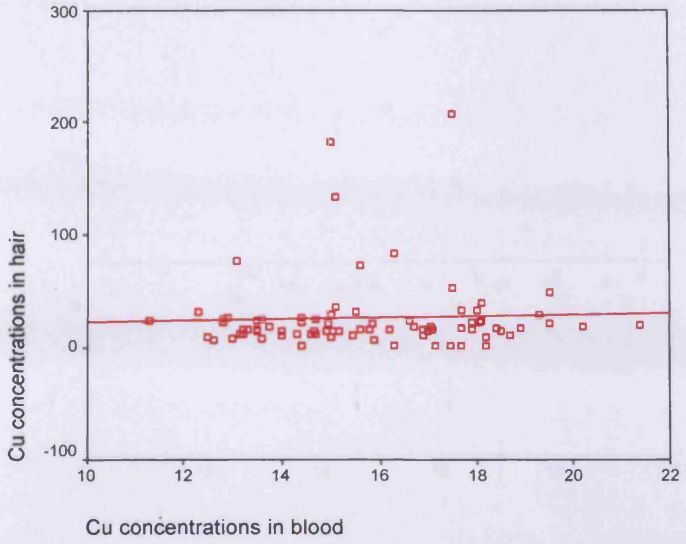


Figure 4.49: Scatterplot showing correlations between copper concentrations in all hair and blood samples (n=80).

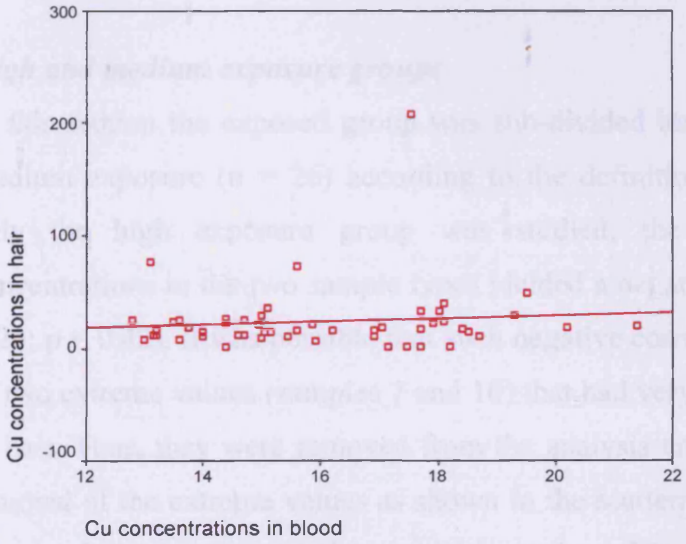


Figure 4.50: Scatterplot showing correlations between copper concentrations in hair and blood samples from participants residing in exposed areas (n=51).

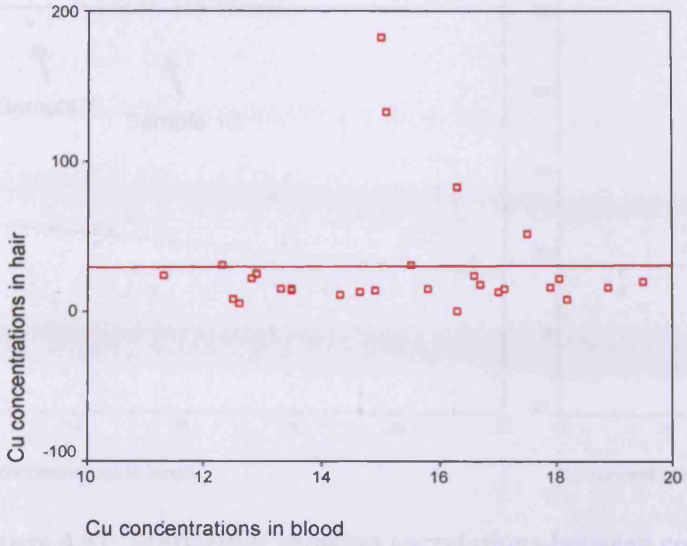


Figure 4.51: Scatterplot showing correlations between copper concentrations in hair and blood samples from participants residing in control areas (n=29).

High and medium exposure groups

In this section the exposed group was sub-divided into high exposure (n = 25) and medium exposure (n = 26) according to the definition discussed previously. When only the high exposure group was studied, the correlation between copper concentrations in the two sample types yielded a negative value of -0.17 (r = -0.17; n = 25; p = 0.42). It was possible that such negative correlation was due to the presence of two extreme values (samples 7 and 10) that had very high concentrations of copper in hair. Thus, they were removed from the analysis and the test was rerun. After the removal of the extreme values as shown in the scatterplot on the right of figure 4.52, the correlation was reversed to a positive value of 0.08 (r = 0.08; n = 23; p = 0.71). The correlation was found to be relatively stronger when only samples from the medium exposure group were studied (figure 4.53), although in overall the correlation was still weak (r = 0.21; n = 26; p = 0.3). Nevertheless, all of the correlation coefficients found failed to reach statistical significance.

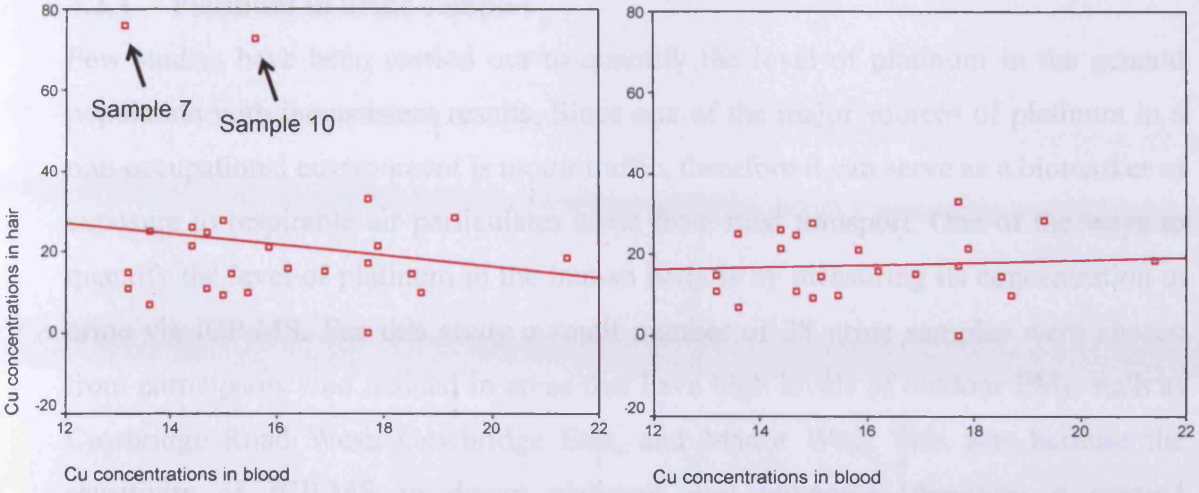


Figure 4.52: Scatterplot showing correlations between copper concentrations in hair and blood samples from participants residing in high exposure areas (n=25). Extreme values "7" and "10" were removed from the figure on the right.

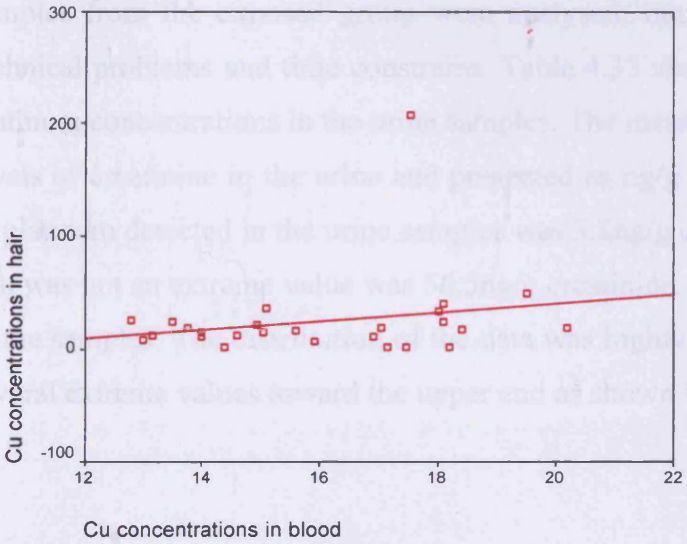


Figure 4.53: Scatterplot showing correlations between copper concentrations in hair and blood samples from participants residing in medium exposure areas (n=26).

4.2.4 Platinum in urine samples

Few studies have been carried out to quantify the level of platinum in the general population with inconsistent results. Since one of the major sources of platinum in a non-occupational environment is motor traffic, therefore it can serve as a biomarker of exposure to respirable air particulates arose from road transport. One of the ways to quantify the level of platinum in the human body is by measuring its concentration in urine via ICP-MS. For this study a small number of 28 urine samples were chosen from participants who resided in areas that have high levels of outdoor PM_5, such as Cowbridge Road West, Cowbridge East, and Manor Way. This was because the sensitivity of ICP-MS to detect platinum was unknown, therefore it seemed reasonable in the first instance to select samples from individuals residing in more polluted areas and assumed that the levels of platinum biomarker should be higher. Initially a set of samples from the control group was scheduled to follow once samples from the exposed group were analysed, but it was later cancelled due to technical problems and time constrains. Table 4.33 shows the descriptive statistics of platinum concentrations in the urine samples. The measurements were adjusted for the levels of creatinine in the urine and presented as ng/g of creatinine. The lowest level of platinum detected in the urine samples was 3.8ng/g creatinine, and the highest level that was not an extreme value was 56.5ng/g creatinine. Platinum was not detected in 3 of the samples. The distribution of the data was highly skewed due to the presence of several extreme values toward the upper end as shown in figure 4.54.

	Pt concentration (ng/g creatinine)
N	28
Mean	150.8
Median	12.0
Minimum	0
Maximum	1411.6
Percentiles 25th	6.0
75th	88.7

Table 4.33: Concentrations of platinum in urine samples.

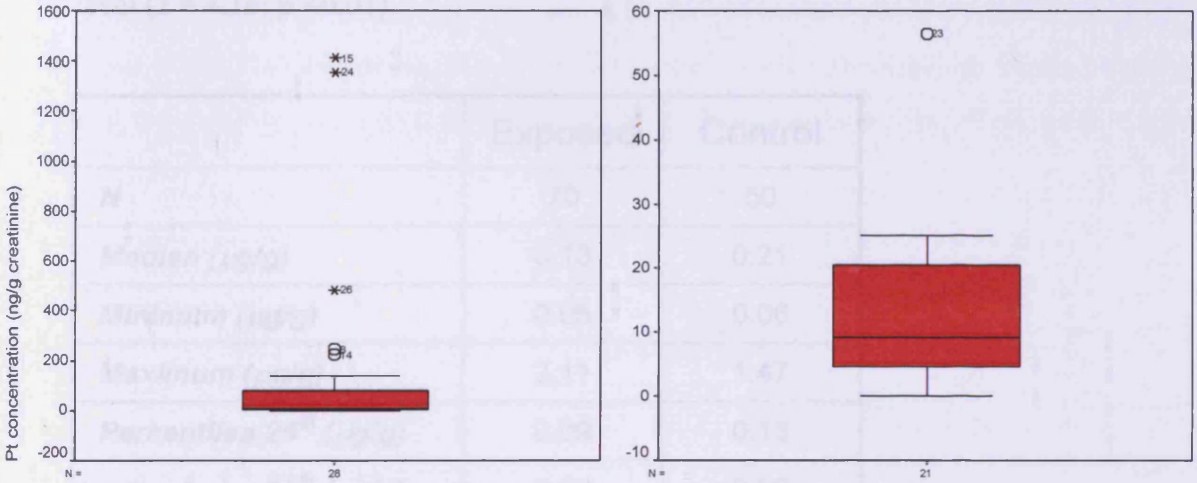


Figure 4.54: Platinum concentrations in urine samples. Extreme values "8", "15", "24", "26", "22", and "27" were removed from the figure on the right.

4.2.5 1-hydroxypyrene (1-HP) in urine samples

In this study, urine samples were collected from participants residing in different exposure areas and biomarkers of PAH uptake from the environment were compared. Throughout the study two urine samples that were 6 months apart were collected from each participant. A total of 120 sets of urine samples were received for the analysis of 1-HP in urine, of which 70 were from the exposed group and 50 were from the control group. Biomarkers for the absorbed dose of PAH, which were presented as 1-HP in urine, were analysed by HPLC. The concentrations of 1-HP derived from the two samples of each subject were averaged for the analysis. Because the data were not evenly distributed, therefore medians were tested instead of means, using the non-

parametric Mann-Whitney test and Kruskal-Wallis tests. Any samples that contained insufficient amount of 1-HP and undetected by HPLC were regarded as zero, and any extreme values were included in the analysis.

Differences in exposed and control groups

Table 4.34 shows the descriptive statistics of 1-HP concentrations in urine samples. All samples contained detectable levels of 1-HP, the median concentrations were calculated and it was found to be higher in the control group (0.21μg/g of creatinine) than the exposed group (0.13μg/g). Three extreme values were present in the exposed group (figure 4.55). When tested by Mann-Whitney test the difference in medians observed between the two groups was found to be statistically significant at the 1% level ($z = 4.16$; $p < 0.01$).

	Exposed	Control
N	70	50
Median (μg/g)	0.13	0.21
Minimum (μg/g)	0.05	0.06
Maximum (μg/g)	2.11	1.47
Percentiles 25th (μg/g)	0.09	0.13
75th (μg/g)	0.19	0.50

Table 4.34: 1-HP concentrations in urine, exposed v control.

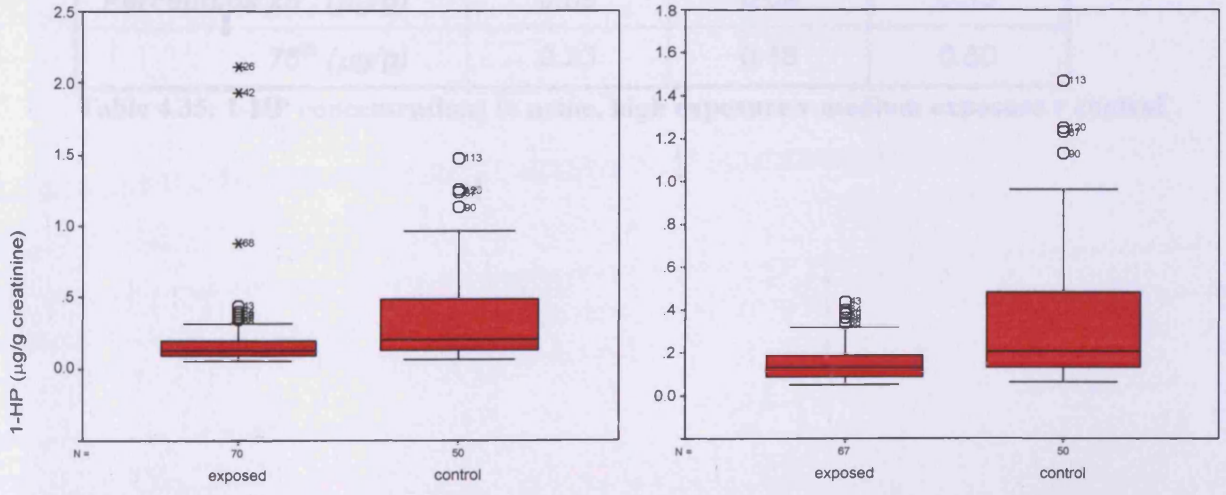


Figure 4.55: 1-HP concentrations in urine, exposed v control. Extreme values "26", "42"and "68" were removed from the figure on the right.

Differences in high exposure, medium exposure, and control groups

For this analysis the exposed group was divided into high exposure group and medium exposure group, with 36 and 34 samples respectively. The control group remained unchanged. The high exposure group has a median of 0.16μg/g, the medium exposure group 0.06μg/g, and the control group 0.21μg/g (table 4.35). The median levels of 1-HP did not resemble a linear trend across the 3 exposure groups. Three extreme values were identified in the high exposure group (figure 4.56). Kruskal-Wallis test showed that the medians between the three groups were significantly different from each other at the 1% level (χ^2 (2) = 17.73; $p < 0.01$). Mann-Whitney tests were also carried out to identify possible differences within groups. Results showed that the high exposure group was not different from the medium exposure group ($z = 0.71$; $p = 0.48$) but was significantly different from the control group ($z = 3.10$; $p < 0.01$). Moreover, the difference seen between the medium exposure group and the controls was also found to be statistically significant at the 1% level ($z = 3.84$, $p < 0.01$).

	High exposure	Medium exposure	Control
N	36	34	50
Median (μg/g)	0.16	0.06	0.21
Minimum (μg/g)	0.05	0.05	0.06
Maximum (μg/g)	2.11	0.40	1.47
Percentiles 25th (μg/g)	0.09	0.09	0.13
75th (μg/g)	0.23	0.18	0.50

Table 4.35: 1-HP concentrations in urine, high exposure v medium exposure v control.

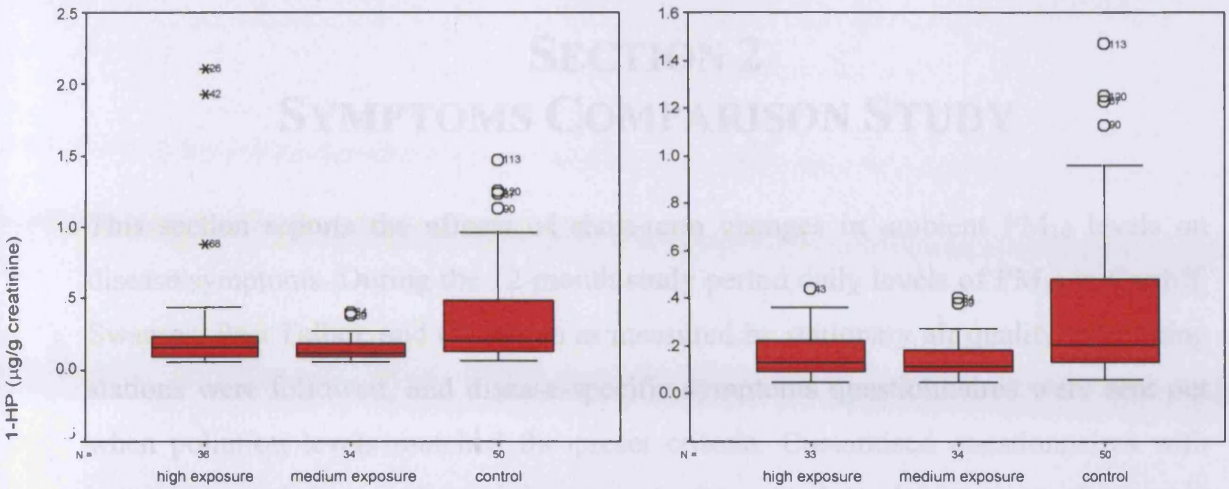


Figure 4.56: 1-HP concentrations in urine,high exposure v medium exposure v control. Extreme values "26", "42"and "68" were removed from the figure on the right.

SECTION 2
SYMPTOMS COMPARISON STUDY

This section reports the effects of short-term changes in ambient PM_{10} levels on disease symptoms. During the 12-month study period daily levels of PM_{10} in Cardiff, Swansea, Port Talbot, and Cwmbran as measured by stationary air quality monitoring stations were followed, and disease-specific symptoms questionnaires were sent out when pollution levels matched the preset criteria. Customised questionnaires with items extracted from validated instruments were used to detect acute changes in disease symptoms in patients with asthma, chronic respiratory diseases excluding asthma, and chronic cardiac diseases that may have been induced by short-term changes in PM_{10} levels in their areas. All subjects were acting as their own controls in the study and thus allowed comparisons to be made at the individual level.

4.3 Asthma symptoms questionnaire analysis

Outcome rates

As shown in table 4.36, a total of 200 copies of invitation letters were given out to all patients visiting the participating asthma clinics in South Wales. Eighty-three asthma patients expressed interests by filling in the cards with their personal and contact details, which were then returned to the researcher via the clinics. Further information were collected from the patients when they were contacted by phone. At the end 65 fulfilled the selection criteria of the study and amongst them 44 agreed to take part. Approximately half of these patients resided in Cardiff (48%), with the rest from Swansea (39%), Port Talbot (7%), and Cwmbran (7%). There were more females than males (16 v 28) and the mean age was 57years old, with the youngest 20yrs old and the oldest 76yrs old. All subjects survived throughout the duration of the study, and all 44 sets of questionnaires were collected that recorded their asthma symptoms through different episodes of air pollution with no missing data. The response rate of the study was 67.7%.

	Number of participants (n)
Letters handed out	200
Response received	83
Eligible responses	65
Respondents agreed to take part	44
Completed questionnaires	44

Table 4.36: Breakdown of responses to recruitment letters, Asthma Symptoms Comparison Study.

4.3.1 Changes in asthma symptoms score between high and normal levels of PM_{10}

A copy of the asthma symptoms questionnaire is listed in appendix 8.1. The questionnaire included items that can be categorised, which focused on disease symptoms (questions 4,5, 7, 13 and 14), medication use (10 and 23), and emotional well-being (questions 1-3, 8, 9, 11, 16, 18-22, 24 and 25). The remaining questions were all "check questions" for the detection of confounding factors that may affect the accuracy of the results. For every question the participants were asked to choose an option between 1 and 7 to represent how their asthma symptoms had been. The only exception was question 23 in which only 4 options were available. The answers they had given were then converted into symptoms scores, with option 1 equivalent to a score of 1, and option 2 equivalent to a score of 2 and so on. Based on this method, a low symptoms score therefore indicated that the patient was experiencing hardship from his or her exacerbated asthma symptoms. Table 4.37 shows a summary of the mean symptoms scores for each question during different pollution episodes. Using the symptoms scores obtained, the influence of air pollution at high levels were expressed by calculating the effect size, which was calculated by dividing the differences of the mean scores following high and normal pollution episodes by the standard deviation (SD) of the results in the corresponding question (figure 4.57). The SD indicated how widely spread the symptoms scores were for each question.

Effect size (%) = [(difference in mean scores) / SD] x 100%

Figure 4.57: Formula for calculating effect size.

Large effect size % represents greater changes observed in the mean symptom scores between normal and high pollution episodes in either direction. Paired-Sample T-Test was used to find out whether the difference in means observed between the two episodes was statistically significant. This statistical method is used for comparing the repeated means of a group of individual. In other words, it compares the means of two variables for a single group, such as before and after an intervention. In this case the mean symptoms scores of the same group of individuals during high and normal pollution episodes were compared. All questions in the asthma symptoms questionnaire were tested except for question 23, because the answers for that question were neither continuous nor categorical, which were not suitable for calculating means.

Changes in asthma symptoms

Out of the 5 questions that focused on changes in asthma symptoms, 3 yielded positive effect sizes (questions 5, 7, and 14) and 2 yielded negative effect sizes (questions 4 and 13). The largest positive effect size was seen in question 7 (+28.3%), meaning the participants were more likely to experience wheeze in the chest during high levels of PM_{10}. On the other hand, the largest negative effect size was seen in question 4 (-10.7%), meaning the participants were suffering from shortness of breathe more frequently at normal period than episodes of high PM_{10} pollution. Mean symptoms score reported by the participants between different occasions of pollution episodes were tested by Paired-Sample T-Test but none of them achieved statistical significance.

Changes in medication use

Result for question 10 showed a positive effect size of 7.1%, which reflected the increased use of asthma medication in the participants when PM_{10} levels were high.

However, when the observed difference was tested by Paired-Sample T-Test it was found to be statistically insignificant ($t(43) = -0.39$; $p = 0.7$).

Changes in emotional well-being

Questions for changes in emotional well-being that yielded positive effect sizes were 1, 19, 20, 21, and 22, of which question 22 had the highest effect size of 41.6%. When results of these 5 questions were tested by Paired-Sample T-Test, only question 22 reached statistical significance ($t(43) = -2.48$; $p = 0.02$), meaning the participants were more likely to feel discomfort and distress due to coughing when PM_{10} level was high. All the remaining questions (2, 3, 8, 11, 16, 18, 24, and 25) yielded negative effect sizes and amongst them the effect was most significant in question 25 (-44.8%), meaning the participants were less bothered by heavy breathing during high levels of ambient PM_{10}. No changes in overall symptoms score between different episodes of particulate pollution were seen in question 9.

Question number	Episode	Mean score	SD	Effect size (%)	p-value
Symptoms					
Pair 4	High	3.27	1.70	-10.7	0.60
	Normal	3.09			
Pair 5	High	3.25	1.87	+4.9	0.79
	Normal	3.34			
Pair 7	High	3.02	1.84	+28.3	0.13
	Normal	3.55			
Pair 13	High	3.16	1.79	-10.2	0.59
	Normal	2.98			
Pair 14	High	2.98	1.84	+12.4	0.51
	Normal	3.20			
Medication use					
Pair 10	High	2.59	1.91	+7.1	0.70
	Normal	2.73			
Emotional well-being					
Pair 1	High	2.52	1.75	+22.1	0.23
	Normal	2.91			
Pair 2	High	3.30	1.95	-4.7	0.79
	Normal	3.20			
Pair 3	High	3.55	1.95	-5.8	0.71
	Normal	3.43			
Pair 8	High	3.27	2.02	-9.0	0.61
	Normal	3.09			
Pair 9	High	2.93	1.75	0	1.00
	Normal	2.93			
Pair 11	High	3.11	1.72	-6.6	0.75
	Normal	3.00			
Pair 16	High	3.66	2.17	-4.2	0.81
	Normal	3.57			
Pair 18	High	3.11	2.03	-20.1	0.16
	Normal	2.70			
Pair 19	High	2.59	1.93	+35.2	0.09
	Normal	3.27			
Pair 20	High	3.18	2.01	+10.2	0.61
	Normal	3.39			
Pair 21	High	2.89	1.87	+18.2	0.31
	Normal	3.23			
Pair 22	High	2.36	1.86	+41.6	**0.02**
	Normal	3.14			
Pair 24	High	3.16	1.96	-16.2	0.40
	Normal	2.84			
Pair 25	High	3.66	1.78	-44.8	**0.01**
	Normal	2.86			

Table 4.37: Mean symptoms scores and statistical significance for each question in the Asthma Symptoms Questionnaire between two occasions of high and normal air pollution levels. Note that question 23 and all "check questions" were omitted.

Question 23 concerned the frequency of inhaler usage amongst the participants and they had 4 options available to choose from. However, because the options were not weighted equally, the comparison of neither means nor medians was suitable for its analysis. Figure 4.58 shows the distribution of the mean symptoms score reported by each participant for question 23, during different episodes of particulate air pollution. The graph shows that more participants have obtained lower symptoms score when air pollution level was high, as indicated by the distribution of the red bars that skewed to the left. In contrast, more participants have obtained higher symptoms score when air pollution level was normal, as reflected by the lower number of participants scoring 1 and 2, and higher number of participants scoring 3 and 4. The hypothesis of this study was that during episodes of high particulate air pollution, the symptoms score obtained by each participant would be lower in contrast to normal episodes of pollution. Thus in an ideal situation when the hypothesis is correct, the distribution of the bars in figure 4.58 should resemble those shown in figure 4.59, i.e. the red bars which represent high episode of air pollution should skew to the left while the green bars which represent normal episodes of air pollution should skew to the right.

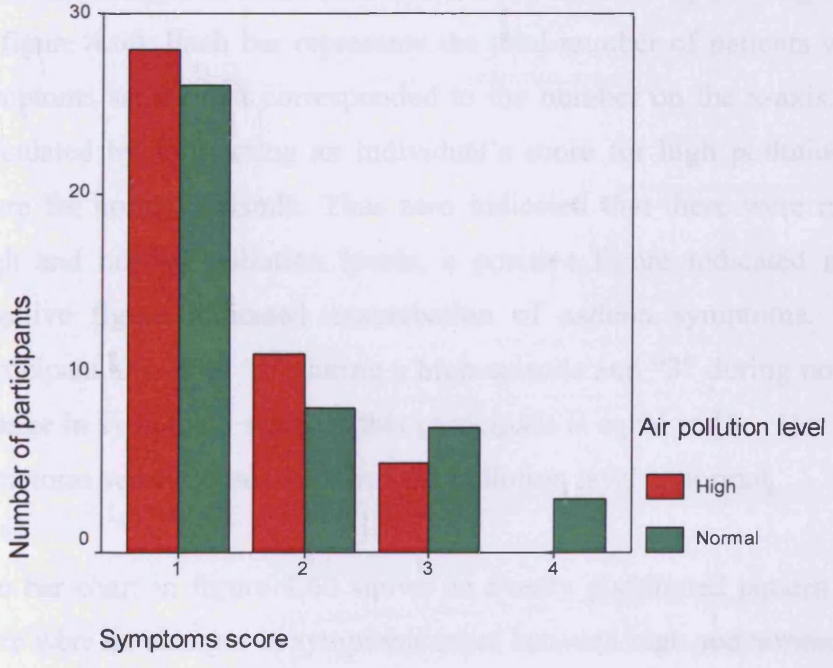


Figure 4.58: Clustered bar chart showing the distribution of symptoms scores for question 23 (n=44), between different episodes of particulate air pollution.

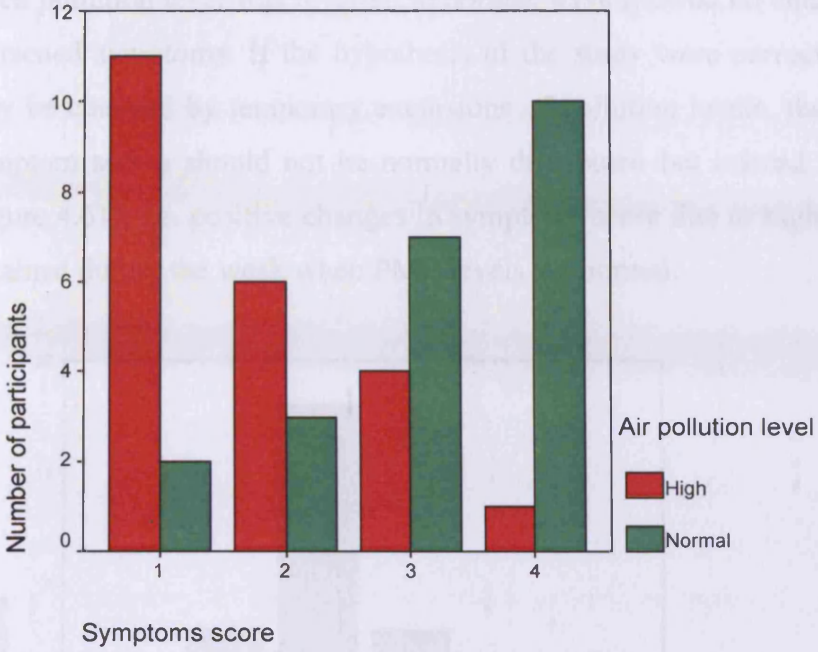


Figure 4.59: A hypothetical clustered bar chart showing the distribution of symptoms score between different episodes of particulate air pollution.

In addition to knowing the overall changes in symptoms scores, it is also important to know the changes at individual levels. This was done by plotting a bar chart as shown in figure 4.60. Each bar represents the total number of patients with their change in symptoms scores that corresponded to the number on the x-axis. The changes were calculated by subtracting an individual's score for high pollution episode from the score for normal episode. Thus zero indicated that there were no changes between high and normal pollution levels, a positive figure indicated improvement and a negative figure indicated exacerbation of asthma symptoms. For example, if a participant answered "1" during a high episode and "3" during normal level, then the change in symptoms score of this participant is equal to [3 – 1] = 2, which means the symptoms were less severe when the pollution level is normal.

The bar chart in figure 4.60 shows an evenly distributed pattern and suggested that there were no changes in symptoms score between high and normal pollution episodes for most participants. Despite the fact that improvements were seen in a number of patients (i.e. those with a change of +1, +2, and +3 in symptoms score) when changing from high to normal pollution levels, there were roughly the same number of patients who suffered from worse asthmatic symptoms (i.e. those with a change of –1 and –2 in symptoms score). Overall, improvement was seen in 34% of the subjects

when pollution level was reverted to normal, 41% showed no changes, and 25% have worsened symptoms. If the hypothesis of the study were correct, that is, symptoms may be changed by temporary excursions of pollution levels, the overall changes in symptom scores should not be normally distributed but instead skewed to the right (figure 4.61), i.e. positive changes in symptoms score due to higher symptoms scores obtained during the week when PM_{10} levels are normal.

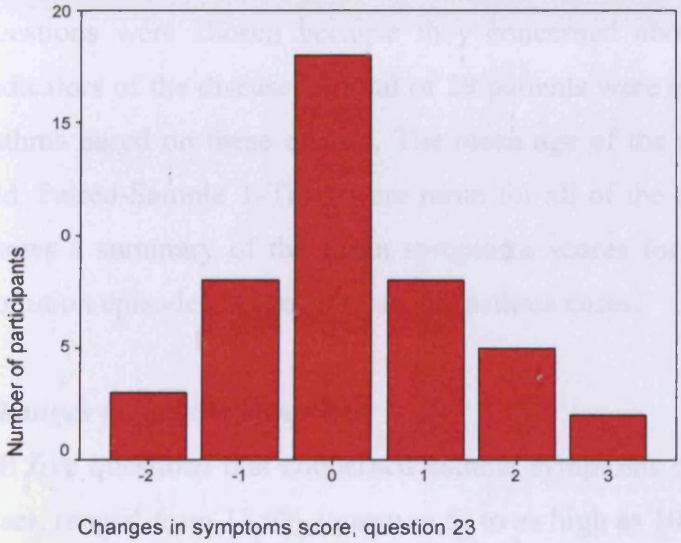


Figure 4.60: Bar chart showing changes in symptoms scores for question 23 (n=44), high v normal pollution episode.

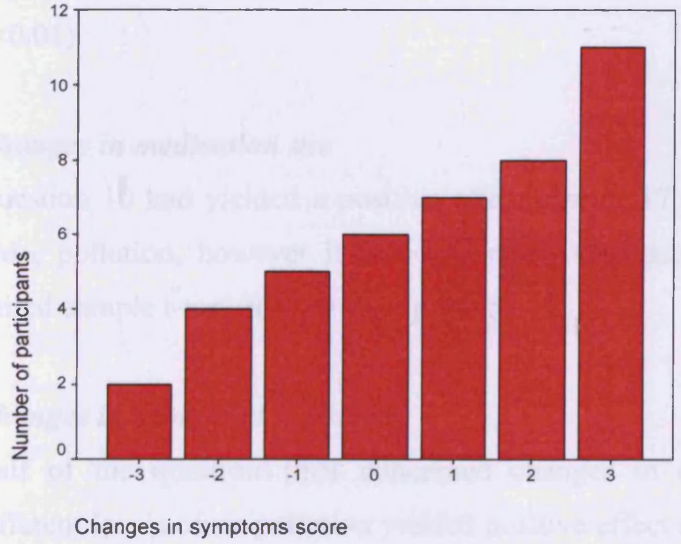


Figure 4.61: A hypothetical bar chart showing changes in symptoms score, high v normal pollution episodes.

4.3.2 Changes in asthma symptoms score amongst the more severe cases between high and normal levels of PM_{10}

It is possible that excursions in pollution differentially affect those individuals with more severe symptoms. Therefore a more sensitive subgroup of asthmatics who were suffering from more severe asthma were chosen from the main group in order to re-examine the effects of PM_{10}. This subgroup of patients was selected based on whether or not they had scored low (options 1 and 2) for questions 4, 7, and 13. These questions were chosen because they concerned about symptoms that were strong indicators of the disease. A total of 29 patients were identified as having more severe asthma based on these criteria. The mean age of the subjects was increased to 59yrs old. Paired-Sample T-Tests were rerun for all of the questions except 23. Table 4.38 shows a summary of the mean symptoms scores for each question during different pollution episodes in the more severe asthma cases.

Changes in asthma symptoms

All five questions that concerned asthma symptoms changes yielded positive effects sizes, ranged from 15.6% (question 5) to as high as 104.9% (question 7). When tested by Paired-Sample T-Test, the difference observed in question 7 was the only one that reached statistical significance, meaning the participants were more likely to experience wheeze in the chest during episodes of high pollution ($t(28) = -3.3$; $p<0.01$).

Changes in medication use

Question 10 had yielded a positive effect size of 17.1% between different levels of PM_{10} pollution, however it failed to reach statistical significance when tested by paired-sample t-test ($t(28) = -0.7$; $p = 0.5$).

Changes in emotional well-being

Half of the questions that concerned changes in emotional well-being between different levels of air pollution yielded positive effect sizes (questions 1, 2, 9, and 19-22) and half yielded negative effect sizes (questions 3, 8, 11, 16, 18, 24, and 25). The largest positive effect size was seen in question 22 (89.1%) and for negative effect size it was seen in question 25 (-71.6%), both of which were found to be statistically significant at the 1% level after being tested by paired-sampled t-test. All remaining

questions were found to be statistically insignificant, although question 1 was only marginally failed to reach significance ($t(28) = -1.9$; $p = 0.06$).

Changes in asthma symptoms score between analyses using data from all cases and from only severe cases is summarised in table 4.39.

Question number	Episode	Mean score	SD	Effect size (%)	p-value
Symptoms					
Pair 4	High	2.31	1.44	+28.7	0.34
	Normal	2.72			
Pair 5	High	2.62	1.54	+15.6	0.60
	Normal	2.86			
Pair 7	High	1.97	1.09	+104.9	<0.01
	Normal	3.10			
Pair 13	High	2.34	1.52	+20.4	0.48
	Normal	2.66			
Pair 14	High	2.31	1.58	+28.3	0.31
	Normal	2.76			
Medication use					
Pair 10	High	2.24	1.62	+17.1	0.50
	Normal	2.52			
Emotional well-being					
Pair 1	High	1.86	1.09	+69.4	0.06
	Normal	2.62			
Pair 2	High	2.55	1.38	+10.0	0.75
	Normal	2.69			
Pair 3	High	2.93	1.67	-10.3	0.68
	Normal	2.76			
Pair 8	High	2.69	1.79	-15.4	0.58
	Normal	2.41			
Pair 9	High	2.28	1.49	+18.6	0.54
	Normal	2.55			
Pair 11	High	2.86	1.64	-10.5	0.70
	Normal	2.69			
Pair 16	High	3.17	2.02	-10.3	0.64
	Normal	2.97			
Pair 18	High	2.45	1.72	-16.0	0.43
	Normal	2.17			
Pair 19	High	2.07	1.51	+52.5	0.15
	Normal	2.86			
Pair 20	High	2.66	1.76	+21.6	0.48
	Normal	3.03			
Pair 21	High	2.10	1.32	+49.7	0.13
	Normal	2.76			
Pair 22	High	1.66	1.04	+89.1	<0.01
	Normal	2.59			
Pair 24	High	2.66	1.90	-32.8	0.19
	Normal	2.03			
Pair 25	High	3.10	1.40	-71.6	<0.01
	Normal	2.10			

Table 4.38: Mean symptoms scores and statistical significance for each question in the Asthma Symptoms Questionnaire amongst the more severe asthma cases, between two occasions of high and normal air pollution levels (n=29). Note that question 23 and all "check questions" were omitted.

Question 23 was analysed using the method explained earlier. Figure 4.62 showes that most of the subjects scored low during both high pollution episodes and normal pollution levels, meaning asthma medication use was unlikely to be affected by the ambient levels of PM_{10}. At individual levels, as shown in figure 4.63, the symptoms scores followed an evenly distributed pattern, with small number of subjects showing either improved or worsen symptoms between high and normal pollution levels. Overall, improvement in symptoms scores was seen 28% of the patients, while 41% of the patients had shown no changes and 31% were worsened.

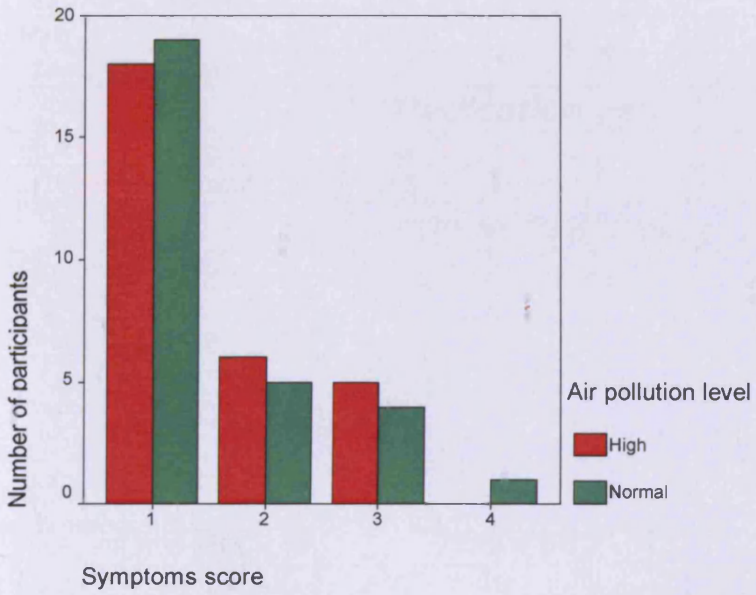


Figure 4.62: Bar chart showing changes in symptoms scores for question 23 (n=29) in the more severe cases, high v normal pollution episode.

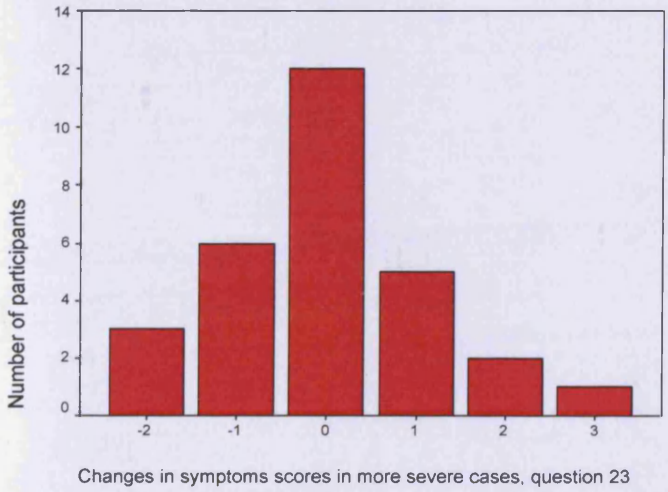


Figure 4.63: Clustered bar chart showing the distribution of symptoms scores for question 23 (n=29) in the more severe cases, high v normal pollution episode.

Question number	Episode	All cases		Only severe cases	
		Mean score	Effect size (%)	Mean score	Effect size (%)
Symptoms					
Pair 4	High	3.27	-10.7	2.31	28.7
	Normal	3.09		2.72	
Pair 5	High	3.25	4.9	2.62	15.6
	Normal	3.34		2.86	
Pair 7	High	3.02	28.3	1.97	104.9
	Normal	3.55		3.10	
Pair 13	High	3.16	-10.2	2.34	20.4
	Normal	2.98		2.66	
Pair 14	High	2.98	12.4	2.31	28.3
	Normal	3.20		2.76	
Medication use					
Pair 10	High	2.59	7.1	2.24	17.1
	Normal	2.73		2.52	
Emotional well-being					
Pair 1	High	2.52	22.1	1.86	69.4
	Normal	2.91		2.62	
Pair 2	High	3.30	-4.7	2.55	10.0
	Normal	3.20		2.69	
Pair 3	High	3.55	-5.8	2.93	-10.3
	Normal	3.43		2.76	
Pair 8	High	3.27	-9.0	2.69	-15.4
	Normal	3.09		2.41	
Pair 9	High	2.93	0	2.28	18.6
	Normal	2.93		2.55	
Pair 11	High	3.11	-6.6	2.86	-10.5
	Normal	3.00		2.69	
Pair 16	High	3.66	-4.2	3.17	-10.3
	Normal	3.57		2.97	
Pair 18	High	3.11	-20.1	2.45	-16.0
	Normal	2.70		2.17	
Pair 19	High	2.59	35.2	2.07	52.5
	Normal	3.27		2.86	
Pair 20	High	3.18	10.2	2.66	21.6
	Normal	3.39		3.03	
Pair 21	High	2.89	18.2	2.10	49.7
	Normal	3.23		2.76	
Pair 22	High	2.36	41.6	1.66	89.1
	Normal	3.14		2.59	
Pair 24	High	3.16	-16.2	2.66	-32.8
	Normal	2.84		2.03	
Pair 25	High	3.66	-44.8	3.10	-71.6
	Normal	2.86		2.10	

Table 4.39: Changes in asthma symptoms score between analyses using data from all cases (n=44) and only severe cases (n=29).

4.4 Cardiac symptoms questionnaire analysis

Outcome rates

The same research method used for studying symptoms changes in asthma patients was applied to this study. The hypothesis was that, short-term increase in ambient PM_{10} levels would exacerbate the symptoms of individuals with cardiac disease. A total of 207 replies were received from potential participants when 324 invitation letters were handed out to patients visiting the participating cardiology outpatient clinics in South Wales (table 4.40). All respondents were followed up by phone and 126 were found to be eligible for the study, of which 84 agreed to take part. However, during the course of the study, 13 were withdrawn from the study; 4 due to death and 7 due to illnesses. At the end a total of 73 complete sets of questionnaires that recorded the participants' cardiac symptoms were collected. Most of the questionnaires were successfully completed with some containing missing data, which were subsequently filled in by contacting the participants via the phone. The mean age of the survived patients was 66years old, and 69% of them were male. Most of the subjects resided in Cardiff (55%), and the others were from Cwmbran (33%), Swansea (11%), and Port Talbot (1%). Response rate of the study was 67%.

	Number of participants (n)
Letters handed out	**324**
Response received	**207**
Eligible responses	**126**
Respondents who agreed to take part	**84**
Withdrawn due to death	**4**
Withdrawn due to illness	**7**
Completed questionnaires	**73**

Table 4.40: Breakdown of responses to recruitment letters given out to cardiac patients.

4.4.1 Changes in cardiac symptoms score between high and normal levels of PM_{10}

The cardiac symptoms questionnaire included items that concerned changes in symptoms (questions 3, 5, 8, 9, and 12), medication use (question 7), and emotional well-being (questions 1, 2, 4, 6, 10, 11, and 13-17). However, the format of the cardiac symptoms questionnaire was different from the asthma symptoms questionnaire due to the format of the options that the participants could choose. A copy of the cardiac symptoms questionnaire is listed in appendix 8.2. For the cardiac symptoms questionnaire, because all of the questions contain answers in ordinal format that were unsuitable for calculating the mean or median scores, a different analytical approach was used. Each individual reported on a particular question, on occasions of high pollution episodes and occasions of low pollution episodes. Therefore the change in symptoms score (i.e. worse or better) or no change between the two occasions was recorded. Then the proportion of participants who changed their reports of a particular symptom between different pollution episodes was calculated by ignoring those individuals whose reporting was constant between the two episodes and calculating a proportional change. The proportion of changes was represented by the net improvement (%), which was calculated by the formula below:

(N of "improved" – N of "worsen") / N of questionnaires completed) x 100%

Thus with reference to question 1 in table 4.39, 22 participants reported that their symptoms had worsened during high pollution episodes, while 20 other reported improved cardiac health during the same pollution episodes. In this case the overall change in cardiac symptom was [(20-22) / 73 x 100%] = -2.7%.

Question number	Symptoms score		Net change (%)
	Worsen	Improved	
Symptoms			
3	23	27	5.5
5	21	27	8.2
8	13	12	-1.4
9	10	18	11.0
12	22	22	0
Medication use			
7	14	12	-2.7*
Emotional well-being			
1	22	20	-2.7
2	21	23	2.7
4	10	21	15.1
6	18	19	1.4
10	13	16	4.1
11	20	19	-1.4
13	26	21	-6.9
14	23	21	-2.7
15	22	22	0
16	23	19	-5.5
17	27	14	-17.8

*Only those who were prescribed nitroglycerin were included (n=32).

Table 4.41: Changes in cardiac symptoms between episodes of high and normal air pollution levels (n=73).

The calculation of net change only involved individuals who had reported changes in their symptoms and excluded those who had reported no changes. In order to compensate for this shortfall, the same analytical method used for studying question 23 of the asthma symptoms questionnaire was used. The breakdown of the answers of each question in the cardiac symptoms questionnaire is presented in appendix 9.1, figure "a" of figures 1-17. The higher the symptoms score (as shown on the x-axes) the better the participants were with regard to their cardiac symptoms. Graphs representing the differences in symptoms score were also presented in appendix 9.1, figure "b" of figures 1-17. Each bar represents the change in symptoms score and was calculated by subtracting the symptoms score obtained during high pollution episodes

from score obtained during normal pollution episodes. A positive value would therefore represent improvement in cardiac symptoms and vice versa, and zero would mean that there were no changes between high and normal pollution levels.

Changes in cardiac symptoms

There were five questions that recorded changes in cardiac symptoms, of which questions 3, 5, and 9 yielded positive net changes that ranged from 5.5% to 11%. The largest positive net change amongst the symptoms questions was seen in question 9, meaning the participants had increased frequency of swelling in the lower limbs when they woke up in the morning during the period when pollution level was high. In contrast question 8 had yielded only a small negative net change of -1.4%, meaning the participants experienced shortness of breath slightly more frequently during episodes of normal air pollution and as a result had to sleep sitting up. No change was seen in question 12 which concerned the frequency of dizziness or light-headed feelings.

Changes in medication use

Question 7 is the only item in the questionnaire for the detection of changes in medication use. Nitroglycerin is a vasodilator that relieves angina pectoris, and only 32 patients in the study were prescribed the drug. A negative net change of -2.7% was recorded, meaning there was a slight increase in the use of nitroglycerin tablets for cardiac symptoms during normal episodes of air pollution.

Changes in emotional well-being

Out of the eleven questions related to emotional well-being, only four yielded positive net changes (questions 2, 4, 6, and 10) with a range of 1.4% to 15.1%. The largest net change was seen in question 4, meaning the participants were more frequently limited by their cardiac symptoms when performing various activities during high levels of pollution. In contrast, 6 questions yielded negative net changes (questions 1, 11, 13, 14, 16, and 17) with question 17 being the largest at -17.8%. This question reflected that the participants were more often felt excluded from doing things with other people due to their cardiac symptoms during normal levels of PM_{10}. Question 15 was the only item that showed no difference between different pollution episodes.

Overall changes in cardiac symptoms score

In appendix 9.1 as shown at the top of the graphs (figure "a", figure 1-17), which were the breakdown of answers of each question, the symptoms score for each question were similar between the two different PM_{10} levels in overall. In general, there were little changes in symptoms score between different pollution episodes, and the distributions of the symptoms score had a tendency to skew towards the right, i.e. majority of the participants did not suffer from severe cardiac symptoms. Although occasionally there was larger number of participants scoring higher in normal days than high pollution days, such pattern was also seen in reverse in some cases. For example in figure 11a, in which there were more participants scoring high, i.e. 4-6, during high levels of air pollution, the pattern was reversed in figure 16a where there were more participants scoring low (i.e. 1-3) during normal pollution levels than high.

For the graphs displayed at the bottom of appendix 9.1 showing difference in symptoms score between high and normal pollution episodes (figure "b", figure 1-17), a normal distribution pattern was seen in all of the graphs, with the most number of subjects having no change in their symptoms score. This indicated that there were little changes in symptoms at the individual level between the pollution episodes, and that the participants' cardiac health was not hugely affected by the short-term increase in PM_{10} levels.

4.4.2 Changes in cardiac symptoms score amongst the more severe cases between high and normal levels of PM_{10}

A sub-sample of 33 participants defined as individuals suffering from more severe cardiac symptoms was chosen for this analysis, based on whether or not they reported low symptom scores of 1 to 3 for either or both questions 3 and 7. The mean age of these 33 patients was slightly lowered to 65years old. Table 4.42 summarises all the results obtained.

Changes in cardiac symptoms

All questions yielded positive net changes including those that had no change (question 12) or negative net change (question 8) when results from all 73 participants were analysed. The range of all positive net changes was 3% to 54.6%. Question 3 had the highest positive net change meaning cardiac symptoms appeared more

frequently during high levels of air pollution. Question 8, which yielded a negative net change previously, was reversed to +3% when only the more severe cases were analysed.

Changes in medication use

The net change of question 7 remained consistent and a larger negative net change of -7.1% was observed when only the more severe cases were analysed (n=14). This represented a slight increase in the use of nitroglycerin tablets for cardiac symptoms during episodes of normal pollution.

Changes in emotional well-being

All but two of the questions concerning emotional well-being yielded positive net changes, ranging from 6.1% to 45.5%. Question 6, which yielded the highest positive net change reflected that the participants' cardiac symptoms had more limitations on their enjoyment of life when pollution level was high. Question 10 was the only item that yielded a negative net change, although the change was small at only -3%. No change was seen in question 16.

Changes in cardiac symptoms score between analyses using data from all cases and from only the severe cases is summarised in table 4.43.

Question number	Symptoms score		
	Worsen	Improved	Net change (%)
Symptoms			
3	5	23	54.6
5	5	17	36.4
8	6	7	3.0
9	4	10	18.2
12	6	13	21.2
Medication use			
7	3	2	-7.1*
Emotional well-being			
1	6	15	27.3
2	7	14	21.2
4	1	12	33.3
6	4	19	45.5
10	9	8	-3.0
11	7	13	18.2
13	6	13	21.2
14	9	11	6.1
15	6	14	24.2
16	10	10	0
17	7	10	9.1

*Only those who were prescribed nitoglycerin were included (n=14)

Table 4.42: Changes in cardiac symptoms amongst the more severe cases between epsidodes of high and normal air pollution levels (n=33).

Question number	Net change (%)	
	All cases	Only severe cases
Symptoms		
3	5.5	54.6
5	8.2	36.4
8	-1.4	3.0
9	11.0	18.2
12	0	21.2
Medication use		
7	-2.7*	-7.1#
Emotional well-being		
1	-2.7	27.3
2	2.7	21.2
4	15.1	33.3
6	1.4	45.5
10	4.1	-3.0
11	-1.4	18.2
13	-6.9	21.2
14	-2.7	6.1
15	0	24.2
16	-5.5	0
17	-17.8	9.1

* Only those who were prescribed nitoglycerin were included (n=32)
# Only those who were prescribed nitoglycerin were included (n=14)

Table 4.43: Changes in cardiac symptoms score between analyses using data from all cases (n=51) and only severe cases (n=33).

Overall changes in cardiac symptoms score

When only the more severe cases were included, as shown in appendix 9.2 figures 1-17, the distributions of the graphs appeared to be different from those when all 73 participants were included. For the graphs that showed the breakdown of answers of each question (figure "a", figure 1-17), larger number of individuals scoring higher during normal pollution levels was seen in a number of questions. This was especially apparent in questions 2-5, 11, and 15, in which the green-coloured bars representing normal pollution levels were skewed to the right and in contrast the red-coloured bars representing high pollution levels were skewed to the left. This means more

participants obtained better symptoms score during episodes of normal air pollution level and vice versa.

As for the graphs showing changes in symptoms score between high and normal pollution episodes (figure "b", figure 1-17), although they were again showing normal distribution patterns with the highest number of participants reporting no change in symptoms score, a number of graphs had tendencies to skew to the right toward the positive change in symptoms score. This means more participants were reporting improvement in their cardiac symptoms when PM_{10} levels were normal, compare to those who reported worsened symptoms.

4.5 Respiratory symptoms questionnaire analysis

Outcome rates

This section focuses on the changes of symptoms in patients with chronic respiratory conditions between high and normal levels of PM_{10} pollution, applying the same research method of both the asthma and cardiac symptoms comparison studies. The hypothesis was that symptoms of individuals with chronic respiratory disease would be worsened by the short-term increase in ambient PM_{10} levels. As shown in table 4.44, a total of 271 invitation letters were given out in various respiratory clinics in south Wales to their visiting patients. Through the clinics 167 replies were returned, of which 109 were eligible for the study. These individuals were then followed-up via the phone and eventually 69 agreed to take part. Throughout the study period, 8 patients died and 10 withdrew due to illness. At the end a total of 51 complete sets of questionnaires were received. Any missing data were swiftly followed-up and subsequently filled in by contacting the patients via the phone. The mean age of the 51 participants who had successfully completed the survey was 66yrs old, of which 49% were male. Most of the participants resided in Cardiff (57%), and the others were from Swansea (29%), Cwmbran (8%), and Port Talbot (6%). Response rate of the study was 63%.

	Number of participants (n)
Letters handed out	271
Response received	167
Eligible responses	109
Respondents who agreed to take part	69
Withdrawn due to death	8
Withdrawn due to illness	10
Completed questionnaires	51

Table 4.44: Breakdown of responses to recruitment letters given out to respiratory patients.

4.5.1 Changes in respiratory symptoms score between high and normal levels of PM_{10}

Items within the respiratory symptoms questionnaire can be divided into those that concerned changes in symptoms, medication use (question 22), and emotional well-being (questions 8, 9, 12, 14, and 17-21). In addition, the symptoms questions were further divided into two subgroups and became items of general respiratory symptoms (questions 1, 2, 3, 5, 7, 13, and 16) and items of specific respiratory symptoms (questions 4, 6, 10, 11, and 15). Questions of general respiratory symptoms consisted of items that concerned the more general respiratory health such as coughs and production of phlegm. On the other hand, questions of specific respiratory symptoms were regarded as stronger indicators of respiratory health such as shortness of breath and chest tightness. The net changes of each item in the questionnaire were calculated and shown in table 4.45.

The breakdown of the answers of each question in the respiratory symptoms questionnaire are listed in appendix 10.1, figure "a" of figures 1-22. Same as those presented in the cardiac symptoms questionnaire analysis, each bar represents the total

number of patients who had given a score for the corresponding question during both high and low pollution episodes, and the higher the symptoms score the better the patients were feeling in terms of their respiratory symptoms. Overall, changes in symptoms score between high and normal levels of air pollution were little, and at individual levels the distributions of the symptoms score frequently skewed towards the left, indicating that majority of the participants were suffering from severe respiratory symptoms (appendix 10.1, figure "b" of figures 1-22).

Changes in general respiratory symptoms

Out of the seven items in this section, questions 1, 2, and 7 had yielded positive net changes ranging from 2% to 9.6%. Question 2 had the largest positive net change meaning the participants were more likely to bring up phlegm during high levels of air pollution. The remaining items (questions 3, 5, 13, and 16) all yielded negative net changes with question 5 being the largest at -13.7%, meaning severe wheezing attacks were more frequently reported in the participants during episodes of normal air pollution levels.

Changes in specific respiratory symptoms

Three of out five items used for the detection of changes in specific respiratory symptoms yielded positive net changes. They were questions 6, 11, and 15, with 11 having the highest net change of 17.7%. This reflected that the participants were more likely to suffer from shortness of breathe during high levels of air pollution. On the other hand, both question 4 and 10 yielded identical value of negative net change of -5.9%. These questions indicated that during normal levels of air pollution the participants had unpleasant attacks of chest troubles (question 4) and chest tightness (question 10) more frequently than during levels of high pollution.

Changes in medication use

Question 22 was the only item for the detection of changes in medication use, which in this case was the frequency of oxygen mask usage between different levels of air pollution. Results from only 31 individuals were included in the analysis because not every participant in the study required oxygen mask for breathing. A positive net change of 22.6% was observed, meaning the use of oxygen mask to help breathing was increased during high levels of PM_{10}.

Changes in emotional well-being

Amongst all the items within this section, questions 8, 17, 18, and 21 yielded positive net changes ranging from 2% to 25.5%. Oppositely questions 12, 14, 19, and 20 yielded negative net changes, and there was no change in question 9. The largest positive net change was seen in question 21, meaning the participants were more often felt excluded from doing things with other people because of their respiratory symptoms. Question 20 was the item that yielded the largest negative net change of -13.7%, meaning the participants were more likely to feel discouraged due to their respiratory symptoms during episodes of normal pollution level.

Question number	Symptoms score		
	Worsen	Improved	Net change (%)
General respiratory symptoms			
1	11	14	5.8
2	11	16	9.6
3	16	11	-9.6
5	19	12	-13.7
7	20	21	2.0
13	17	14	-5.9
16	20	16	-7.8
Specific respiratory symptoms			
4	15	12	-5.9
6	16	17	2.0
10	16	13	-5.9
11	11	20	17.7
15	10	17	13.7
Medication use			
22	2	9	22.6*
Emotional well-being			
8	17	22	9.8
9	17	17	0
12	15	14	-2.0
14	18	12	-11.8
17	13	22	17.7
18	14	15	2.0
19	19	16	-5.9
20	21	14	-13.7
21	10	23	25.5

*Only those who used oxygen were included (n=31)

Table 4.45: Changes in respiratory symptoms between episodes of high and normal air pollution levels (n=51).

Overall changes in respiratory symptoms score

Changes in symptoms score were also examined graphically as shown in appendix 10.1, figure "b" of figure 1-22. In almost all cases the proportion of participants who reported no changes in symptoms was always the largest and normal distribution

patterns were seen in all of the graphs. The only exception was question 7, in which the number of participants who reported no changes in their symptoms score was slightly lower than those who reported a -1 change, and the number was also identical to those who reported a +1 change. Occasionally there may be increase or decrease in symptoms score between different levels of PM_{10} pollution, however the magnitude was always small (+1 or -1) such as those seen in questions 17, 19, 20 and 21.

4.5.2 Changes in respiratory symptoms score amongst the more severe cases between high and normal levels of PM_{10}

Table 4.46 below presents the net changes in symptoms scores obtained from a sub-sample of 13 individuals with more severe respiratory cases. This was based on whether or not they reported low symptoms score of 1 to 2 for both questions 4 and 10. The mean age of this subgroup of patients was slightly increased to 67yrs old.

Changes in general respiratory symptoms

Three out of the seven questions that concerned changes in general respiratory symptoms yielded positive net changes (questions 1, 2, and 13). The range was 7.7% to 23.1% with question 2 being the largest again as previous when all 51 sets of results were analysed. Questions 5, 7, and 16 yielded negative net changes with question 7 being the largest (-38.5%). Question 3 detected no change in symptoms score between different levels of PM_{10}.

Changes in specific respiratory symptoms

Out of the five questions that focused on specific respiratory symptoms, 3 yielded positive net changes ranging from 7.7% to 30.8% (questions 4, 6, and 11). The largest effect size was seen in question 11, meaning shortness of breath was more frequently reported during high levels of PM_{10}. Question 15 was the only item that yielded negative net change (-15.4%) and reflected that the participants had to sleep sitting up more often due to shortness of breathe during episodes of normal pollution. No change was seen in question 10.

Changes in medication use

Eight subjects who regularly required the use of oxygen mask to help breathing were included in the analysis. A positive net change of 12.5% was observed, which was lower than that reported previously.

Changes in emotional well-being

Questions 9, 17, 19, and 20 yielded positive net changes ranging from 7.7% to 15.4%. Both questions 17 and 20 had the highest positive net change, but question 20 yielded a negative net change of -13.7% previously. Four questions yielded relatively large negative net changes, two of which were -23.1% (questions 12 and 18) and the other two were -30.8% (questions 14 and 21). Interestingly, question 21 was the question that had the largest positive net change previously. No change was observed in question 8.

Changes in respiratory symptoms score between analyses using data from all cases and from only the severe cases is summarised in table 4.47.

Question number	Symptoms score		Net change (%)
	Worsen	Improved	
General respiratory symptoms			
1	1	2	7.7
2	1	4	23.1
3	1	1	0
5	3	2	-7.7
7	7	2	-38.5
13	4	6	15.4
16	5	4	-7.7
Specific respiratory symptoms			
4	0	2	15.4
6	3	4	7.7
10	2	2	0
11	2	6	30.8
15	3	1	-15.4
Medication use			
22	0	1	12.5*
Emotional well-being			
8	4	4	0
9	4	5	7.7
12	4	1	-23.1
14	5	1	-30.8
17	2	4	15.4
18	4	1	-23.1
19	4	5	7.7
20	4	6	15.4
21	6	2	-30.8

*Only those who used oxygen were included (n=8).

Table 4.46: Changes in respiratory symptoms amongst the more severe cases between episodes of high and normal air pollution levels (n=13).

Question number	Net change (%)	
	All cases	Only severe cases
General respiratory symptoms		
1	5.8	7.7
2	9.6	23.1
3	-9.6	0
5	-13.7	-7.7
7	2.0	-38.5
13	-5.9	15.4
16	-7.8	-7.7
Specific respiratory symptoms		
4	-5.9	15.4
6	2.0	7.7
10	-5.9	0
11	17.7	30.8
15	13.7	-15.4
Medication use		
22	22.6*	12.5#
Emotional well-being		
8	9.8	0
9	0	7.7
12	-2.0	-23.1
14	-11.8	-30.8
17	17.7	15.4
18	2.0	-23.1
19	-5.9	7.7
20	-13.7	15.4
21	25.5	-30.8

* Only those who used oxygen were included (n=31).
\# Only those who used oxygen were included (n=8).

Table 4.47: Changes in respiratory symptoms score between analyses using data from all cases (n=51) and only severe cases (n=13).

Overall changes in respiratory symptoms score

The breakdown of the answers of each question in the respiratory symptoms questionnaire amongst the more severe cases are listed in appendix 10.2, figure "a" of figures 1-22. Same as previously when all 51 cases were analysed, the overall changes in symptoms score between episodes of high and normal PM_{10} levels were little, and majority of the participants reported low symptoms score regardless of the pollution episodes. In appendix 10.2, figure "b" of figures 1-22 shows the change in symptoms score at individual levels between high and low pollution levels. Again, the graphs resembled a normal distribution pattern with the highest number of participants reporting no change in nearly all of the case. Occasionally there were increase or decrease in symptoms score between different levels of PM_{10} pollution, however the magnitude was always small (+1 or -1) such as those seen in questions 8, 9, 13, 14, and 19-21.

CHAPTER 5 – DISCUSSION AND CONCLUSION
SECTION 1
EXPOSURE COMPARISON STUDY

This study was carried out in the city of Cardiff which has 305,200 inhabitants according to the 2001 Census figures. It was estimated by the Cardiff Council that 44,000 commuters travel to work in Cardiff each day of whom approximately 80% commute by car or by bus. Cardiff is also a popular tourist area with large number of visitors entering and leaving the city everyday. Development in recent years had demolished most of the heavy industries in the city. As a result of the city's size and degree of economic activity, air quality has been an issue in certain parts of Cardiff caused by pollutants emitted from road transport. These are highlighted by high volumes of traffic queuing and buildings situated close to the roads. Main, arterial routes used to move people and goods are also areas of concern. Having said that, data from stationary air quality monitoring stations showed that the PM_{10} air pollution level in Cardiff is not as significant as larger cities such as London. The mean annual level of PM_{10} as measured by stationary monitoring station was 19.8μg/m^3 in 2004 and 19.7μg/m^3 in 2005, which were approximately 10μg/m^3 lower than the level measured in London Westminster. The PM_{10} level of Cardiff centre is projected to reduce to 18.0μg/m^3 in 2010.

5.1.1 Classification of street types and definition of exposure status of subjects

In order to investigate whether microenvironments, in terms of particulate pollution caused by local traffic, exist within an urban area, a number of streets from Cardiff were chosen in the study which were subsequently classified into exposed and control groups. Ideally the classification of streets into the appropriate group should be based on real data such as traffic flow volume or levels of air particulates in those areas, to ensure that the particulate levels in the exposed streets are truly different from the controls. However, traffic flow data was only available for a small number of high trafficked streets in Cardiff and the levels of air particulates were only monitored at fixed sites. As a result extra streets had to be introduced into the study using long-term local knowledge of traffic queues and flow in order to bring up the total number of streets in the study. To prove that groups of chosen streets were actually different

from each other in terms of pollution level, environmental survey work was carried out using portable equipment to provide information on particulate concentrations of various areas in relative terms. It is well know that levels of air particulates vary greatly during the course of the day and can be affected by a number of factors such as weather. Theoretically the best approach to quantify the levels of air particulates of a street is by long-term continuous monitoring. However, due to limited resources and time, only a limited number of measurements were made in the target areas. This led to the variations seen in air particulate levels within the same area during different period of time, as expressed by the different SE% obtained that ranged from 4% to 12%. Nevertheless, these measurements were all made at random times between 9am and 6pm Monday to Friday when traffic within the city was busiest. One of the most effective ways of reducing variability is by increasing the number of measurements made in the same street. Throughout the study a total of 373 measurements were made in all target streets, with an average of 16 times per street. Each time 20mins of sampling was carried out and thus this converts into 320mins, or 5.3hrs of sampling time per street on average. Based on the findings obtained through the environmental survey work, the mean PM_5 concentration of the exposed areas was 17.5μg/m^3 and the control areas was 11.8μg/m^3. Since the proportion of PM_5 in PM_{10} in terms of total particle mass was estimated to be approximately 75% [DTI 1999], assuming that the proportion is constant, the level of ambient PM_{10} found in the study would therefore be around 23.3μg/m^3 and 15.7μg/m^3 for the exposed and control areas respectively. The annual mean urban background PM_{10} concentration in Cardiff as measured by fixed monitoring site was 19.7μg/m^3 in 2005, which was about 15% lower than the PM_{10} level estimated in the exposed areas, and about 25% higher than the PM_{10} level estimated in the control areas.

5.1.2 Indoor levels of air particulates and its relationship with outdoor levels

The variation of indoor PM_5 was not as large as that observed in outdoors, as shown by the smaller standard deviations of the indoor measurements. In exposed areas, the SD of all outdoor PM_5 measurements was 40% higher than indoors, and similarly in control areas, the SD of outdoor PM_5 levels was 13% higher than indoors. The median indoor PM_5 concentration of the houses located in the exposed areas was 13.2μg/m^3 and in the control areas was 9.4μg/m^3, in which both values were around 80% of their

corresponding outdoor median PM_5 concentrations. Therefore it may be possible that a proportion of up to 80% of the outdoor PM_5 penetrated into the houses, and that the higher level of indoor PM_5 observed in the exposed group may be attributable to the higher level of PM_5 outdoor. In fact, a moderate correlation ($r = 0.57$) was found between indoor and outdoor PM_5 levels in overall. Although correlations between two variables do not provide information on causality, in this case it was apparent that particulates entered the houses which led to the increased indoor levels and not the other way. This was because levels of PM_5 was always higher in outdoors and thus the concentration gradient would have driven the particles inside the houses. Furthermore, larger concentration gradients would be able to drive more particles indoor, thus explaining the finding that the correlation between indoor and outdoor PM_5 in the exposed group ($r = 0.53$) was higher than the controls ($r = 0.36$), because the difference between indoor and outdoor median PM_5 was higher in the exposed areas ($3.5\mu g/m^3$) than controls ($2.1\mu g/m^3$). Based on the assumption that the frequency of gas or electricity appliances usage for cooking and heating were at similar levels in all sampled houses (i.e. the background levels of PM_5 generated indoors), and since all the participating houses were non-smoking households, then the differences in PM_5 seen across different houses were very likely to be due to particles in the ambient air entering the house from the outside, especially when the architectural design of the house was found to have no influence on the levels of indoor PM_5.

5.1.3 Trace element concentrations in environmental PM_{10} samples

Environmental PM_{10} samples were collected and four elements that are known specific markers of motor vehicles were analysed by ICP-MS – vanadium is produced by fuel combustion; copper is produced from wearing of brake linings; bromine used to be a component of fuel additive but has been phased out; and antimony is released through engine wear and from lubricants in brake pads. Since ICP-MS is capable of analysing a suite of elements simultaneously other elements were also studied. The hypothesis was that the levels of these elements in air particulates would be higher in exposed than control areas. However, both vanadium and bromine were found to be higher in control areas, with only vanadium reached statistical significance. Antimony was only found in a small number of samples and comparison was not carried out. Higher levels of copper found in exposed areas reflected the possibility of increased

emissions from motor vehicles in those microenvironments, and the lack of statistical significance may be explained by the small sample size. However, if truly this was the case, the levels vanadium, bromine, and antimony should have followed the same trend since they were all emitted from motor vehicles, thus it was difficult to explain why one marker was higher in the exposed areas and the others were not. It was possible that copper was the best marker for vehicular emissions among the four, after all its median concentration found in the environmental PM_{10} samples was relatively higher than the rest of the elements. Another possibility was that the higher level of copper observed in the exposed areas was due to unknown sources other than motor traffic. Interestingly the levels of sodium and chlorine were found to be significantly higher in the exposed areas. Any contamination of samples from salt on the surface of the skin would be expected to result in an overall increase in sodium and chlorine in all samples universally and not just those from the exposed areas. The other possible explanation is that Cardiff is a coastal city and therefore the sodium and chlorine found were very likely to be sea salt. But why were they significantly higher in exposed areas? At first it was thought that this may be related to the distance to the coast, which is on the eastern and south-eastern side of the city. However, all exposed and control areas (except Marshfield) were at similar distance to the coast, and levels of sodium and chlorine were not particularly higher in the Marshfield samples compared with the other control samples. Thus the distance from the coast of where the samples were taken could not explain the findings. Finally, the most probable explanation would be that salt were used during cold weather to melt ice on road surfaces, and being a major road with high traffic volume, i.e. streets from exposed group, are more likely to be treated than small streets or cul-de-sacs in the control areas.

5.1.4 Trace element concentrations in indoor dust samples

Dust were collected from inside the houses for the analysis of trace elements by ICP-MS. Eight known specific markers of motor vehicles including vanadium, manganese, iron, copper, zinc, barium, cerium, and lead were selected, and in addition a suite of other elements were also analysed. Vanadium, manganese, and cerium are used as fuel additives, lead is found in resuspended road dust due to long-term environmental pollution caused by the use of leaded fuel in the past; copper and barium are from brake wear; and iron and zinc are from engine wear. Results showed that the levels of

almost all these elements were found to be higher in the exposed group than the control, ranged from 33% as seen in vanadium and cerium, to as high as 200% as seen in lead. Copper was the only exception in which the median concentration found in the control group was nearly 30% higher than the exposed group. In addition the levels of aluminium, cobalt, and tin were also found to be higher in samples from the exposed group. Although none of the differences found achieved statistical significance possibly due to small sample size, these data suggested two possibilities, a) that air particulates were entering the house from outdoor and b) harmful elements that were attached on the surfaces of the particles settled and accumulated in the house. However, it is worth mentioning that iron, copper, and zinc are common metals which may have been generated from indoor, and traces of lead can often be found in the old paint work of older houses. Finally, because the dust samples were collected over a much longer period of time than the environmental PM_{10} samples (6mths v 24hrs), therefore the higher levels of trace elements found in the dust samples of the exposed group would indicate long-term increased exposure to air particulates generated from outdoors.

5.1.5 Trace element concentrations in blood and hair

Study subjects were allocated into the appropriate group according to the exposure status of the streets they resided in. Trace elements were analysed in both blood and hair samples collected from subjects residing in exposed and control areas. Whole blood samples were separated into sera for the analysis of copper, iron, zinc, and lead by ICP-MS. Hair samples were washed and analysed by NAA for the presence of vanadium, manganese, copper, bromine, antimony, and a suite of other elements. Except for copper, manganese, and bromine in hair, none of the elements in any of these samples demonstrated differences between their median concentrations in the exposed and control groups. Although manganese and bromine have median levels being 35% and 48% higher respectively in exposed than controls, none of the observed differences reached statistical significance. Lead was not detected in a large number of samples because sera were used instead of whole blood. As demonstrated in a Swedish study involving 372 adolescents, the median levels of lead found were 16μg/l in whole blood but only 0.33μg/l in serum [Barany *et al* 2002]. Although the minimum detection for lead in serum (0.1μg/l) is 10-fold higher than blood, the low

levels of lead found in serum means that it is not an ideal choice for quantifying this metal in blood. The trace element concentrations found in both blood and hair showed that these biomarkers of exposure were not being taken up, despite the fact that subjects from the exposed group were exposed to higher levels of respirable particles in both indoor and outdoor environments. The possibility was that particles with trace elements adhered to the surface failed to penetrate into the deepest regions of the lungs and/or dissolve into the bloodstream, either due to particle size or the solubility of the elements. The American Conference of Governmental Industrial Hygienists (ACGIH) has assigned percentages of different particle fractions that can be carried to the various regions of the lungs, and in the case of PM_5 it was estimated that only 30% of the particles are within the respirable fraction that can penetrate deep into the alveolar of the lungs [ACGIH 1999]. In relative terms, hair is a better long-term dosimeter of exposure than blood, not only because hair is an inert and chemically homogeneous substance and are able to fix trace elements once they are incorporated into it, but their extraction and storage are also easier than blood. Blood in contrast reflects exposure to trace elements in a shorter-term, and thus the levels found in blood are largely determined by the subject's exposure to air pollutants shortly before (hours or days) the sample is extracted. A laboratory study showed that the concentrations of blood lead peaked after 4-5hrs of inhaling lead particles, and after reaching its maximum the level declined exponentially [Chamberlain *et al* 1978]. Hence blood is more suitable for the immediate measurement of exposure to trace elements, as it gives no indications of the cumulative levels of these elements in the body. Therefore unless subjects residing in the exposed areas inhaled large doses of copper-containing particles within the respirable fraction, significant differences in copper concentrations found in blood and hair seemed unlikely. The lack of correlation in copper concentrations between blood and hair suggested that the copper found in hair were due to long-term deposition of the metal from blood, rather than days before the blood samples were being taken.

5.1.6 Concentrations of platinum in urine

Platinum is released into the atmosphere from the catalytic converters of motor vehicles, and hence is an ideal indicator for exposure to road traffic. Twenty-eight samples from individuals residing in the exposed areas were analysed by ICP-MS for their presence of platinum. The median concentration of platinum found was 12ng/g

creatinine with a range of 3.8-1412ng/g creatinine. The mean concentration was 151ng/g creatinine, reflecting the presence of several extreme values toward the upper end. Urinary levels of platinum found in this study were similar to those found in a group of non-occupationally exposed individuals in London, UK (mean 113ng/g creatinine, range 48-224ng/g) [Farrago *et al* 1998], but were significantly higher than those found in Munich, Germany (mean 6.5ng/g creatinine; median 4.3ng/g creatinine) [Schierl 2000], Budapest, Hungry (mean 10.1ng/g creatinine; median 7.8 ng/g creatinine) and Vienna, Austria (mean 3.7ng/g creatinine; median 3.2ng/g creatinine) [Zaray *et al* 2004]. The fact that only samples from the exposed areas were included in the analysis may have resulted in the relatively higher median level of platinum found compared to other European studies. Platinum concentrations were also quantified in several other European studies [Bocca *et al* 2004, Spezia *et al* 2005], but the authors did not control for the levels of creatinine in the urine and the levels were therefore incomparable. Two urine samples, one from Manor Way and the other Western Avenue, contained unexpectedly high levels of platinum that were almost 10-fold higher than the median platinum concentration found in the study. Traces of platinum can always be found in contaminated food and water, and according to Vaughan and Florence diet was the main route for platinum intake in Australia [Vaughan and Florence 1992]. However, the levels platinum in foodstuff are often low and therefore cannot explain the huge differences observed in the study by dietary intake alone. Another possible source of platinum is from dental alloy restorations that contain platinum, which has been found to increase the body load of platinum by more than 10-fold [Herr *et al* 2003].

5.1.7 Levels of PAH in the environment and 1-HP concentrations in urine

Nine environmental samples were collected for the detection of PAH by HPLC. However, all of them contained insufficient quantities that were above the minimum detection limit (5ng/m^3). In contrast, levels of 1-HP were detected in the urine samples, which are metabolites of one of the most abundant PAH in the environment pyrene. Higher median concentration of 1-HP was found in the control group by 62%. This finding was not consistent with the fact that no PAH were detected in the environmental samples. One of the possibilities was that the 1-HP found in the body was through intake of food and water that were contaminated by PAH. As discussed in chapter 1, food is one of the major sources of PAH found in the body and they can

be found in substantial quantities in some foods depending on the mode of cooking, preservation, and storage. As for the significant difference in 1-HP found in samples from exposed and control subjects, it could be explained by the different dietary habits of the subjects, which in certain extent is linked to social status.

Recommendation for future work

This section summarises the shortcomings and difficulties encountered in the Exposure Comparison Study in retrospect, and discusses the possibilities of how it can be improved should studies of the similar kind be carried out.

Recruitment

As with most epidemiological studies the most challenging issue in the Exposure Comparison Study was the recruitment of subjects. In the study over 8,000 invitation letters were sent out within a window of 24mths of which only 5% were returned. The bottleneck of the recruitment process was due to the lack of respondents when the invitation letters were sent out. These letters were mass-mailed to all households in the target streets with no information on the names of the residents. With the number of commercial advertising junk mails each household receives nowadays, it was likely that most of the invitation letters were discarded even before being read. At first the use of GP records for information on the people who reside in the target streets had been proposed. However, due to the Data Protection Act the clinics were not allowed to release contact information of their patients unless permissions were granted. Another way was to ask the clinics to send out invitations on the researcher's behalf, but with the extra administrative works required and no clear benefits to the clinics it was doubtful if cooperation could be obtained. In the future if recruitment of such kind is required, it may be possible to employ research assistants to cover all target areas and speak to the residents in person. Although the process will be time consuming and labour intensive, this method can largely increase the number of people who will be given the information and thus potentially increase the number of participating subjects. Moreover, the eligibility status of those who refused to participate can also be obtained for the calculation of response rate.

Collecting environmental PM_{10} samples

Much difficulty was encountered when collecting environmental PM_{10} samples for trace elements and PAH analyses. The task required the setting up of heavy duty air pumps inside the participating households that had to operate for 24hrs continuously. Not only were the pumps noisy and cumbersome to set up, the need of placing the inlet head outdoors meant that windows had to be opened throughout the night. As a result security was the main reason of why the request of setting up the pumps inside the houses was declined by majority of the participants. While this problem was minimised in the control areas because most houses had garages which was an ideal place to setup the pumps with minimal distraction and inconvenience, such option was not available in most of the houses in the exposed areas. The recent requisition of a mobile air monitoring vehicle in the department would have solved the problem should it have been available prior to the beginning of the study. This vehicle is capable of automatically carrying out environmental surveys without the need of external power supply. By simply parking the vehicle in the target streets PM_{10} samples can therefore be easily collected at anytime and for long durations.

Measuring indoor and outdoor air particulate levels

In the study both indoor and outdoor levels of PM_5 were measured by the portable QCM for a short period inside and outside the participating households respectively. While this method provided information on the particulate levels inside the sampled house and its corresponding outdoor environment, the short sampling time may not have been able to capture the short-term variance in particulate level such as during rush hours, and therefore may not have reflected accurately the true indoor level of the house. Ideally the sampling time should be at least 24hrs so that any short-term changes in particulate levels can be monitored. This would require a piece of monitoring equipment that is capable of registering real-time particulate levels like the QCM, but with a higher maximum operating time and lower noise level to minimise distraction. Most importantly, sampling should take place simultaneously in indoor and outdoor in order to provide the most accurate data for studying correlations of air particulates inside and outside the house.

Collecting biological samples

Out of the three types of biological samples that had to be collected in the study, i.e. blood, hair, and urine, collecting blood sample was the one that presented most concerns. Throughout the duration of the study, only 84 out of the possible 123 sets of blood samples were collected. The main reason was that due to health and safety issues blood samples could only be extracted by a qualified medical staff, which means the participants had to attend the phlebotomy clinic at the University Hospital of Wales in order to donate a blood sample. This was found to be extremely inconvenient for the participants not only because some of them resided or work far away from the hospital, but also because the clinic only opens between 9am and 5pm Monday to Friday, while most people were at work. Effort have been made to increase the number of blood samples donated by sending out reminder letters and making follow-up phone calls, as well as providing travel expense reimbursements, but the decision of whether to attend the clinic or not was entirely the subjects' own wishes. In future studies when blood samples are required a nurse or phlebotomist can be employed to carry out the task at the participant's home or work place. In addition the use of other biological samples such as urine for the analysis of trace elements can be considered as an alternative to blood.

Even if blood samples were donated they present another concern. As discussed previously blood is a short-term dosimeter of exposure to air particulates arise from motor traffic, therefore the concentrations found in blood would only reflect the subjects' exposure to air particulates several days prior to giving blood. This potential problem can be overcome by asking the subjects to keep an activity diary several days before donating a blood sample. This would allow detailed records of each individual's daily activities be examined and any unusual patterns such as prolonged travelling in motor vehicles or exposure to environmental tobacco smoke can be accounted for. In addition this can also be accompanied by the use of personal particulate samplers that can monitor the levels of air particulates to which each individual was exposed to, since the trace elements of interest are most likely associated with particles. However, these would have to be specially designed and built as equipment of such kind is not commercially available at present. The same research method can be applied to the analysis of 1-HP in urine samples since they are both short-term biomarkers of exposure to motor vehicles.

5.1.9 Conclusion

Results of the Exposure Comparison Study have shown that levels of PM_5 vary between microenvironments within a city by approximately 50%, and higher levels of particulate air pollution were associated with high volumes of local traffic. Moderately high correlation between indoor and outdoor particulate levels, together with the higher levels of several trace elements specific to motor vehicles found in indoor dusts suggested that harmful substances emitted from traffic were able to penetrate into houses and settled in the indoor environments. Having said that, there was no evidence showing human uptake of any of these harmful substances despite increased exposure. This was reflected by the null findings in the study that none of the biomarkers of exposure have shown any significant differences in concentrations from biological samples of subjects residing in different exposure areas. Having said that, because each individual is exposed to a number of different microenvironments, it was difficult to conclude if the exposure biomarkers found in the biological samples could truly reflect the levels of exposure from their local area. Due to the relatively small sample size compared to other large-scale ecological studies, this study was unable to demonstrate any major findings with high levels of statistical significance. Nevertheless this study has shown that microenvironments with different levels of respirable air particulates attributable to local traffic volume can be found within a city, which was independent to whether a difference in biological uptake existed. Therefore the research work carried out can be regarded as a pilot study which has managed to find some evidence of the existence of microenvironments, and further studies will be required to establish the possibility of increased uptake of biological markers of exposure to motor vehicles as a result of residing within proximity to motor traffic.

SECTION 2
SYMPTOMS COMPARISON STUDY

5.2.1 Asthma symptoms questionnaire

Changes in symptoms

Different changes in asthma symptoms were observed in the study which lacked consistency across symptoms. The most significant change was seen in wheezing which is one of the strongest indicators of one's asthma condition. Improvement was also seen in shortness of breath despite discrepancies between "short of breath" and "very short of breath", that is, improvement was only seen in "very short of breath" and not the other. This suggested that short-term increase in PM_{10} levels appeared to have larger affects on the more severe asthma symptoms such as very short of breath and less on milder asthma symptoms such as difficulties in breathing. Indeed, when only cases of severe asthma were studied positive effect sizes were seen in all items, which coincides with the explanation that respirable particulate air pollution has more significant effects on patients suffering from severe asthma.

Changes in medication use

The frequency of asthma medication use reflects how asthma symptoms are affecting an individual. Positive effect size for medication use was seen when all cases of asthma subjects were studied, and the effect was further increased when only the extreme cases were included. This again suggested that increase in PM_{10} levels has more significant negative effects on patients with more severe asthma, and resulted in the increased medication use for their exacerbated symptoms.

Changes in emotional well-being

A number of items in the questionnaire concerned about changes in emotional well-being. Different degrees of changes in each item were observed but an overall improvement was seen in those focused on activities and symptoms-related emotions. In terms of activities, little changes were seen between high and normal pollution episodes in patients when they were carrying out moderate and social activities. However, when it comes to performing strenuous activities, less limitation was reported during normal levels of PM_{10} as reflected by a large positive effect size. The effect seen was further increased when only the severe cases were included, which is

consistent with previous findings that air particulate levels have larger effects on severe asthma. In terms of symptoms-related emotions, high pollution levels have caused distress or discomfort due chest tightness and coughs in patients and with a much higher magnitude in the more severe cases. Because these were emotional well-being questions that were related to symptoms, therefore they further support the finding that high levels of particulate air pollution exacerbate asthma symptoms, and especially in the severe cases. Although it has been shown that both asthma symptoms and the need of asthma medications were improved during normal episodes of air pollution, the subjects appeared to be concerned about their asthma symptoms and had always felt bothered by heavy breathing regardless of the level of PM_{10}. This suggested that they worried about having asthma all the time and that the concerns were independent to whether or not their symptoms were affected by air pollution.

5.2.2 Cardiac symptoms questionnaire

Changes in symptoms

Some improvement in cardiac symptoms was seen in patients during normal episodes of air pollution as represented by the positive net changes seen in several questions that concerned symptoms. The effect was further amplified when only the severe cases were included, suggesting that individuals with more severe cardiac symptoms were more likely to be affected by high levels of PM_{10} pollution. Furthermore, the effects of air pollution was particularly apparent in the more specific cardiac symptoms including chest pain, chest tightness, angina, and shortness of breath.

Changes in medication use

While cardiac symptoms have appeared to improve during normal episodes of air pollution, little changes were observed in the use of nitroglycerin for the relief of angina symptoms. Since nitoglycerins are prescribed by doctors and can either be taken regularly or only when required, it was therefore possible that majority of the patients were taking the drug regularly and as a result only little changes were seen between different pollution episodes. Another explanation was that those who were prescribed the drug were possibly suffering from more severe cardiac symptoms and required constant medical usage at all time.

Changes in emotional well-being

Results from questions that focused on changes in emotional well-being were consistent with the symptoms questions. Nearly all items in the questionnaire have shown little changes between episodes of air pollution, however when only the severe cases were included the magnitude of change was markedly increased in nearly all items, which coincides with the previous suggestion that high levels of particulate air pollution have stronger effects on individuals suffering from more severe cardiac symptoms.

5.2.3 Respiratory symptoms questionnaire

Changes in symptoms

Items of the general and specific respiratory symptoms have shown different levels of net changes in both directions. It was difficult to determine the overall effects of air pollution on respiratory symptoms with absolute certainty. However, the moderately large positive net changes observed in two of the specific respiratory symptoms items suggested that high levels of PM_{10} had greater effects on more specific respiratory symptoms such as shortness of breath than general respiratory symptoms such as cough and production of phlegm. It was when only the severe cases were studied that improvement was seen in some of the general respiratory symptoms when pollution level was normal.

Changes in medication use

Positive net change in medication use as represented by the decreased use of oxygen mask to help breathing in normal air pollution episode was seen in the study. However the magnitude of the net change was decreased when only the severe cases were studied. This was due to the fact that only a very small number of patients were identified as severe cases and that all but one of them reported no changes in oxygen use between high and normal levels of PM_{10}.

Changes in emotional well-being

Changes in emotional well-being were similar to those observed in symptoms because changes were seen in different directions and at different levels. In overall however, the patients' abilities to perform activities seemed to have benefited from lower levels of PM_{10}, and in contrast their enjoyment of life appeared to have been affected by

normal levels of air pollution. Large negative net changes were observed in a number of items when only the severe cases were included in the analysis, thus showing the patients' emotional well-being was worse during normal pollution episodes. However they must be treated with caution since the number of individuals included was very small and therefore any small changes in symptoms score will be magnified and appeared to be large.

5.2.4 Recommendation for future work

Recruitment

The decision of using specialist hospital outpatient clinics for the recruitment of subjects in the study seemed to have served the purpose well. However, in retrospect the use of invitation letters was rather passive and inefficient. It appeared that some patients failed to reply to the invitation letters as reflected by the difference in the number of letters given out and the number of actual replies received. It was possible that the patients were either not interested in the study or that they did not read the invitation letters while waiting for their consultations. In the future, this problem can be solved by having research assistants stationed at the clinics and speak to the patients in person. The advantage is that the patients can definitely be informed of the study and it also compensates the inefficiency of the invitation letters. Moreover, the research assistants can also collect their contact information immediately and answer any questions they may have, thereby reducing the workload on follow-ups and the risk of the patients forgetting to include their contact details when returning the reply cards.

Episodes of particulate air pollution

One of the issues most frequently raised by the participants of the Symptoms Comparison Study was that of whether it was possible to let them know in advance as to when the questionnaires will be sent out. Some participants reported difficulties in answering questions that concerned about their symptoms during the week of interest, despite the fact that the questionnaires were received before the end of the target week. Because it was impossible to predict changes in PM_{10} levels, therefore a different approach will be required should this study be repeated in the future. One of the solutions is by the use of symptoms diaries to record their changes in symptoms between episodes of air pollution. Key questions from the symptoms questionnaires

can be extracted and modified to form a disease specific symptoms diary. Each subjects can be asked to complete a daily diary which can then be matched to the changes in PM_{10} levels retrospectively.

Questionnaire design

All the items were extracted from validated instruments which strengthened the validity and usefulness of the symptoms questionnaires used in the study. However, the items were extracted from different instruments and hence the standard analytical methods of these questionnaires as devised by their authors could not be used. While this represent little problems with the asthma symptoms questionnaire, difficulties were encountered when analysing results of the cardiac and respiratory questionnaires. Because the answers of these questionnaires were in ordinal format and were unsuitable for the calculation of means and medians, no statistical tests were able to inspect the differences observed. Therefore if these questionnaires are to be used again in the future, the format of the answers should be revised to allow the calculations of mean symptoms score as well as the use of statistical tests to examine the differences observed.

5.2.5 Conclusion

Results of the Symptoms Comparison Study showed that the levels of respirable particulate air pollution have displayed effects on symptoms, medication use, and emotional welling-being on individuals who were suffering from asthma, chronic cardiac disease, and chronic respiratory disease. While most results of the asthma symptoms questionnaire appeared to be statistically insignificant, this could be explained by the fact that all studies involved only a small number of patients and unless the sample size can be increased it would be difficult to achieve statistical significance. Majority of the patients reported no changes in symptoms score between high and normal episodes of air pollution, although the results suggested that individuals with more severe asthma and cardiac disease appeared to benefit more from normal levels of air pollution. The fact that respiratory patients were less benefited was because their quality of life, as reflected by disease symptoms, was generally poorer than those suffering from asthma and heart disease, and therefore slight changes in air pollution levels was unlikely to have any significant improvements on their symptoms. In summary this study can be considered as a pilot

study that has successfully demonstrated some of acute health effects caused by short-term changes in PM_{10} levels.

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APPENDIX 1

Coleg Meddygaeth Prifsgol Cymru
University of Wales College of Medicine

The Resident
«House_number» «street»
«area»
«town»
«postcode»

«ID»

Dear Resident

A Research Study of the Levels of Exposure to Air Pollution from Motor Vehicles

The University of Wales College of Medicine is investigating the ways that air pollution might affect breathing and heart problems. We are asking healthy men between the ages of 50 and 70, who do not smoke, if they would be willing to take part in this study. If you are male between these ages with no history of chest disease, heart disease, diabetes or arthritis we would be grateful if you would consider taking part. A researcher will then describe the study to you in more detail and answer any questions you may have.

Please answer the questions below and return this sheet in the **FREEPOST** envelope enclosed, you do **NOT** need to use a stamp.

	YES	NO
I am happy to have a member of the research team contact me to discuss my taking part in the study	☐	☐
I am male and between the ages of 50 and 70	☐	☐
Are you a smoker	☐	☐
Do you suffer from chest or heart disease, diabetes or arthritis	☐	☐
My name is	----------	
My date of birth is	----------	
My telephone number is	----------	

THANK YOU FOR YOUR HELP

Professor Ian Matthews

INFORMATION SHEET

A Research Study of the Levels of Exposure to Air Pollution from Motor Vehicles

We invite you to take part in a research study which is investigating the links between air pollution caused by motor vehicles and health. Before you decide we would like to explain why the research is being done and what it will involve. Please take time to read the following information carefully and ask us if you would like more information.

There is growing evidence to suggest that very small and invisible particles from motor vehicle exhausts may cause minor but long term inflammation of the lung. In turn this may, over a period of years, lead to breathing problems and possibly heart symptoms.

The purpose of this research is to investigate whether the levels of certain pollutants from vehicle exhausts in their blood, urine, and hair are different in healthy people living in different areas of the city.

We would like healthy men between the ages of 50 and 70 who do not smoke, to take part in this study. We are writing to households close to roads and households distant from roads and aim to recruit a total of one hundred and fifty men.

If you decide to take part then a researcher from the University of Wales College of Medicine will answer any questions which you may have and you will be asked to sign a consent form and you will be given a copy of this to keep. If you decide to take part you are still free to withdraw at any time and without giving a reason.

If you do take part this will involve:

- answering a short questionnaire
- donating a venous blood sample on two occasions which are six months apart
- donating a urine sample on two occasions which are six months apart
- donating a few fibres of head hair on two occasions which are six months apart

We will arrange for a clinician to take the blood sample in the University Hospital of Wales, Heath Park, at a date and time convenient to you and reimburse you for your travel expenses. Any information which you provide is kept strictly confidential.

This research is needed to decide if the current legal standard for air quality is adequate to protect health and the results of the research may show that air pollution should be reduced below current levels.

The research is organised by the Housing and Neighbourhood and Health (HANAH) research team at the University of Wales College of Medicine. HANAH is funded by the Medical Research Council, the National Asthma Campaign and the Welsh Office of Research and Development. We intend to publish the result of this study in approximately eighteen months time in a medical research journal and at that time we will also inform all participants of the results. If you would like any further information then please telephone Professor Ian Matthews on 029 20 742324.

September 2002

APPENDIX 2

A)Previous day's activities (in the past 24hrs):

1. Details of your whereabouts.

_____

_____

_____

2. Have you been travelling in motor vehicles, if so how long?

_____

_____

3. Have you been exposed to other peoples' tobacco smoke, if so how long?

_____

_____

B) Travel history:

1. Have you been away from your residence overnight in the past month? If so when was it and for how long?

_____

_____

_____

C) About your house:

1. How many sheltered sides does the house have?

_____

2. How many windows are there in the house?

_____

3. How many of these windows are regularly opened during the day?

_____

4. How many of these windows are double-glazed?

_____

5. How many external doors are there in the house?

_____

APPENDIX 3

CONSENT FORM

A Research Study of the Levels of Exposure to Air Pollution from Motor Vehicles

Participant identification number of this research project.....

I confirm that I have read and understood the information sheet dated September 2002 for the above study and have had the opportunity to ask questions.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.

I agree to take part in the above study.

Name **Date:.....**

Signature.....

Researcher **Date:.....**

Signature.....

APPENDIX 4

Site name	Cardiff Briardene
Site type	Roadside
Note	Located adjacent to the heavily trafficked North Road with a daily traffic flow of 49,000

Site name	Cwmbran
Site type	Urban background
Note	Based in playing fields adjacent to school buildings which is an urban / semi-rural environment

Site name	Port Talbot
Site type	Urban background
Note	Located within the grounds of a small hospital 75m from the M4 motorway and 700m from a large steelworks

Site name	Swansea
Site type	Urban centre
Note	Located in a pedestrian area 30-40m from a busy dual carriageway

(Source: www.welshairquality.co.uk)

APPENDIX 5

«Title» «FirstName» «LastName»
«JobTitle»
«Company»
«Address1»
«Address2»
«Address3»
«City»
«PostalCode»

Dear «Title» «LastName»

Re: Research study into the effects of episodes of high ambient air pollution upon the quality of life of susceptible patients.

We have a number of research programmes underway in the department funded by the MRC which are investigating various aspects of the health effects of ambient air pollution.

There is good epidemiological evidence that when ambient air pollution increases markedly in a short time period the incidence of hospital admissions and mortality increases in the sub-population with underlying respiratory disease. We wish to investigate how large an effect such pollution peaks have upon the quality of life of patients. We are, therefore, seeking to recruit individuals into a research study to investigate this. I have discussed the research with Professor Dennis Shale (UWCM) and I write to seek your co-operation.

I attach, for your information, the application which we have submitted for ethical approval and which describes the methodology to be used. We first request that clinic attendees read an information sheet describing what the study involves (i.e. completion of quality of life/symptoms questionnaires). Then if they think that they may wish to participate we ask them to supply contact details on a card which they leave in the clinic for subsequent collection by our researcher. Further contact with the patient and obtaining of informed consent etc. is all undertaken by the research group and clinic staff will have no demand placed upon them.

Please would you inform me if you are prepared for patients to be recruited from your clinic. If so, one of our researchers would arrange a visit to speak to your clinic manager and leave the information sheets and contact cards.

I will of course be happy to answer any queries you may have.

Yours sincerely

Professor Ian Matthews

Enc.

APPENDIX 6

Dear Sir or Madam,

A research study of the effects of air pollution on heart, asthma, and other lung symptoms

We are carrying out a study of the effects of air pollution on heart, asthma, and other lung symptoms. We are looking to recruit people who would be willing to complete a short questionnaire about their symptoms on six separate occasions throughout the year.

An information sheet giving full details of the study is attached with the letter.

Please complete the purple card with this letter and leave it at the clinic to let us know whether or not you are willing to take part in this study. If you think that you may be willing to take part a researcher will contact you in the future on the phone number you provide to answer any questions you may have.

Thank you very much.

Ian Matthews

Professor Ian Matthews

July 03, V1.01

INFORMATION SHEET

A RESEARCH STUDY OF THE EFFECTS OF AIR POLLUTION ON HEART, ASTHMA, AND OTHER LUNG SYMPTOMS

Who are we?
We are a group of scientists based at the University of Wales College of Medicine in Cardiff and we carry out research into how the environment affects our health.

Why are we studying air pollution and heart and lung symptoms?
Many studies carried out in Europe and the USA have shown that when background levels of air pollution increase there is an increase in admissions to hospital for people with heart and breathing problems. It is also likely that symptoms may be worse at these times for people who are not admitted to the hospital.

We wish to find out if heart and lung symptoms are worse when air pollution is high.

Why are we studying air pollution and asthma symptoms?
The UK Government's Committee on the Medical Effects of Air Pollutants (COMEAP) have reviewed the scientific research evidence concerning the effects upon asthmatics at a rise in environmental air pollution. COMEAP concludes that there is a relationship between increased air pollution and symptoms of asthma.

How will we carry out the study?
We will find out the levels of air pollution everyday in the next 12 months. We will also need help of individuals with heart or lung symptom, who live in South Wales.

How can you help?
We would like you to complete a short questionnaire (it takes about fifteen minutes) about your symptoms. We will send the questionnaire to you in the post four times in the next 12 months and it will ask you about your symptoms at that time.

What about privacy and confidentiality?
Your privacy and confidentiality will be respected at all times. Your questionnaires will be identified by a number and your personal details will not be disclosed. Your questionnaire responses will be held securely and confidentially at the Department of Epidemiology, Statistics, and Public Health in full compliance with the Data Protection Act.

What happens next?
Please fill out the green card and leave it with the clinic clerk/receptionist. If you have indicated a possible willingness to take part in this research then a researcher will contact you in the future on the phone number you provide to answer any questions you may have.

Further information
If you would like any further information please contact *Christopher Au-Yeung* on 02920-743637 or 07787-545414.

July 03, V1.01

Reply Card

Please read the letter and the information sheet provided before filling in the form.

I am interested in knowing more about the study.

Yes* ☐ **No** ☐

*If you have answered yes please also fill in the following:

Print name: Mr/Ms/Mrs/Others

_____

Date of birth: _____

Phone number (Including area code):

_____

Consultant's name: _____

APPENDIX 7

CONSENT FORM

A RESEARCH STUDY OF THE EFFECTS OF AIR POLLUTION ON HEART, ASTHMA, AND OTHER LUNG SYMPTOMS

Participant identification number of this research project.....

I confirm that I have read and understood the information sheet dated July 2003 for the above study and have had the opportunity to ask questions.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.

I agree to take part in the above study.

Name **Date:.....**

Signature.....

Researcher **Date:.....**

Signature.....

APPENDIX 8.1

Asthma Symptoms Questionnaire

Department of Epidemiology, Statistics and Public Health
University of Wales College of Medicine
Heath Park
CF14 4XN

July 2003 (V1.01)

Asthma

Asthma Symptoms Questionnaire

We are interested in the symptoms you have experienced in the week following the date mentioned in the enclosed letter. We refer to this in the questionnaire as the "week of interest". This questionnaire is designed to help us learn much more about how your asthma is troubling you and how it affects your life.

Please complete all questions by circling the number that best describes how you have been during the week of interest as a result of your asthma, like this:

EXAMPLE:

How limited have you been over the week of interest in these activities as a result of your asthma?

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
1. Strenuous activities (such as hurrying, exercising etc)	1	2	(3)	4	5	6	7

The numbers inside the boxes are just to make it easier to type in the information when all the booklets have been collected, they have no special meaning.

Asthma

Before you begin...

Please print name: _____

1. Over the week of interest, have you had a respiratory infection that affected your chest?

☐ 1 Yes

☐ 2 No

2. Over the week of interest, did you stay overnight somewhere further than 10miles from your home for more than 3 days?

☐ 1 Yes

☐ 2 No

If you have answered "Yes" for any of the questions above please DO NOT continue to complete the questionnaire and return it to us using the prepaid envelope provided.

If you have answered "No" for both questions above then please proceed to the next page and fill in the questionnaire accordingly.

Asthma

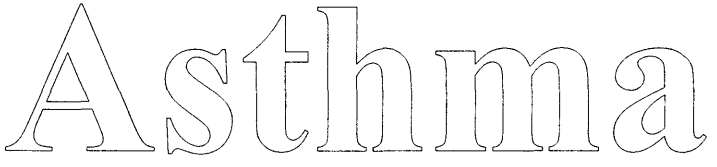
Section 1: Your symptoms

How limited have you been over the week of interest in these activities as a result of your asthma?

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
1. Strenuous activities (such as hurrying, exercising etc)	1	2	3	4	5	6	7
2. Moderate activities (such as walking, housework, gardening, shopping, climbing stairs, bathing and dressing)	1	2	3	4	5	6	7
3. Social activities (such as talking, playing with pets/children, visiting friends/relatives)	1	2	3	4	5	6	7

In general, how much of the time over the week of interest did you:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
4. Feel short of breath as a result of your asthma?	1	2	3	4	5	6	7
5. Feel **VERY** short of breath as a result of your asthma?	1	2	3	4	5	6	7



	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
6. Experience asthma symptoms as a result of being exposed to cigarette smoke?	1	2	3	4	5	6	7
7. Experience a wheeze in your chest?	1	2	3	4	5	6	7
8. Feel frustrated as a result of your asthma?	1	2	3	4	5	6	7
9. Experience a feeling of chest heaviness?	1	2	3	4	5	6	7
10. Need to use medication for your asthma?	1	2	3	4	5	6	7
11. Feel the need to clear your throat?	1	2	3	4	5	6	7
12. Experience asthma symptoms as a result of being exposed to dust?	1	2	3	4	5	6	7
13. Experience difficulty breathing out as a result of your asthma?	1	2	3	4	5	6	7

Asthma

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
14. Wake up in the morning with asthma symptoms?	1	2	3	4	5	6	7
15. Experience asthma symptoms as a result of the weather or air pollution outside?	1	2	3	4	5	6	7
16. Avoid or limit going outside because of the weather or air pollution?	1	2	3	4	5	6	7
17. Experience asthma symptoms as a result of being exposed to strong smells or perfume?	1	2	3	4	5	6	7
18. Did you get interfered with getting a good night's sleep by your asthma?	1	2	3	4	5	6	7

Asthma

How limited have you been over the week of interest:

	Most Activities Not Done		Several Activities Not Done		Very Few Activities Not Done		No Activity Limitation
19. Think of all the overall range of activities that you would have liked to have done over the week of interest. How much has your range of activities been limited by your asthma?	1	2	3	4	5	6	7

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at All Limited
20. Overall, among all the activities that you have done over the week of interest, how limited have you been by your asthma?	1	2	3	4	5	6	7

In general, how much discomfort or distress have you felt over the week of interest:

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
21. As a result of chest tightness?	1	2	3	4	5	6	7
22. As a result of coughing?	1	2	3	4	5	6	7

Over the week of interest how many times did you:

	Everyday	3 or more times, but not everyday	1-2 times	Never over the week
23. Use inhalers to help breathing?	1	2	3	4

Asthma

In general, how much of the time over the week of interest did you:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
24. Feel concerned about having asthma?	1	2	3	4	5	6	7
25. Feel bothered by heavy breathing?	1	2	3	4	5	6	7

Asthma

That's it! Thank you.

Would you please check that you have answered all the questions.

We would be most grateful if you could return the questionnaire to us at your earliest convenience.

Please remember to use the self-addressed prepaid envelope when returning your questionnaire.

If you have any questions about the study or need any help, please ring:
Christopher Au-Yeung on ☎02920 743637 or 07787 545414.

Or write to:

Christopher Au-Yeung
Department of Epidemiology, Statistics & Public Health
University of Wales College of Medicine
Heath Park
Cardiff
CF14 4XN

Or email to:

AU-YEUNGHC@CF.AC.UK

Asthma

APPENDIX 8.2

Cardiac Symptoms Questionnaire

Department of Epidemiology, Statistics and Public Health
University of Wales College of Medicine
Heath Park
CF14 4XN

July 2003 (V1.01)

Cardiac Symptoms Questionnaire

We are interested in the symptoms you have experienced in the week following the date mentioned in the enclosed letter. We refer to this in the questionnaire as the "week of interest". This questionnaire is designed to help us learn much more about how your heart symptoms are troubling you and how they affect your life.

Please complete all the questions by putting a tick in the box next to the answer that best describes how you have been doing over the week of interest as a result of your heart symptoms, like this:

EXAMPLE:

1. How limited have you been over the week of interest when doing strenuous activities (such as hurrying, exercising etc) as a result of your heart symptoms?

- ☐ 1 Totally limited
- ☐ 2 Extremely limited
- ☑ 3 Very limited
- ☐ 4 Moderate limitation
- ☐ 5 Some limitation
- ☐ 6 Not at all limited

The numbers next to the boxes are just to make it easier to type in the information when all the booklets have been collected, they have no special meaning.

Cardiac

Before you begin...

Please print name: _____

1. Over the week of interest, have you had a bug (an infection) that affected your chest?

☐ 1 Yes

☐ 2 No

2. Over the week of interest, did you stay overnight somewhere further than 10miles from your home for more than 3 days?

☐ 1 Yes

☐ 2 No

If you have answered "Yes" for any of the questions above please DO NOT continue to complete the questionnaire and return it to us using the prepaid envelope provided.

If you have answered "No" for both questions above then please proceed to the next page and fill in the questionnaire accordingly.

1. How limited have you been over the week of interest when doing strenuous activities (such as hurrying, exercising etc) as a result of your heart symptoms?

- ☐ 1 Totally limited
- ☐ 2 Extremely limited
- ☐ 3 Very limited
- ☐ 4 Moderate limitation
- ☐ 5 Some limitation
- ☐ 6 Not at all limited

2. How limited have you been over the week of interest when doing Moderate activities (such as walking, housework, gardening, shopping, climbing stairs, bathing, dressing) as a result of your heart symptoms?

- ☐ 1 Totally limited
- ☐ 2 Extremely limited
- ☐ 3 Very limited
- ☐ 4 Moderate limitation
- ☐ 5 Some limitation
- ☐ 6 Not at all limited

3. Over the week of interest, on average, how many times have you had chest pain, chest tightness, angina, or shortness of breath?

I had chest pain, chest tightness, angina, or shortness of breath...

- ☐ 1 All of the time
- ☐ 2 Several times per day
- ☐ 3 At least once a day
- ☐ 4 3 or more times over the week
- ☐ 5 1-2 times over the week
- ☐ 6 Never over the week

Cardiac

4. Over the week of interest, on average, how many times has chest pain, chest tightness, angina, or shortness of breath limited your ability to do what you want?

- ☐ 1 Everyday
- ☐ 2 3 or more times, but not everyday
- ☐ 3 1-2 times
- ☐ 4 Never over the week

5. Over the week of interest, how often did you have chest pain, chest tightness, angina, or shortness of breath when doing your most strenuous level of activity?

I have had chest pain, chest tightness, angina, or shortness of breath...

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

6. Over the week of interest, how much has your chest pain, chest tightness, angina, or shortness of breath limited your enjoyment of life?

- ☐ 1 It has limited my enjoyment of life extremely
- ☐ 2 It has limited my enjoyment of life quite a bit
- ☐ 3 It has limited my enjoyment of life moderately
- ☐ 4 It has limited my enjoyment of life slightly
- ☐ 5 It has not limited my enjoyment of life at all

Cardiac

7. Over the week of interest, on average, how many times have you had to take nitros (nitroglycerin tablets) for your chest pain, chest tightness, or angina?

- ☐ 1 4 or more times per day
- ☐ 2 1-3 times per day
- ☐ 3 3 or more times over the week, but not everyday
- ☐ 4 1-2 times over the week
- ☐ 5 None over the week
- ☐ 6 I am not prescribed nitros

8. Over the week of interest, how many times have you been forced to sleep sitting up in a chair or with pillows to prop you up because of shortness of breath?

- ☐ 1 Every night
- ☐ 2 3 or more times, but not everyday
- ☐ 3 1-2 times
- ☐ 4 Never over the week

9. Over the week of interest, how many times did you have swelling in your feet, ankles or legs when you woke up in the morning?

- ☐ 1 Every morning
- ☐ 2 3 or more times, but not everyday
- ☐ 3 1-2 times
- ☐ 4 Never over the week

10. Over the week of interest, how much has swelling in your feet, ankles or legs bothered you?

It has been...

- ☐ 1 Extremely bothersome
- ☐ 2 Quite a bit bothersome
- ☐ 3 Moderately bothersome
- ☐ 4 Slightly bothersome
- ☐ 5 Not bothersome at all
- ☐ 6 I've had no swelling

Cardiac

11. Over the week of interest, how often have you been bothered by aching or tired legs?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

12. Over the week of interest, how often have you felt dizzy or light-headed?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

13. Over the week of interest, on average, how many times has fatigue limited your ability to do what you want?

- ☐ 1 All of the time
- ☐ 2 Several times per day
- ☐ 3 At least once a day
- ☐ 4 3 or more times, but not everyday
- ☐ 5 1-2 times
- ☐ 6 Never over the week

Cardiac

14. Over the week of interest, how much has fatigue bothered you?

- ☐ 1 Extremely bothersome
- ☐ 2 Quite a bit bothersome
- ☐ 3 Moderately bothersome
- ☐ 4 Slightly bothersome
- ☐ 5 Not bothersome at all
- ☐ 6 I've had no fatigue

15. Over the week of interest, in general, how much of the time have you felt frustrated or impatient as a result of your heart symptoms?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

16. Over the week of interest, in general, did you feel discouraged or down in the dumps because of your heart symptoms?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

17. Over the week of interest, how often have you felt excluded from doing things with other people because of your heart symptoms?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

That's it! Thank you.

Would you please check that you have answered all the questions.

We would be most grateful if you could return the questionnaire to us at your earliest convenience.

Please remember to use the self-addressed prepaid envelope when returning your questionnaire.

If you have any questions about the study or need any help, please ring: Christopher Au-Yeung on ☎02920 743637 or 07787 545414.

Or write to:

Christopher Au-Yeung
Department of Epidemiology, Statistics & Public Health
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Cardiff
CF14 4XN

Or email to:

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Cardiac

APPENDIX 8.3

Respiratory Symptoms Questionnaire

Department of Epidemiology, Statistics and Public Health
University of Wales College of Medicine
Heath Park
CF14 4XN

July 2003 (V1.01)

Respiratory Symptoms Questionnaire

We are interested in the symptoms you have experienced in the week following the date mentioned in the enclosed letter. We refer to this in the questionnaire as the "week of interest". This questionnaire is designed to help us learn much more about how your breathing is troubling you and how it affects your life.

Please complete all the questions by putting a tick in the box next to the answer that best describes how you have been doing over the week of interest as a result of your chest, like this:

EXAMPLE:

1. Over the week of interest, I have coughed...

- ☐ 1 Everyday
- ☐ 2 3 or more days but not everyday
- ☑ 3 1-2 days
- ☐ 4 Only with chest infections
- ☐ 5 Not at all

The numbers next to the boxes are just to make it easier to type in the information when all the booklets have been collected, they have no special meaning.

Respiratory

Before you begin...

Please print name: _____

1. Over the week of interest, have you had a respiratory infection that affected your chest?

☐ 1 Yes

☐ 2 No

2. Over the week of interest, did you stay overnight somewhere further than 10miles from your home for more than 3 days?

☐ 1 Yes

☐ 2 No

If you have answered "Yes" for any of the questions above please DO NOT continue to complete the questionnaire and return it to us using the prepaid envelope provided.

If you have answered "No" for both questions above then please proceed to the next page and fill in the questionnaire accordingly.

Respiratory

1. Over the week of interest, I have coughed...

- ☐ 1 Everyday
- ☐ 2 3 or more days but not everyday
- ☐ 3 1-2 days
- ☐ 4 Only with chest infections
- ☐ 5 Not at all

2. Over the week of interest, I have brought up phlegm (sputum)...

- ☐ 1 Everyday
- ☐ 2 3 or more days but not everyday
- ☐ 3 1-2 days
- ☐ 4 Only with chest infections
- ☐ 5 Not at all

3. Over the week of interest, I have had attacks of wheezing...

- ☐ 1 Everyday
- ☐ 2 3 or more days but not everyday
- ☐ 3 1-2 days
- ☐ 4 Only with chest infections
- ☐ 5 Not at all

4. Over the week of interest, how many severe or very unpleasant attacks of chest trouble have you had?

- ☐ 1 More than 3 attacks
- ☐ 2 3 attacks
- ☐ 3 2 attacks
- ☐ 4 1 attack
- ☐ 5 No attacks

Respiratory

5. Over the week of interest, how many severe or very unpleasant wheezing attacks have you had?

- ☐ 1 More than 3 attacks
- ☐ 2 3 attacks
- ☐ 3 2 attacks
- ☐ 4 1 attack
- ☐ 5 No wheezing

6. Over the week of interest, how long did the worst attack of chest trouble last?

- ☐ 1 3 or more days
- ☐ 2 1-2 days
- ☐ 3 Less than a day
- ☐ 4 I've had no severe attacks

7. Over the week of interest, how many good days (with little chest trouble) have you had?

- ☐ 1 Less than a day
- ☐ 2 1-2 days
- ☐ 3 3 or more days but not everyday
- ☐ 4 Everyday

8. How limited have you been over the week of interest when doing strenuous activities (such as hurrying, exercising etc) as a result of your chest?

- ☐ 1 Totally limited
- ☐ 2 Extremely limited
- ☐ 3 Very limited
- ☐ 4 Moderate limitation
- ☐ 5 Some limitation
- ☐ 6 Not at all limited

9. How limited have you been over the week of interest when doing moderate activities (such as walking, housework, gardening, shopping, climbing stairs, bathing, dressing etc) as a result of your chest?

- ☐ 1 Totally limited
- ☐ 2 Extremely limited
- ☐ 3 Very limited
- ☐ 4 Moderate limitation
- ☐ 5 Some limitation
- ☐ 6 Not at all limited

10. Over the week of interest, on average, how many times have you had shortness of breath?
I had shortness of breath …

- ☐ 1 All of the time
- ☐ 2 Several times per day
- ☐ 3 At least once a day
- ☐ 4 3 or more times over the week
- ☐ 5 1-2 times over the week
- ☐ 6 Never over the week

11. Over the week of interest, on average, how many times have you had chest tightness?
I had chest tightness…

- ☐ 1 All of the time
- ☐ 2 Several times per day
- ☐ 3 At least once a day
- ☐ 4 3 or more times over the week
- ☐ 5 1-2 times over the week
- ☐ 6 Never over the week

12. Over the week of interest, on average, how many times has chest tightness or shortness of breath limited your ability to do what you want?

- ☐ 1 Everyday
- ☐ 2 3 or more times, but not everyday
- ☐ 3 1-2 times
- ☐ 4 Never over the week

13. Over the week of interest, how often did you have chest tightness or shortness of breath when doing your most strenuous level of activity?
I have had chest tightness or shortness of breath...

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

14. Over the week of interest, how much has your chest tightness or shortness of breath limited your enjoyment of life?

- ☐ 1 It has limited my enjoyment of life extremely
- ☐ 2 It has limited my enjoyment of life quite a bit
- ☐ 3 It has limited my enjoyment of life moderately
- ☐ 4 It has limited my enjoyment of life slightly
- ☐ 5 It has not limited my enjoyment of life at all

15. Over the week of interest, how many times have you been forced to sleep sitting up in a chair or with pillows to prop you up because of shortness of breath?

- ☐ 1 Every night
- ☐ 2 3 or more times, but not every night
- ☐ 3 1-2 times
- ☐ 4 Never over the week

16. Over the week of interest, how often have you felt dizzy or light-headed?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

17. Over the week of interest, on average, how many times has fatigue limited your ability to do what you want?

- ☐ 1 All of the time
- ☐ 2 Several times per day
- ☐ 3 At least once a day
- ☐ 4 3 or more times, but not everyday
- ☐ 5 1-2 times
- ☐ 6 Never over the week

18. Over the week of interest, how much has fatigue bothered you?

- ☐ 1 Extremely bothersome
- ☐ 2 Quite a bit bothersome
- ☐ 3 Moderately bothersome
- ☐ 4 Slightly bothersome
- ☐ 5 Not bothersome at all
- ☐ 6 I've had no fatigue

19. Over the week of interest, in general, how much of the time have you felt frustrated or impatient as a result of your chest?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

20. Over the week of interest, in general, did you feel discouraged or down in the dumps as a consequence of your chest?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

21. Over the week of interest, how often have you felt excluded from doing things with other people because of your chest?

- ☐ 1 All of the time
- ☐ 2 Most of the time
- ☐ 3 A good bit of the time
- ☐ 4 Some of the time
- ☐ 5 Hardly any of the time
- ☐ 6 None of the time

22. Over the week of interest, how many times did you use oxygen mask to help breathing?

☐ 1 Everyday

☐ 2 3 or more times, but not everyday

☐ 3 1-2 times

☐ 4 Never over the week

☐ 5 I do not use oxygen

That's it! Thank you.

Would you please check that you have answered all the questions.

We would be most grateful if you could return the questionnaire to us at your earliest convenience.

Please remember to use the self-addressed prepaid envelope when returning your questionnaire.

If you have any questions about the study or need any help, please ring: Christopher Au-Yeung on ☎02920 743637 or 07787 545414.

Or write to:

Christopher Au-Yeung
Department of Epidemiology, Statistics & Public Health
University of Wales College of Medicine
Heath Park
Cardiff
CF14 4XN

Or email to:

AU-YEUNGHC@CF.AC.UK

Respiratory

APPENDIX 9.1

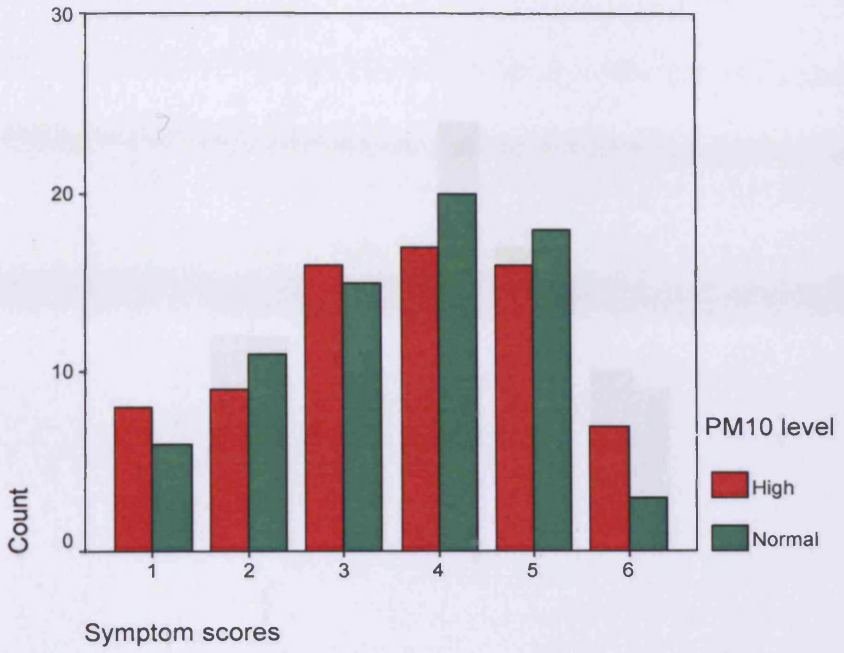

Figure 1a: Breakdown of cardiac symptoms score of question 1 and count of participant number, high v normal levels of PM_{10}.

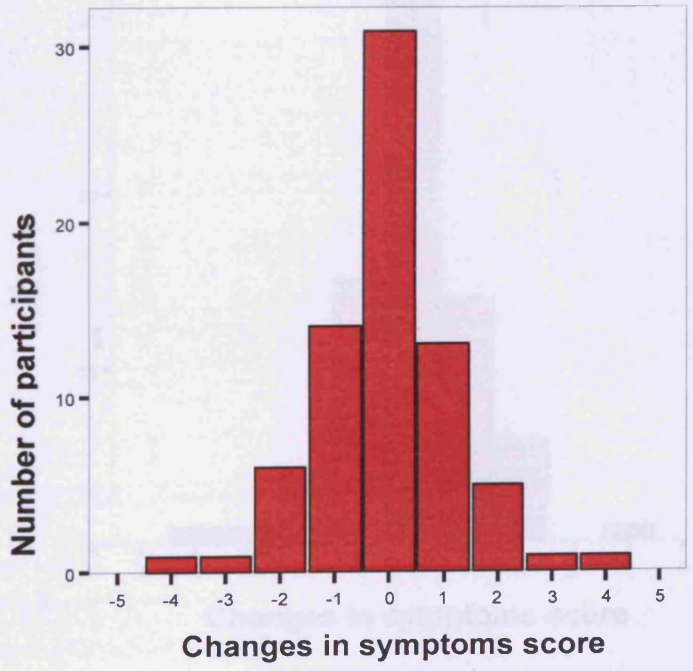

Figure 1b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 1.

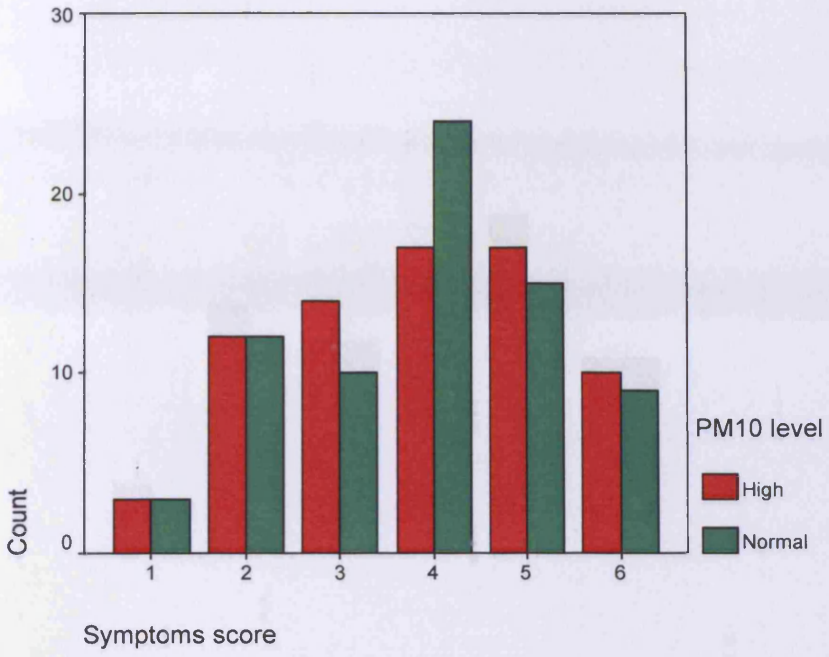

Figure 2a: Breakdown of cardiac symptoms score of question 2 and count of participant number, high v normal levels of PM_{10}.

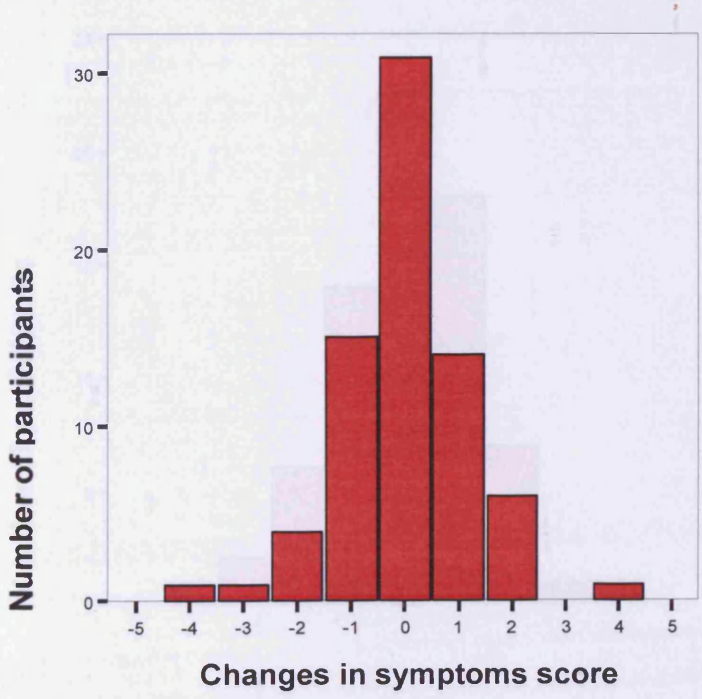

Figure 2b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 2.

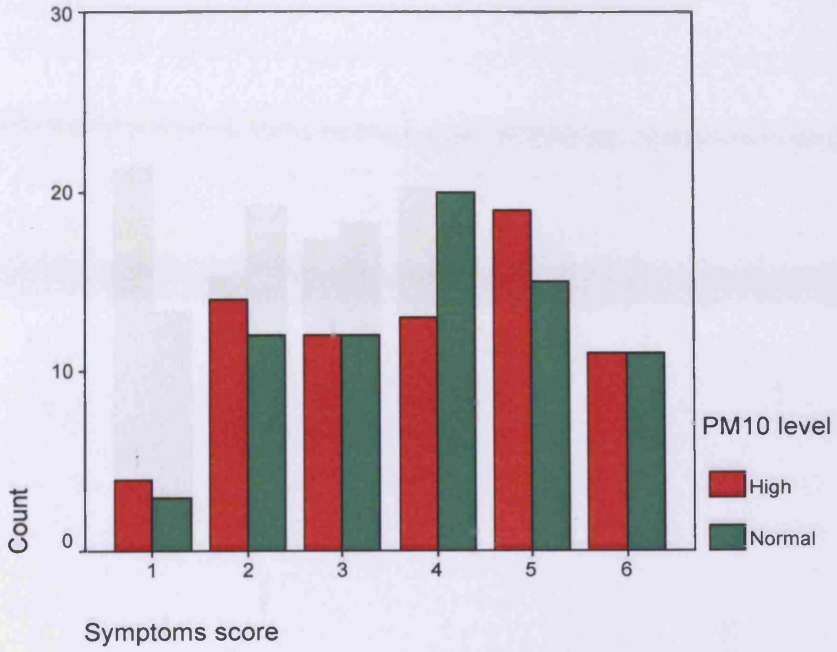

Figure 3a: Breakdown of cardiac symptoms score of question 3 and count of participant number, high v normal levels of PM_{10}.

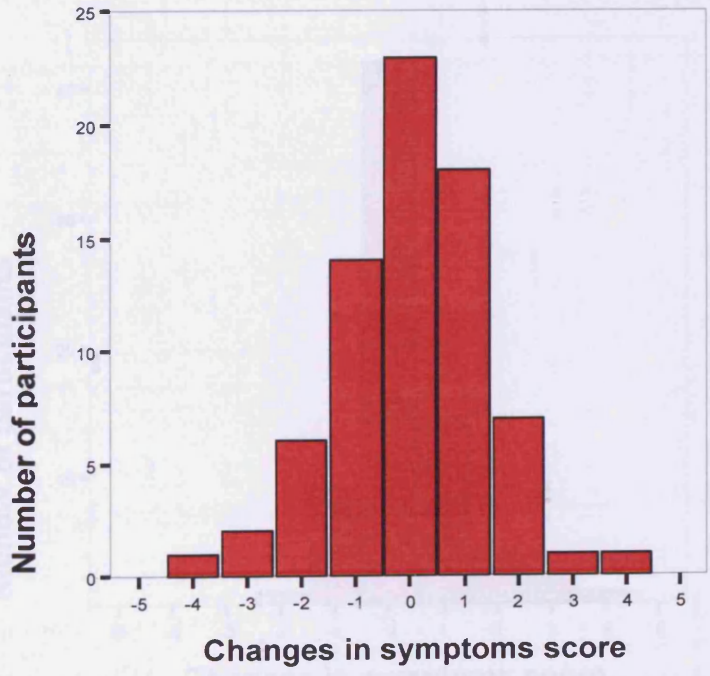

Figure 3b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 3.

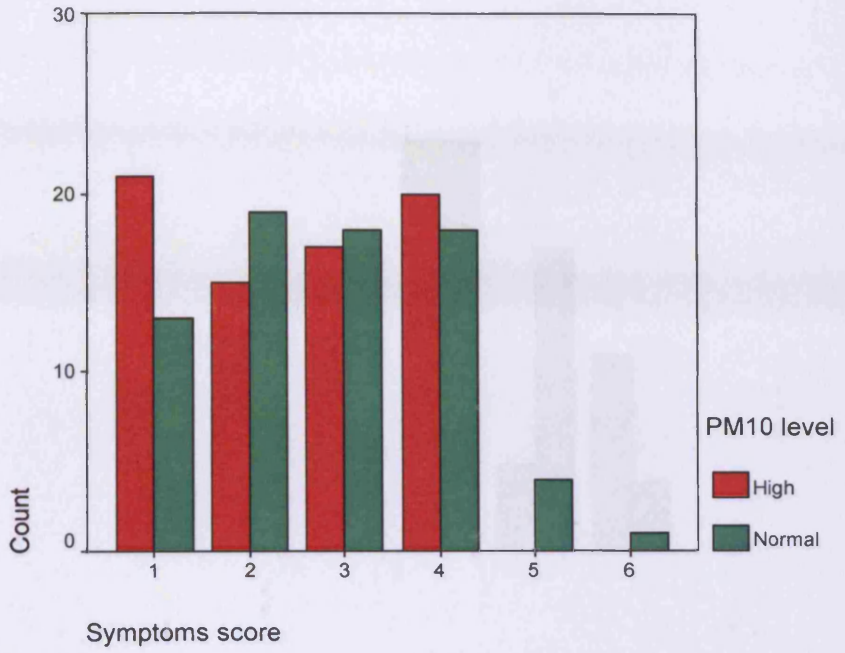

Figure 4a: Breakdown of cardiac symptoms score of question 4 and count of participant number, high v normal levels of PM_{10}.

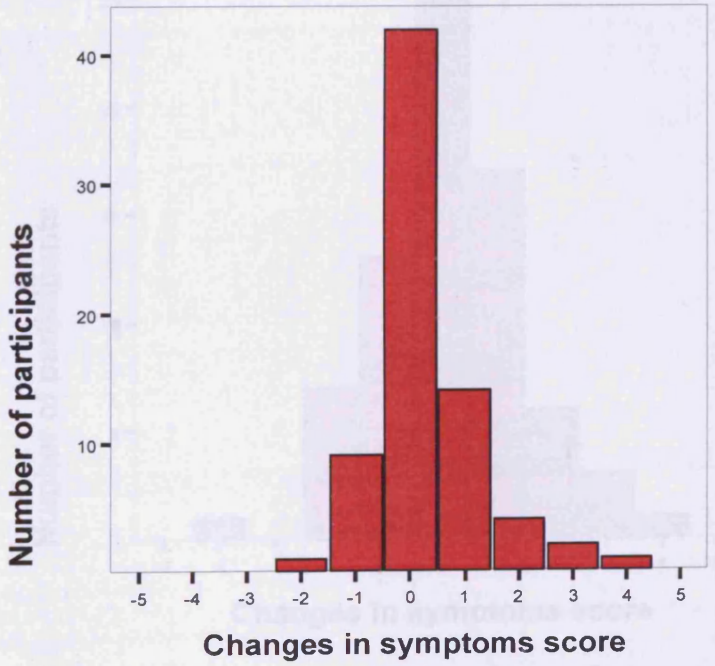

Figure 4b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 4.

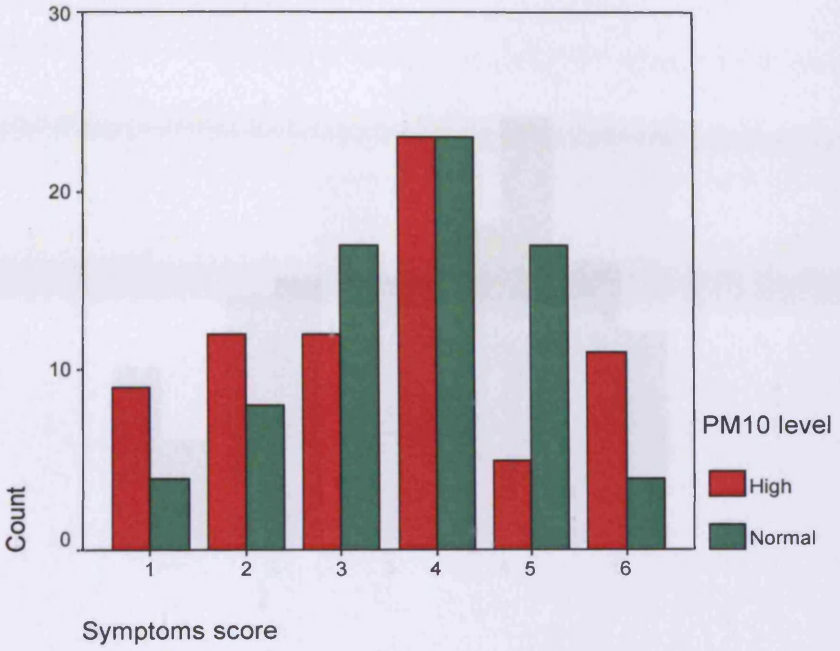

Figure 5a: Breakdown of cardiac symptoms score of question 5 and count of participant number, high v normal levels of PM_{10}.

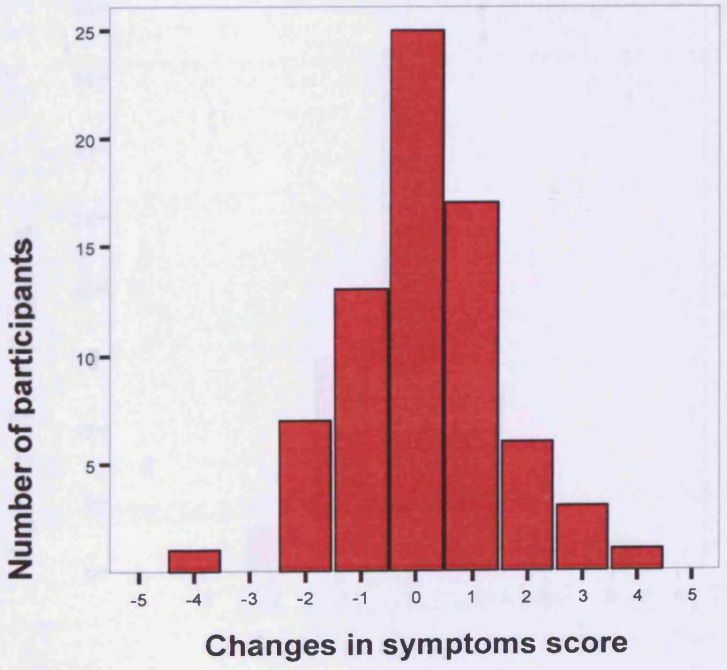

Figure 5b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 5.

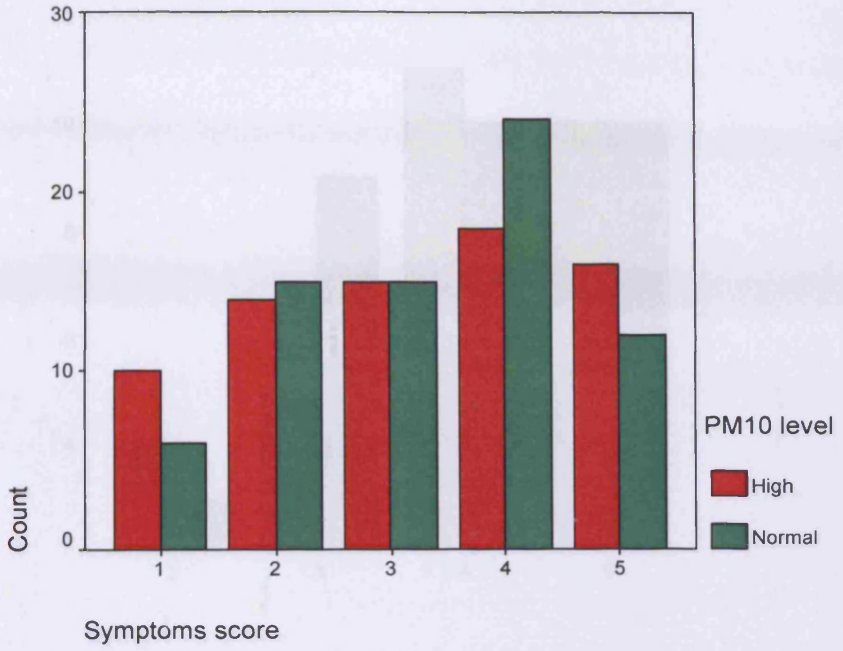

Figure 6a: Breakdown of cardiac symptoms score of question 6 and count of participant number, high v normal levels of PM_{10}.

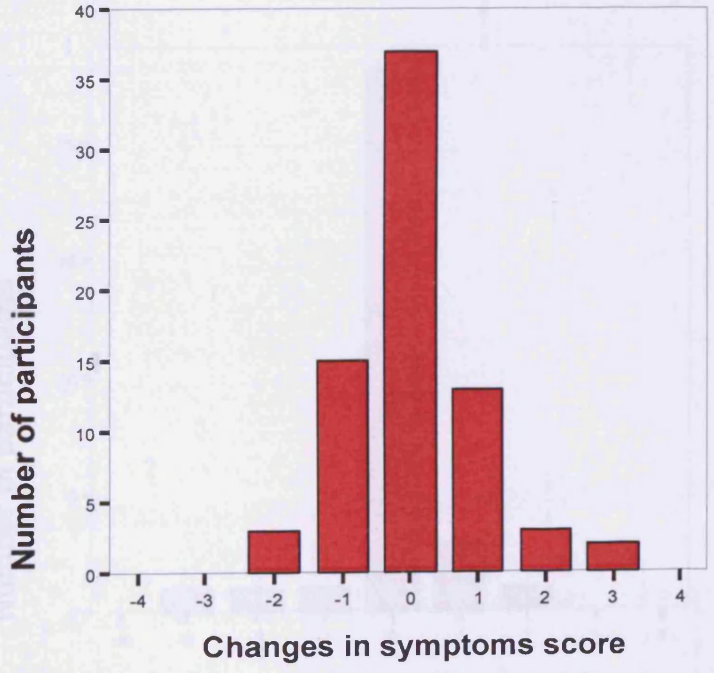

Figure 6b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 6.

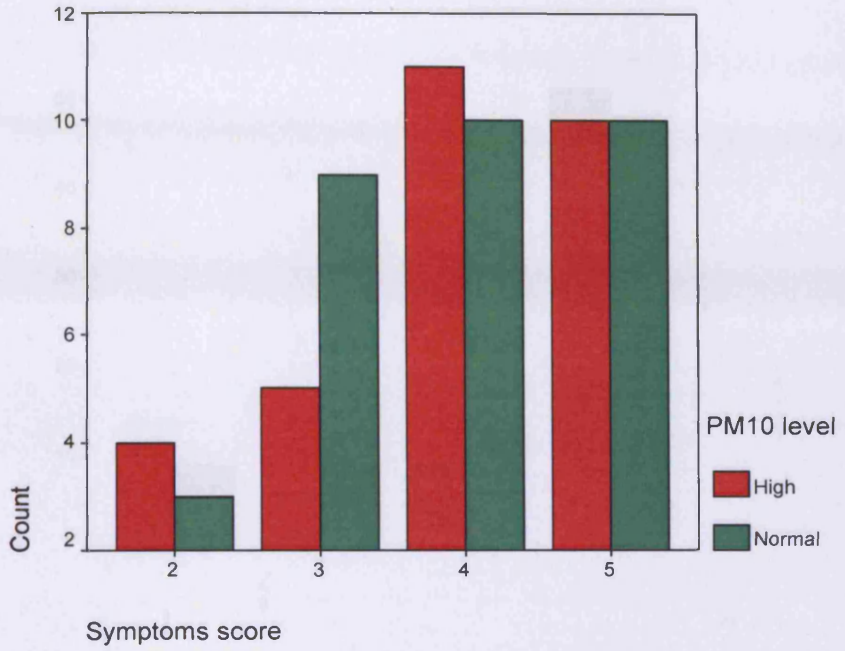

Figure 7a: Breakdown of cardiac symptoms score of question 7 and count of participant number, high v normal levels of PM_{10}.

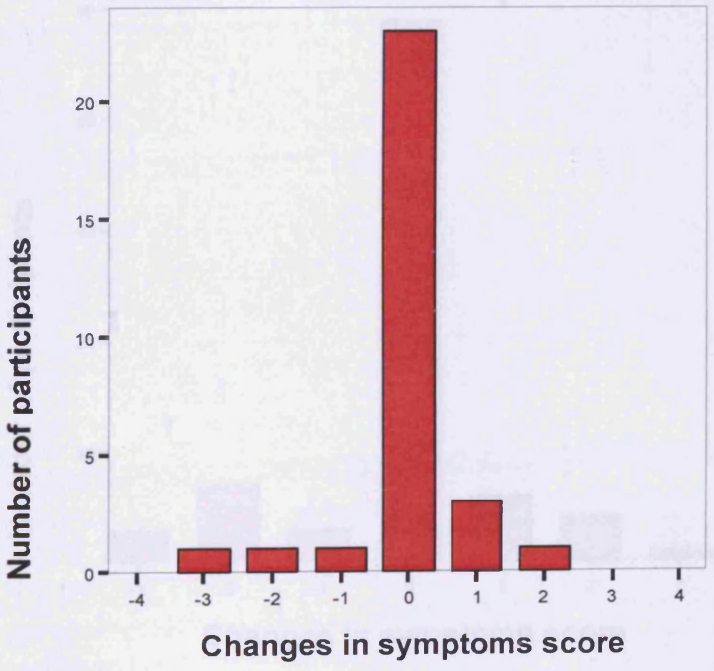

Figure 7b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 7.

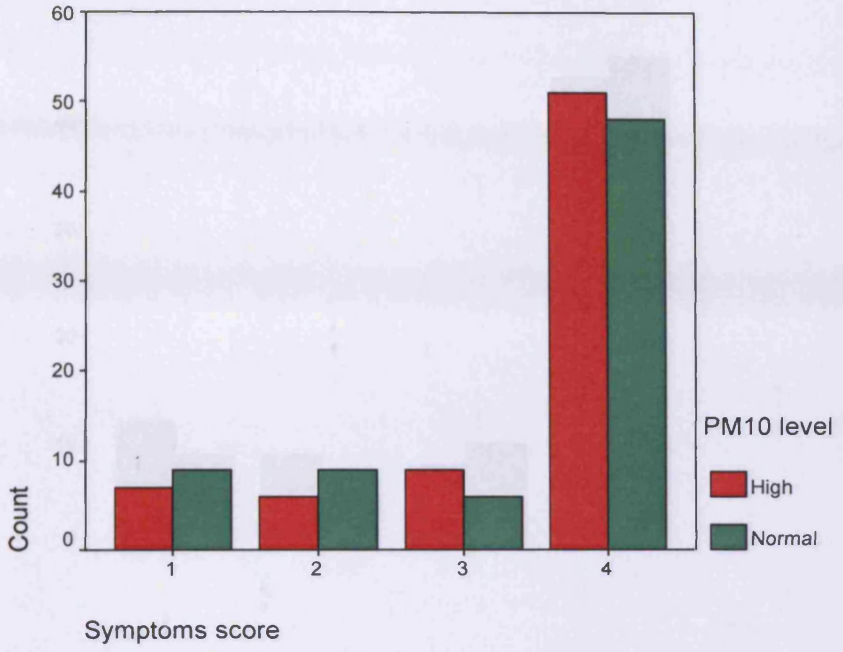

Figure 8a: Breakdown of cardiac symptoms score of question 8 and count of participant number, high v normal levels of PM_{10}.

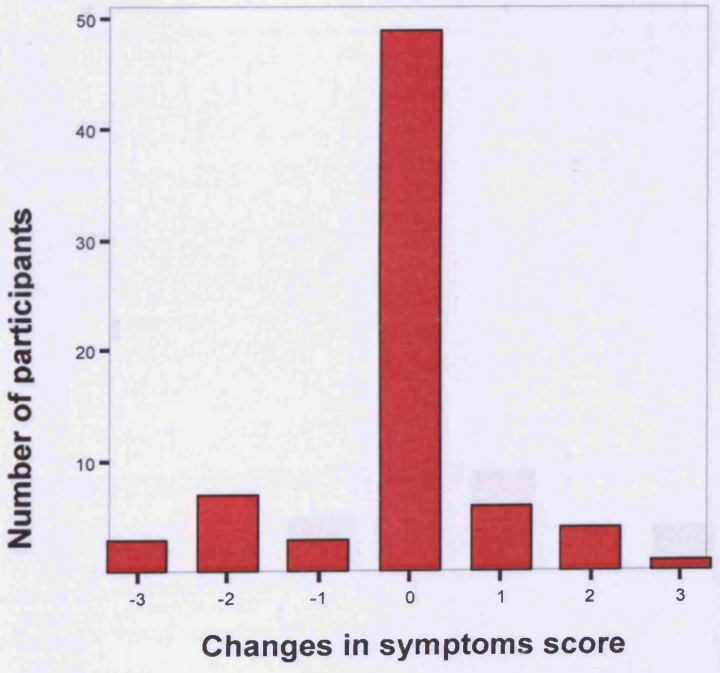

Figure 8b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 8.

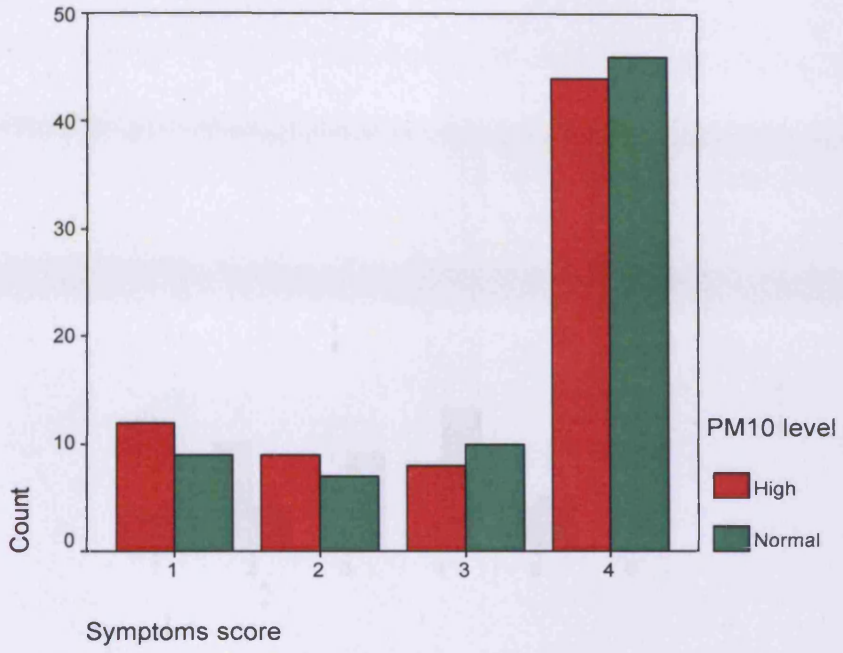

Figure 9a: Breakdown of cardiac symptoms score of question 9 and count of participant number, high v normal levels of PM_{10}.

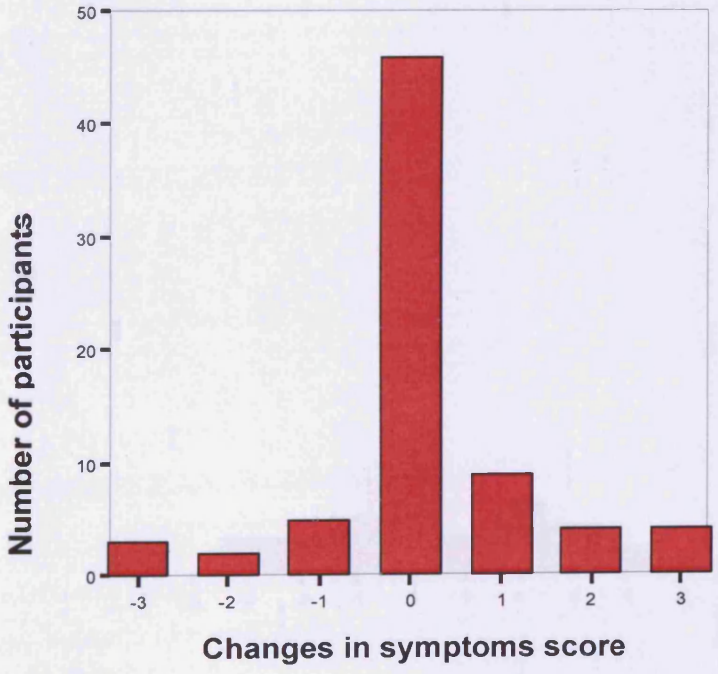

Figure 9b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 9.

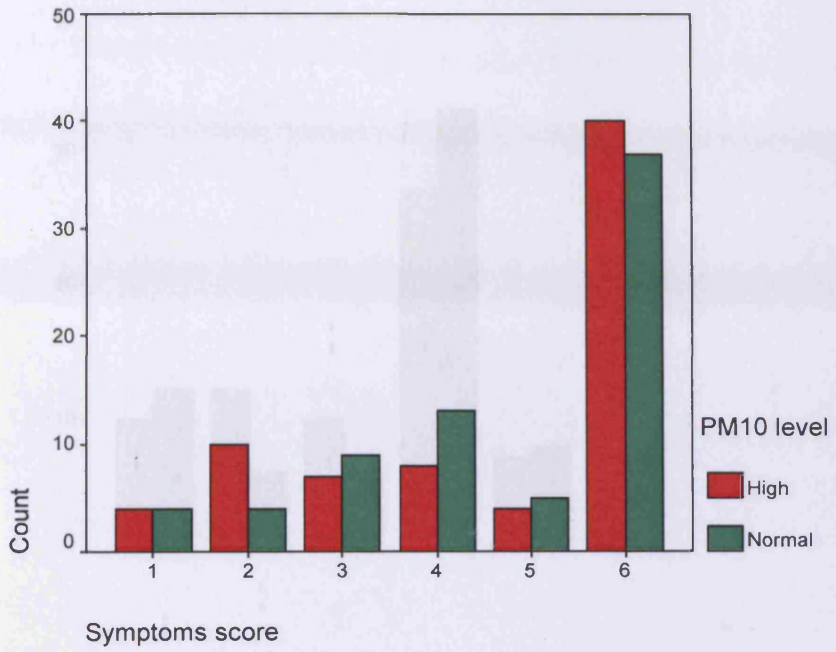

Figure 10a: Breakdown of cardiac symptoms score of question 10 and count of participant number, high v normal levels of PM_{10}.

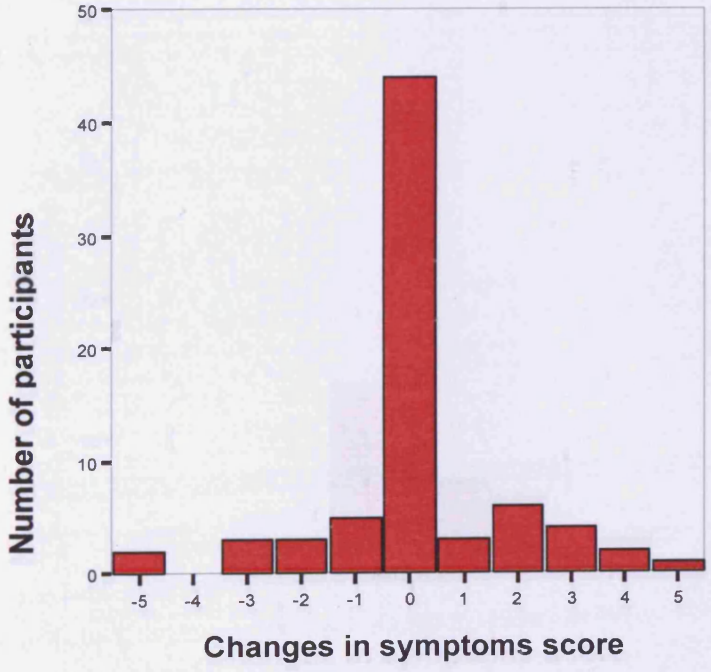

Figure 10b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 10.

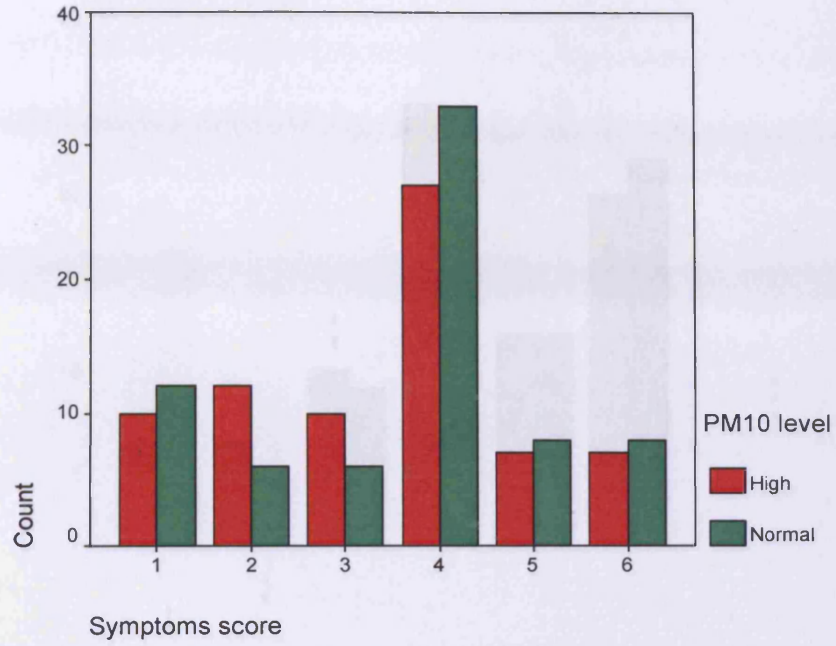

Figure 11a: Breakdown of cardiac symptoms score of question 11 and count of participant number, high v normal levels of PM_{10}.

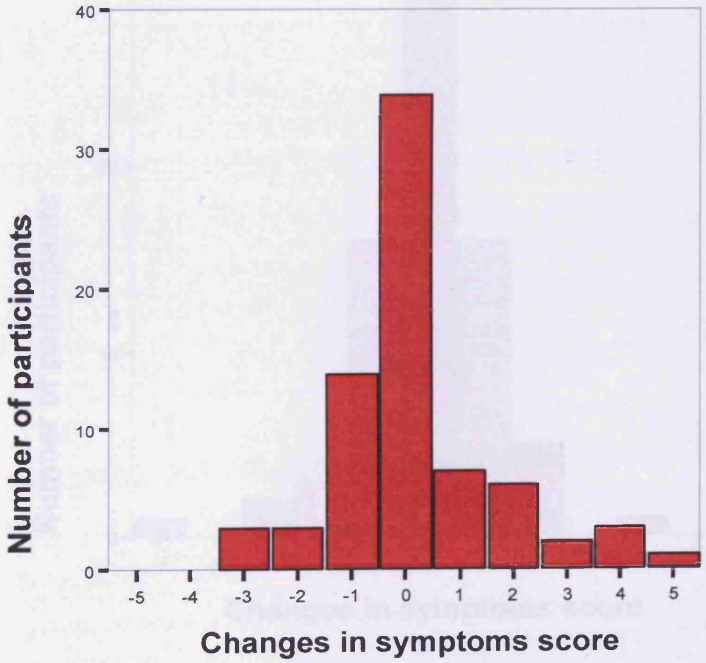

Figure 11b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 11.

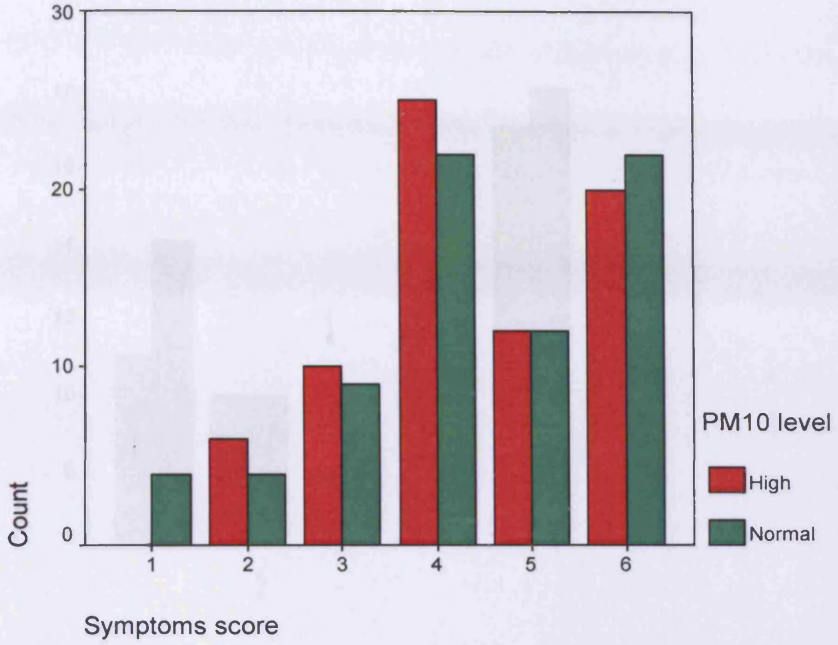

Figure 12a: Breakdown of cardiac symptoms score of question 12 and count of participant number, high v normal levels of PM_{10}.

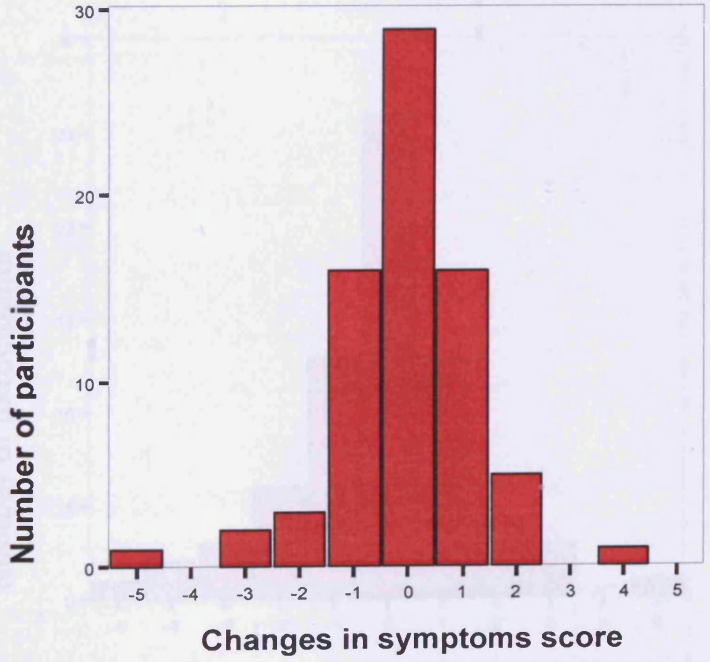

Figure 12b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 12.

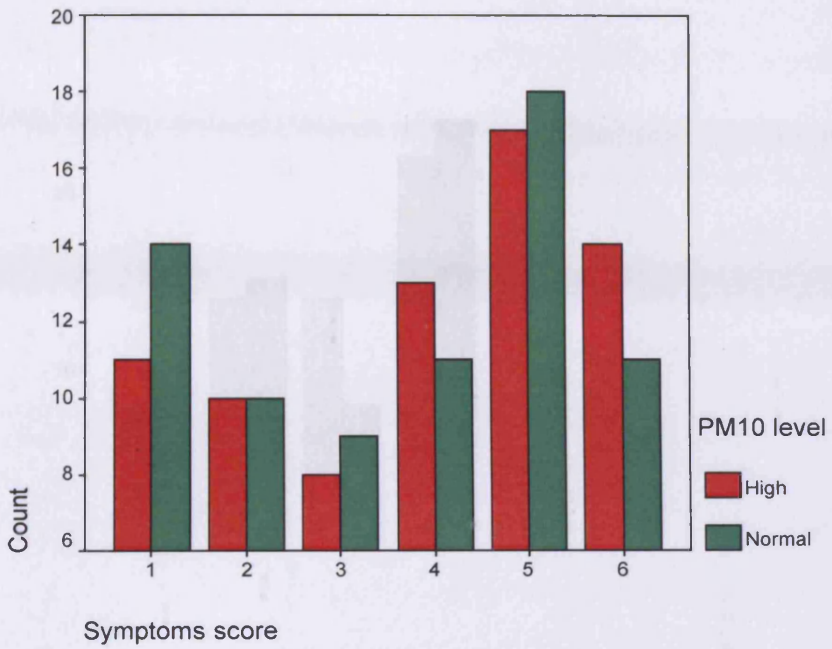

Figure 13a: Breakdown of cardiac symptoms score of question 13 and count of participant number, high v normal levels of PM_{10}.

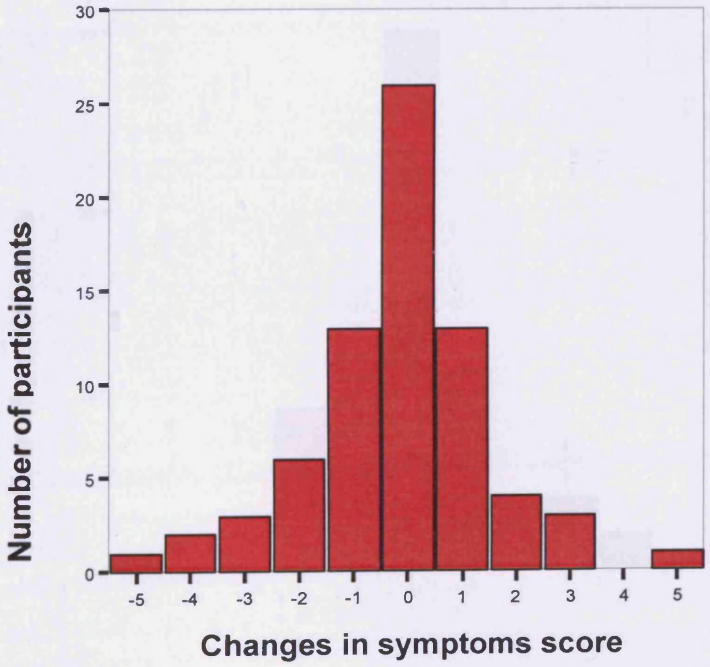

Figure 13b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 13.

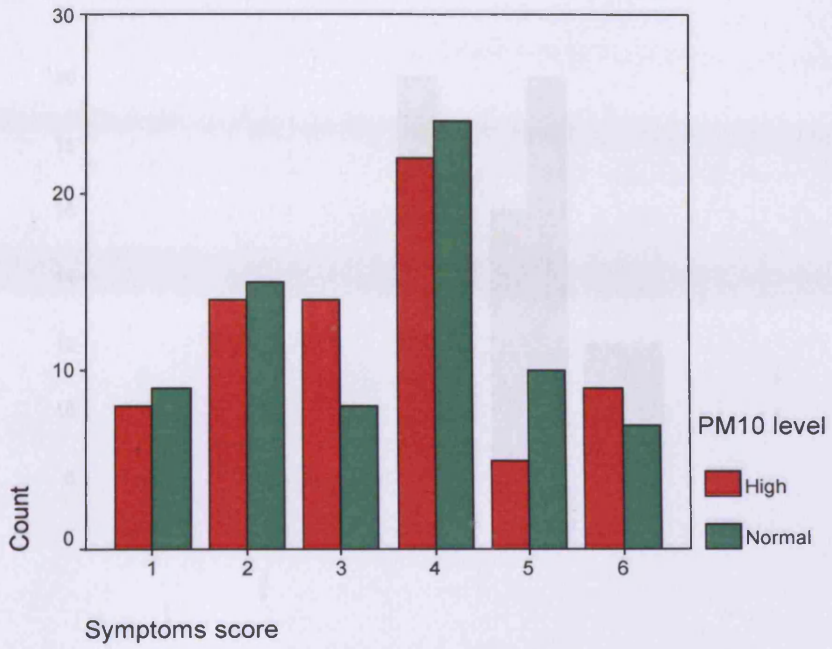

Figure 14a: Breakdown of cardiac symptoms score of question 14 and count of participant number, high v normal levels of PM_{10}.

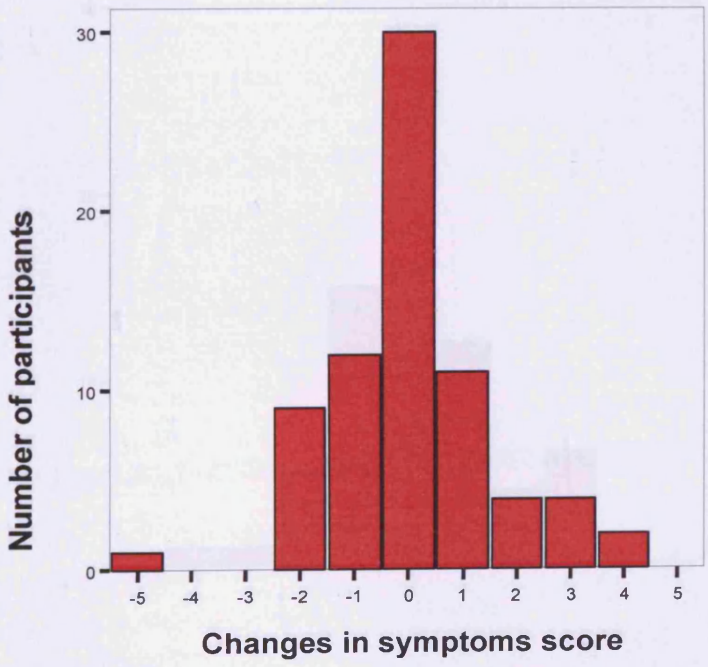

Figure 14b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 14.

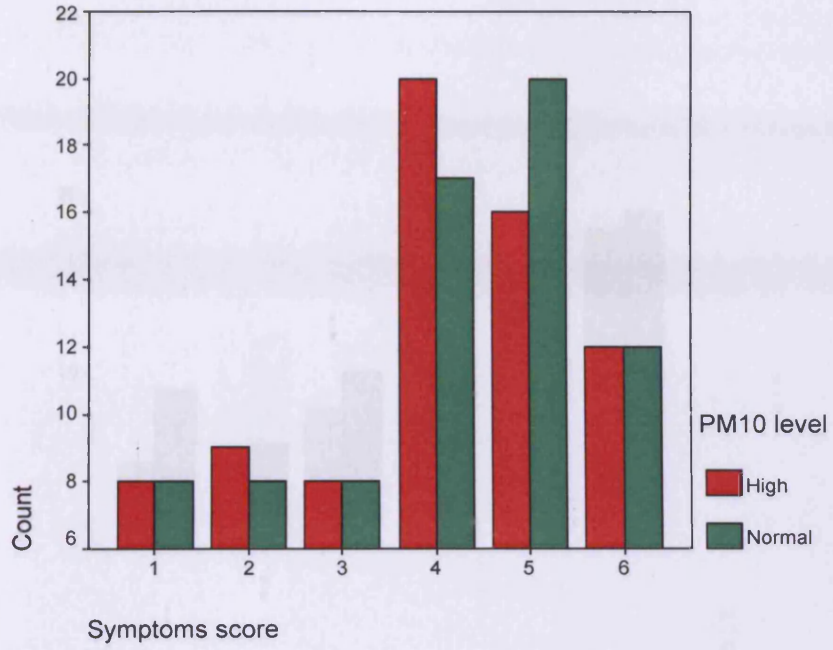

Figure 15a: Breakdown of cardiac symptoms score of question 15 and count of participant number, high v normal levels of PM_{10}.

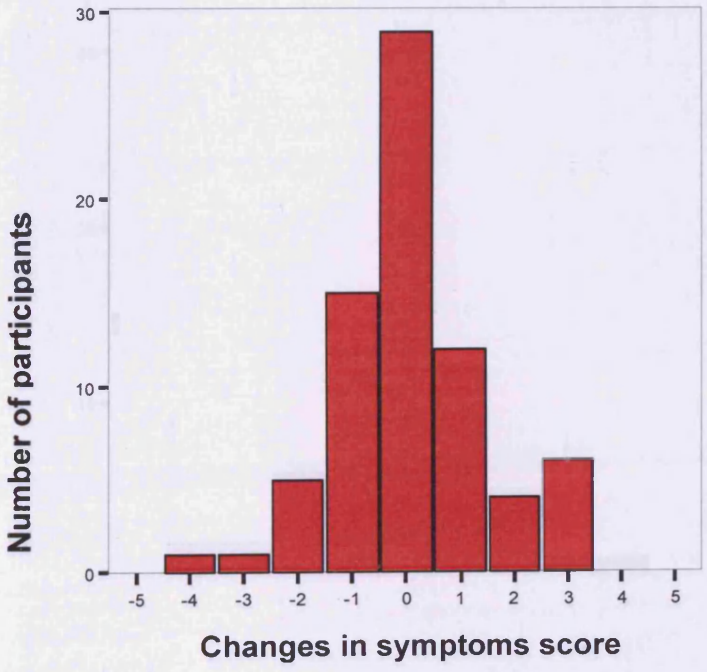

Figure 15b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 15.

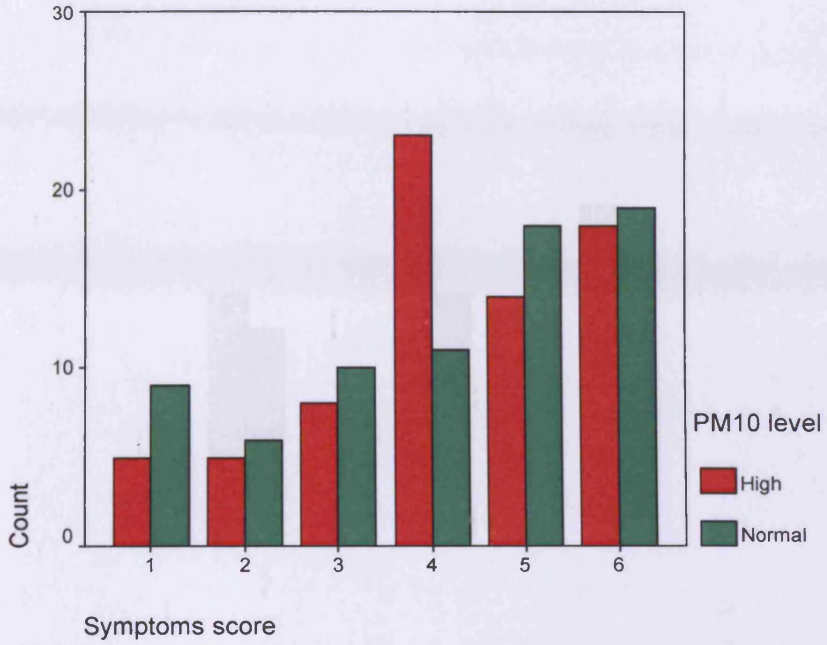

Figure 16a: Breakdown of cardiac symptoms score of question 16 and count of participant number, high v normal levels of PM_{10}.

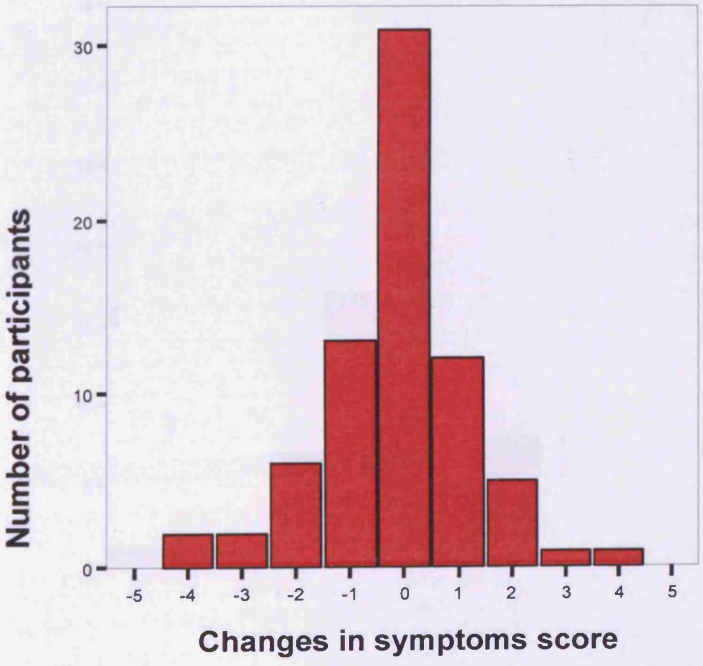

Figure 16b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 16.

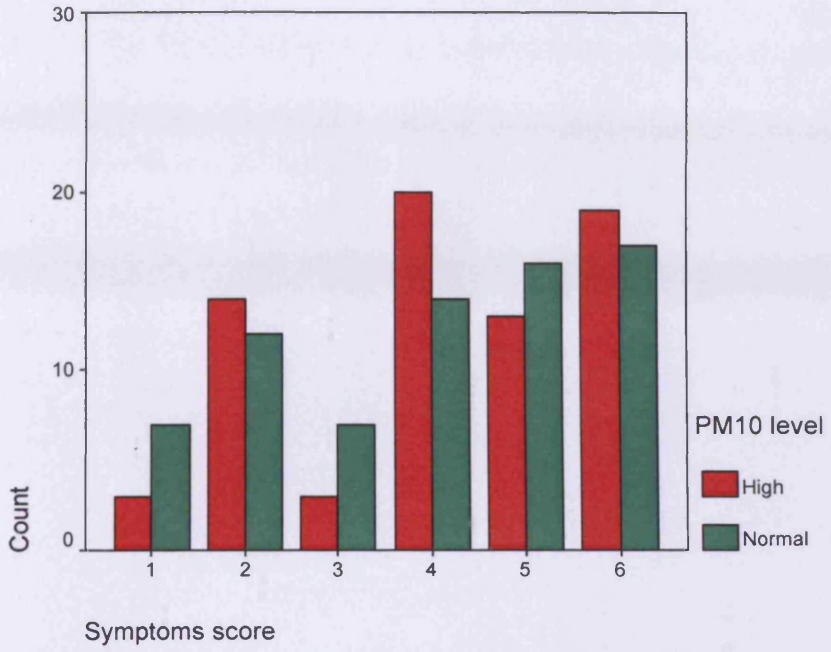

Figure 17a: Breakdown of cardiac symptoms score of question 17 and count of participant number, high v normal levels of PM_{10}.

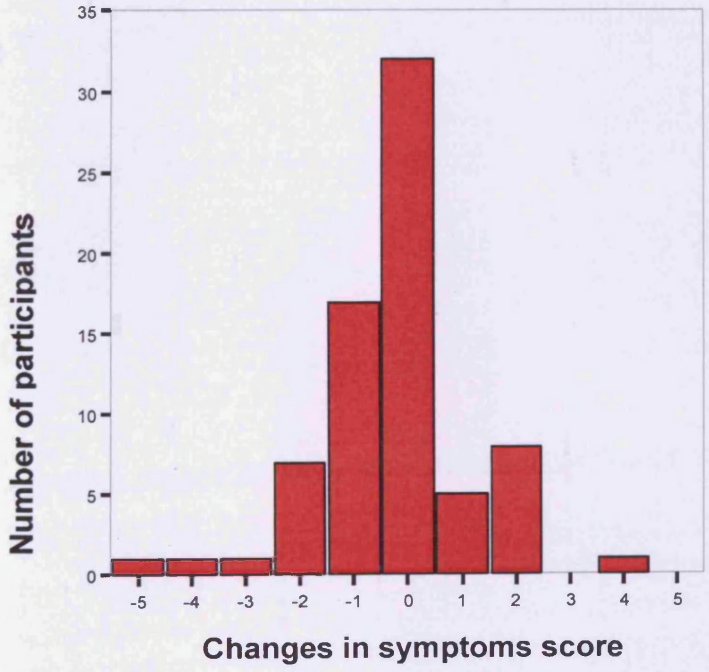

Figure 17b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution, question 17.

APPENDIX 9.2

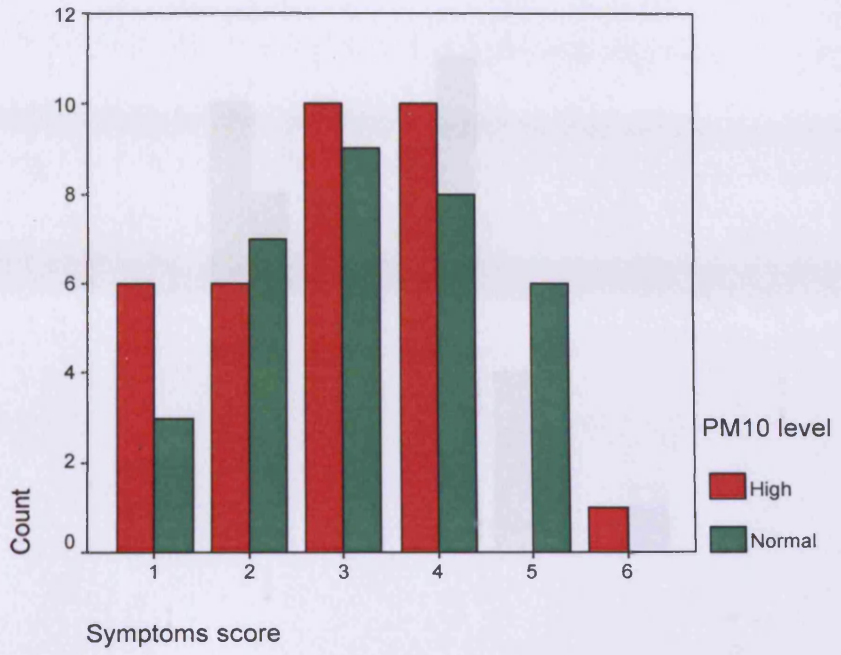

Figure 1a: Breakdown of cardiac symptoms score of question 1 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

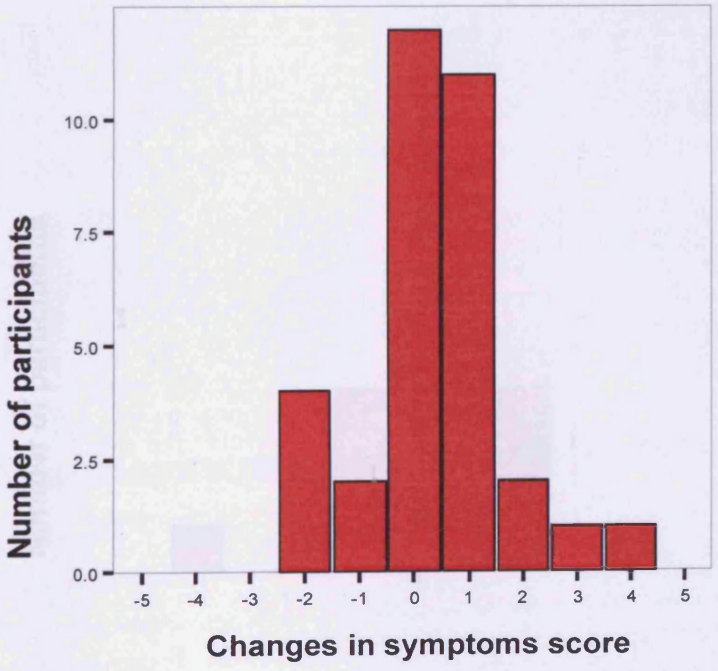

Figure 1b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 1.

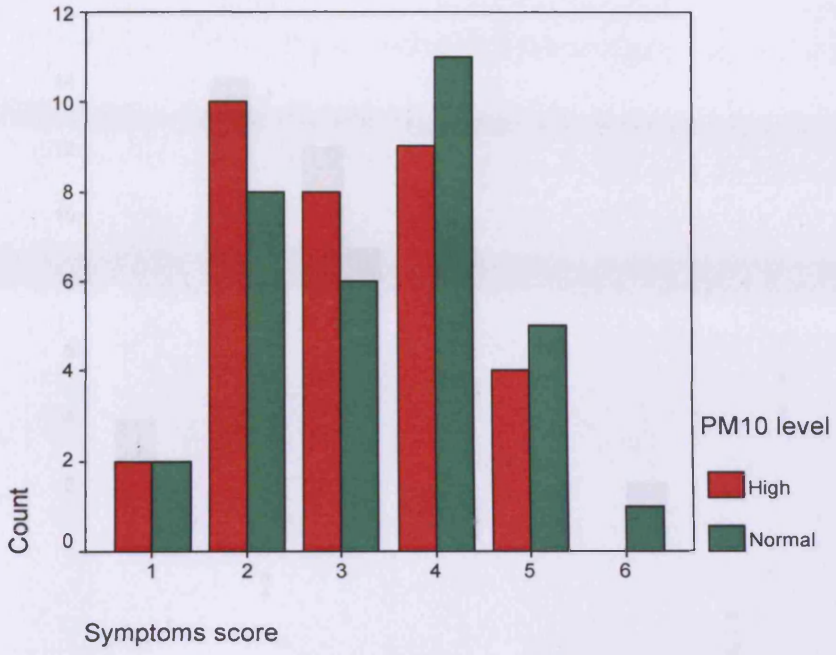

Figure 2a: Breakdown of cardiac symptoms score of question 2 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

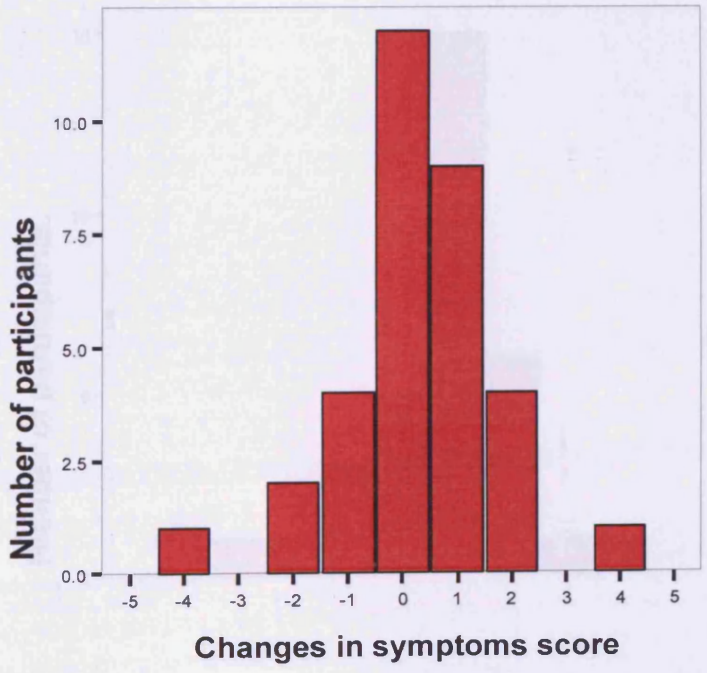

Figure 2b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 2.

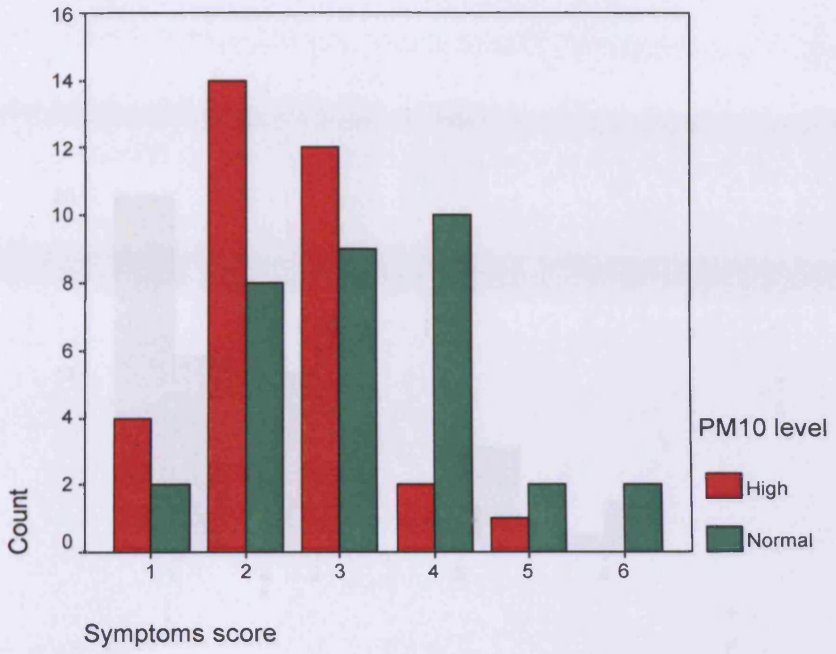

Figure 3a: Breakdown of cardiac symptoms score of question 3 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

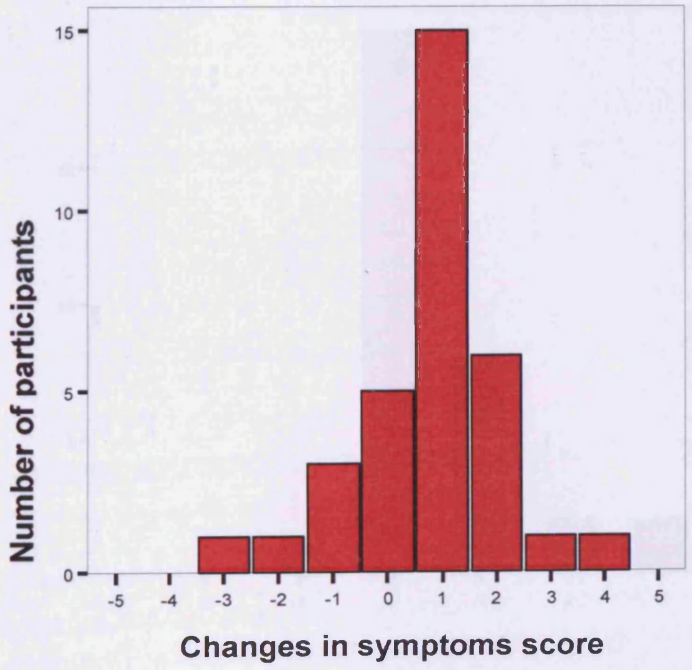

Figure 3b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 3.

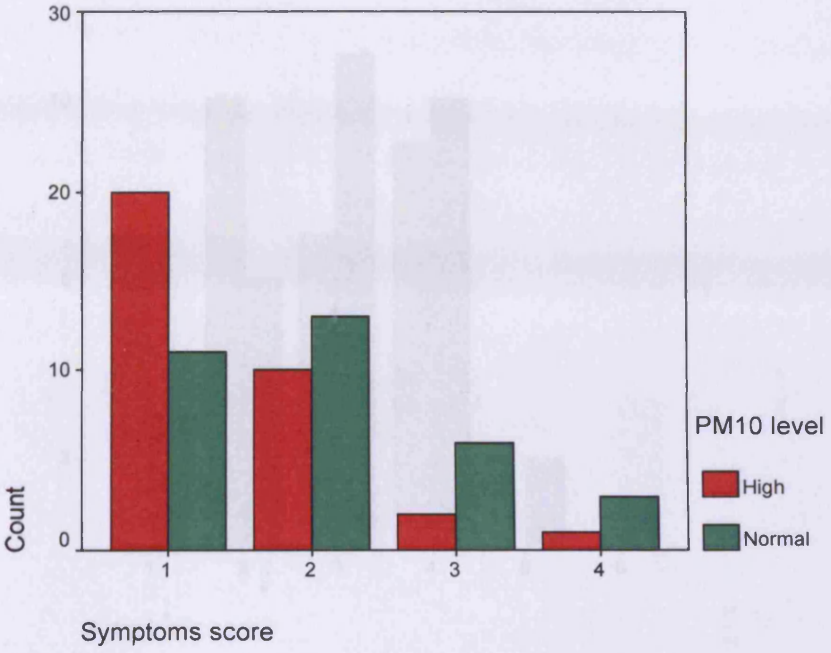

Figure 4a: Breakdown of cardiac symptoms score of question 4 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

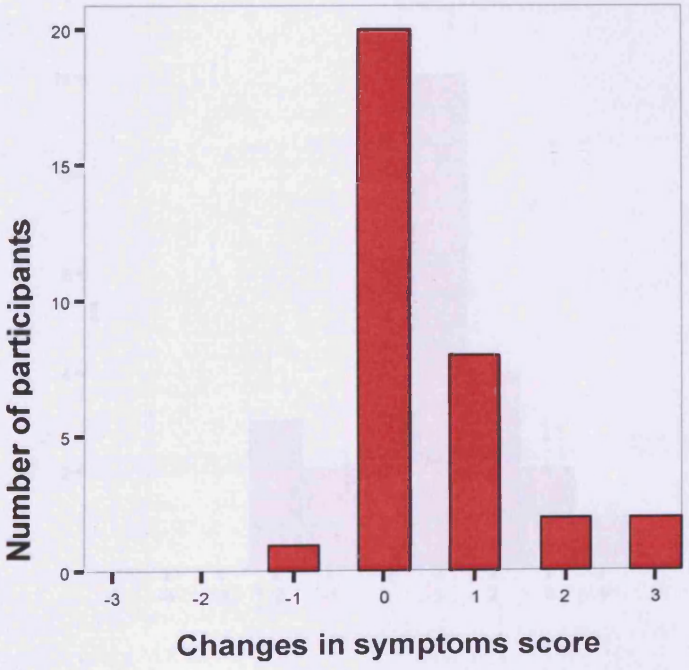

Figure 4b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 4.

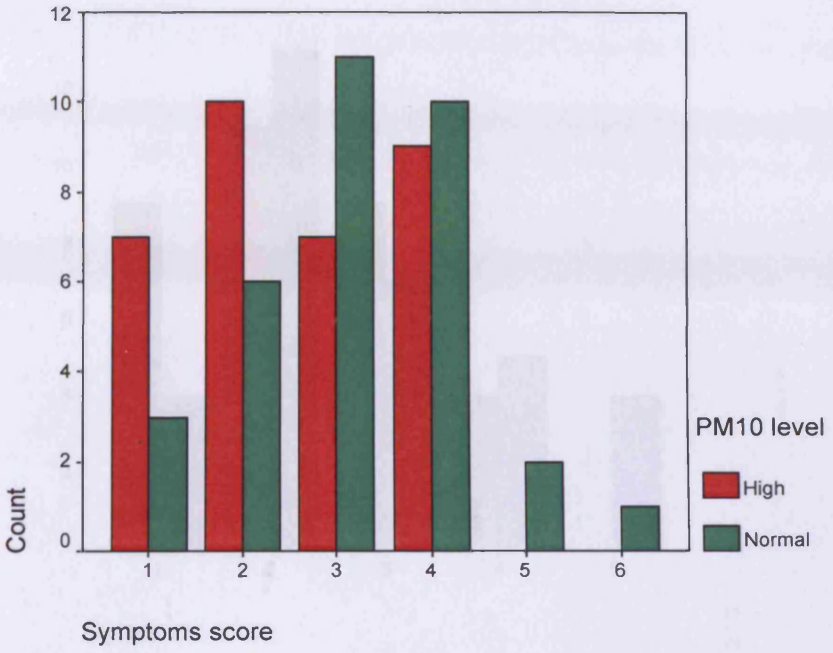

Figure 5a: Breakdown of cardiac symptoms score of question 5 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

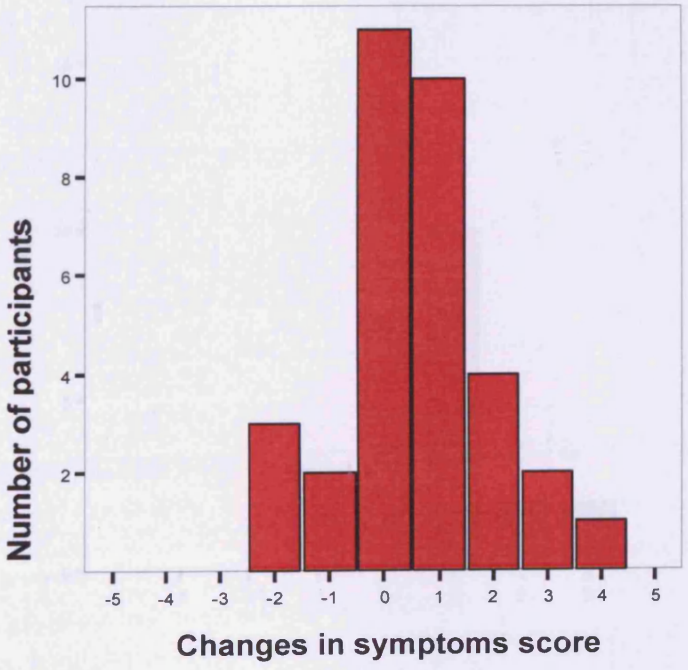

Figure 5b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 5.

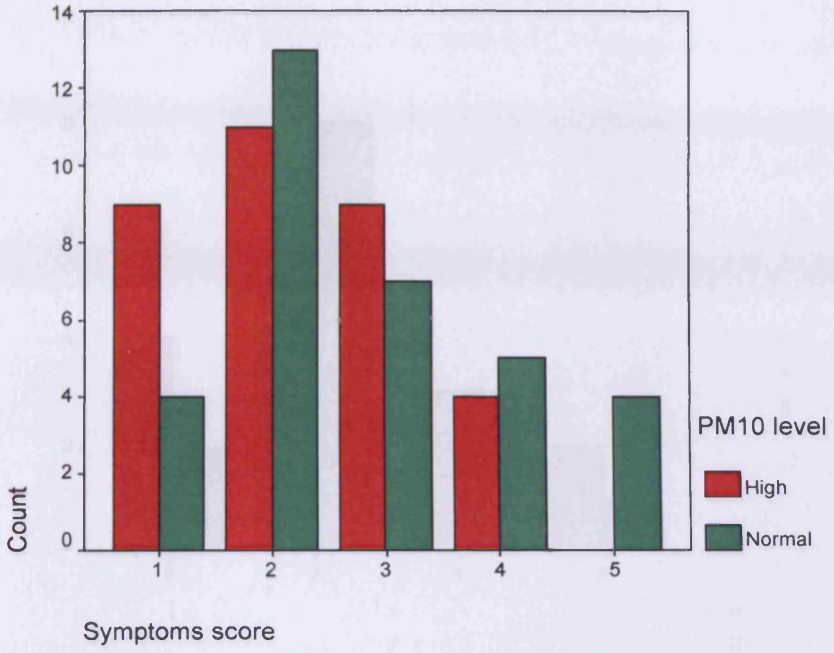

Figure 6a: Breakdown of cardiac symptoms score of question 6 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

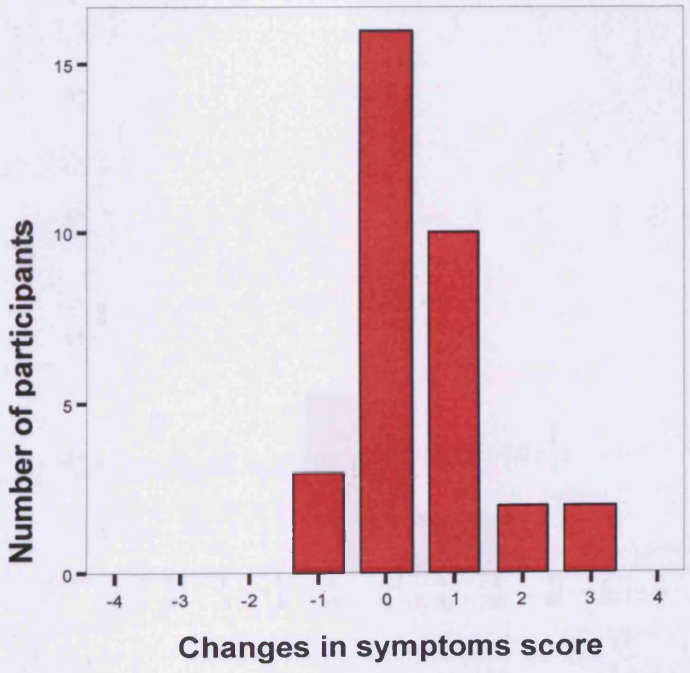

Figure 6b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 6.

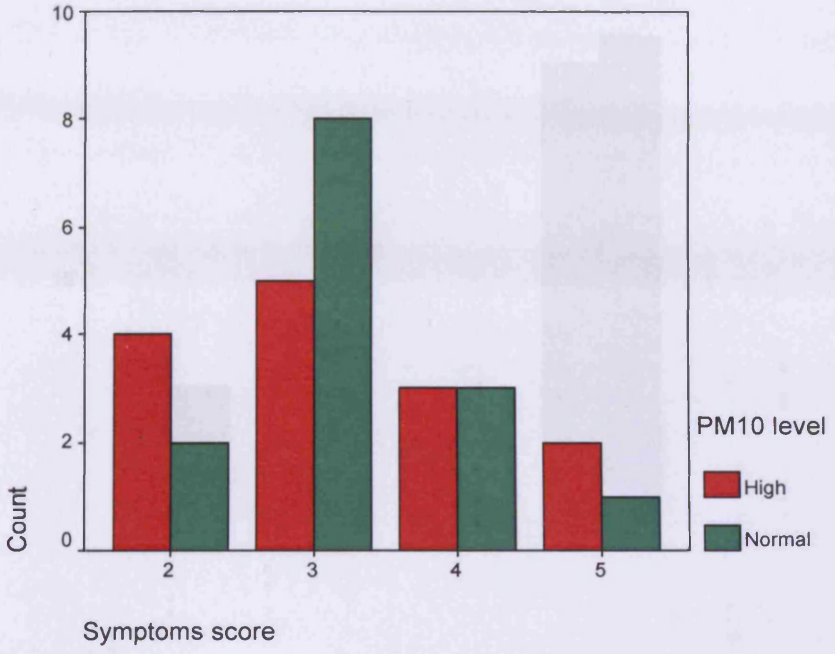

Figure 7a: Breakdown of cardiac symptoms score of question 7 and count of participant number amongst the more severe cases, high v normal levels of PM_{10} (n=14).

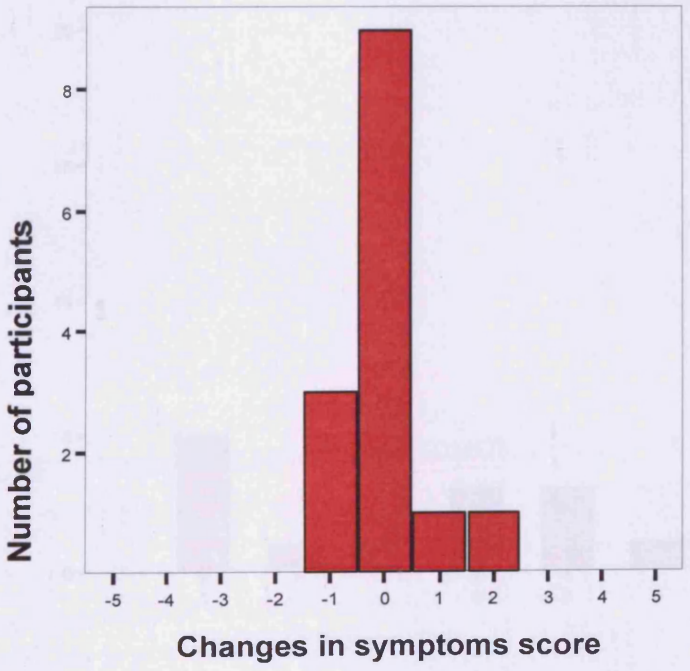

Figure 7b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 7 (n=14).

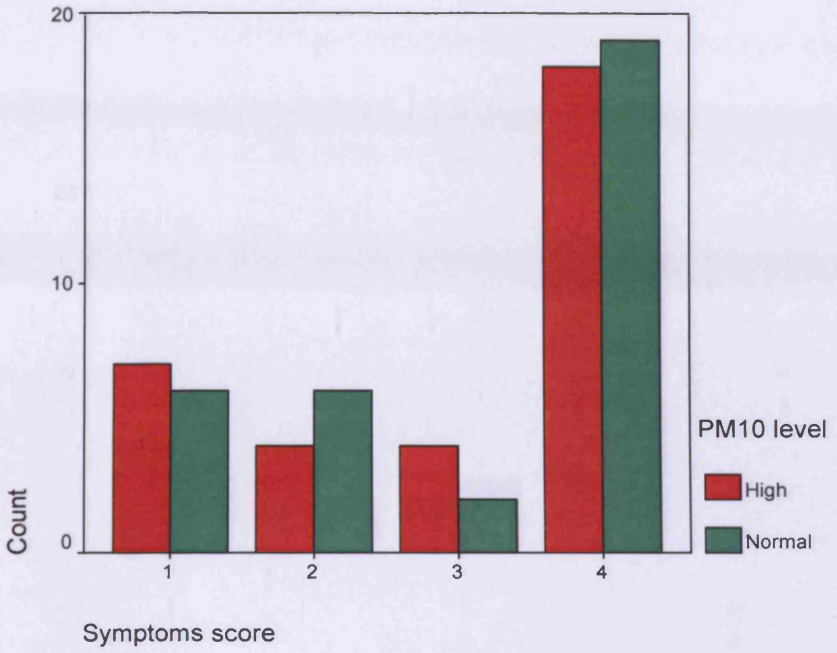

Figure 8a: Breakdown of cardiac symptoms score of question 8 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

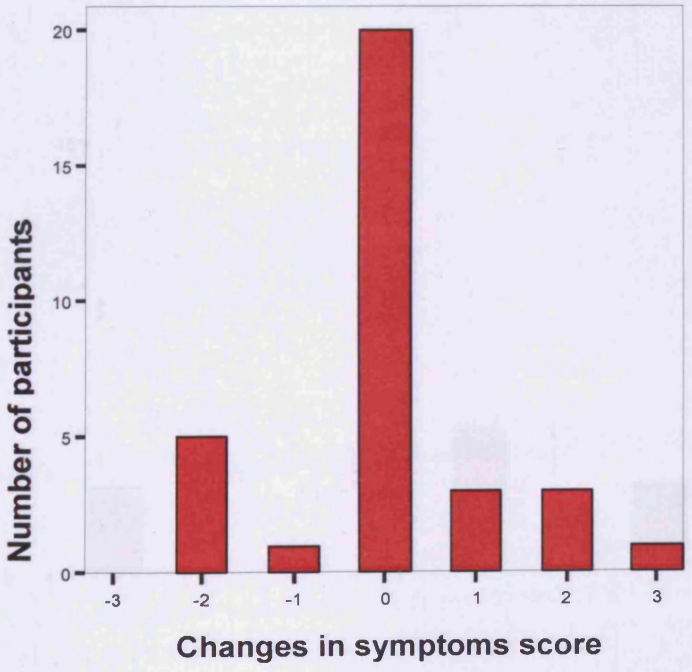

Figure 8b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 8.

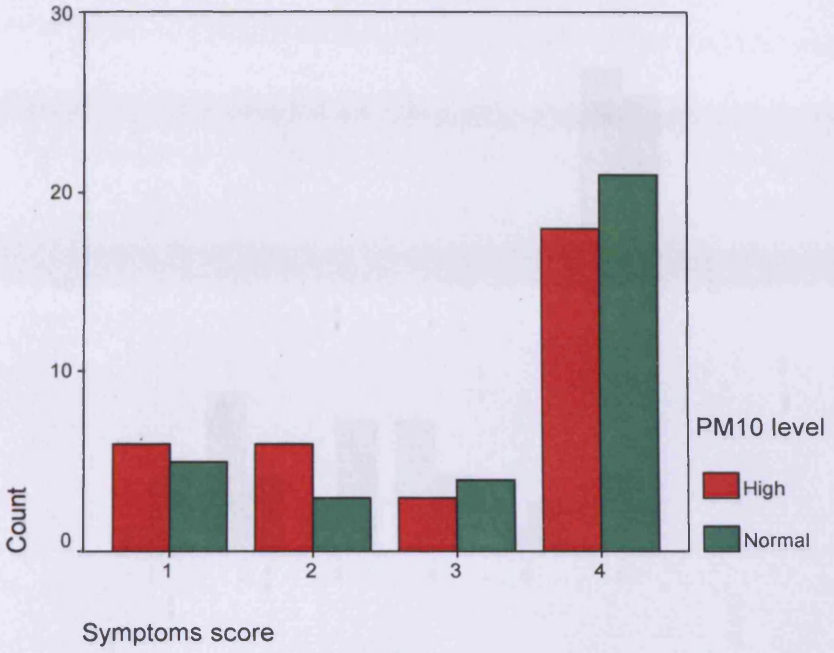

Figure 9a: Breakdown of cardiac symptoms score of question 9 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

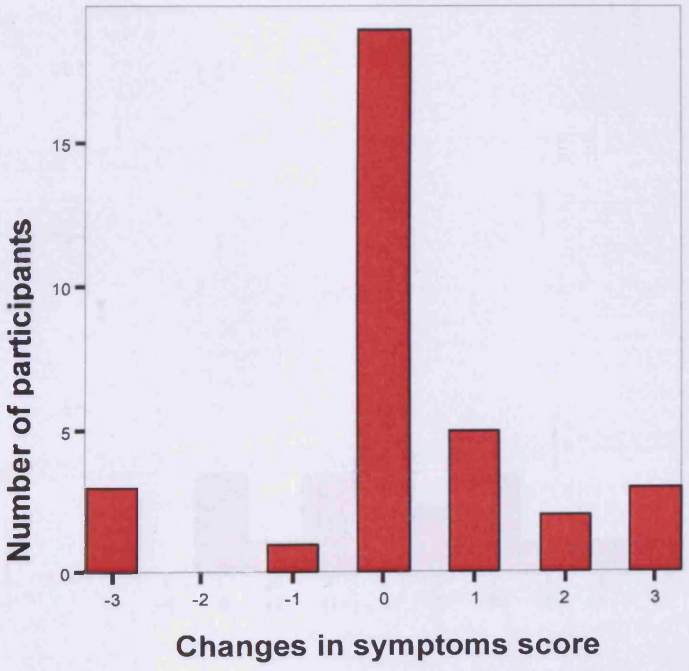

Figure 9b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 9.

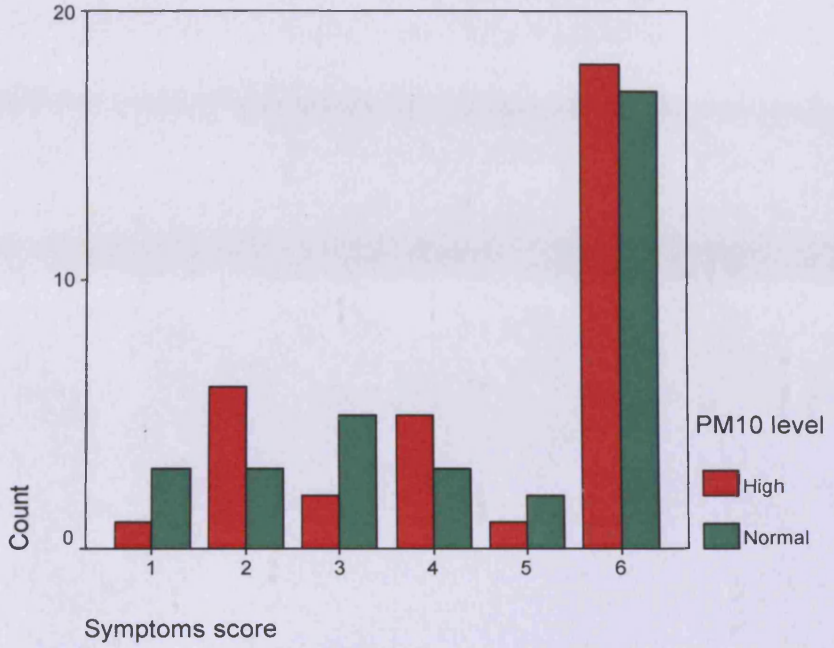

Figure 10a: Breakdown of cardiac symptoms score of question 10 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

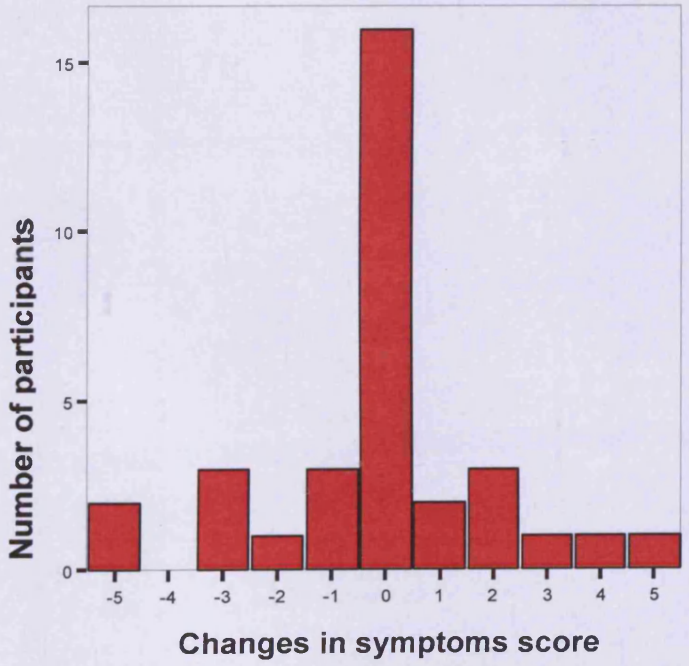

Figure 10b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 10.

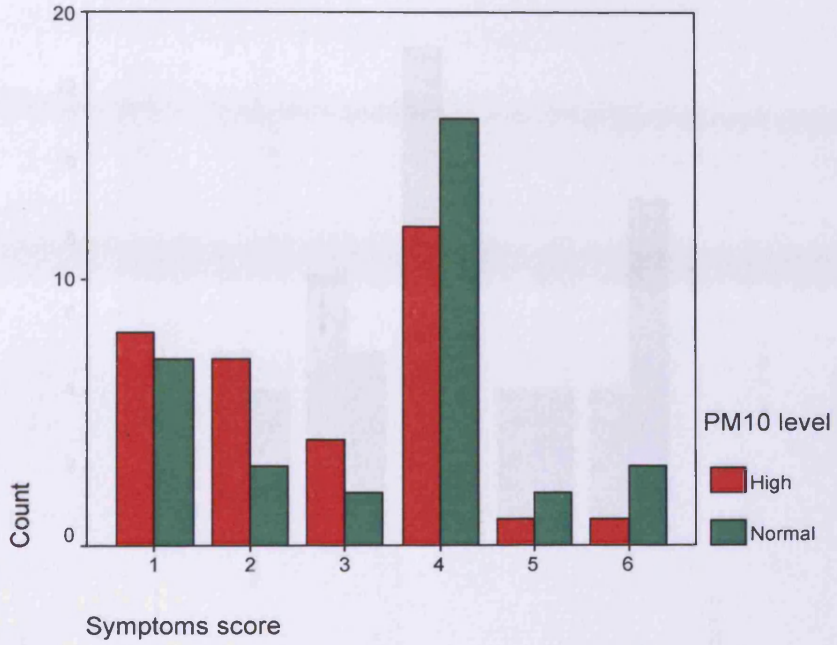

Figure 11a: Breakdown of cardiac symptoms score of question 11 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

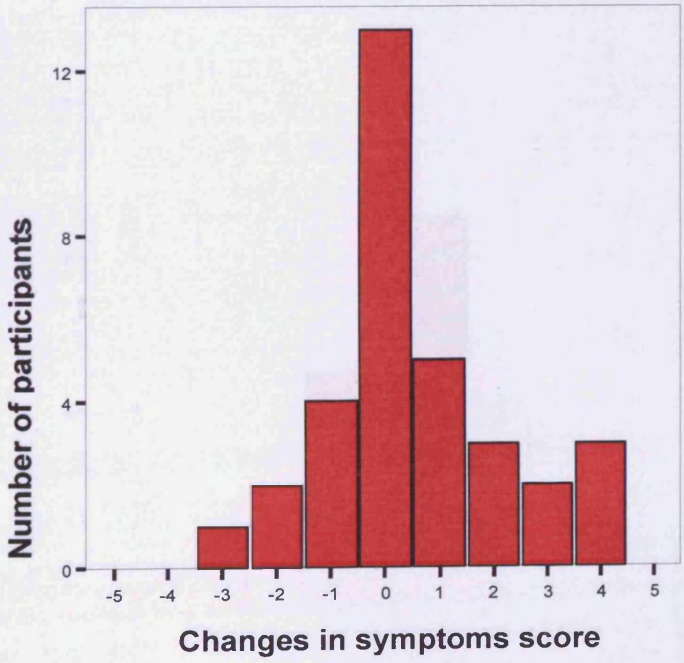

Figure 11b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 11.

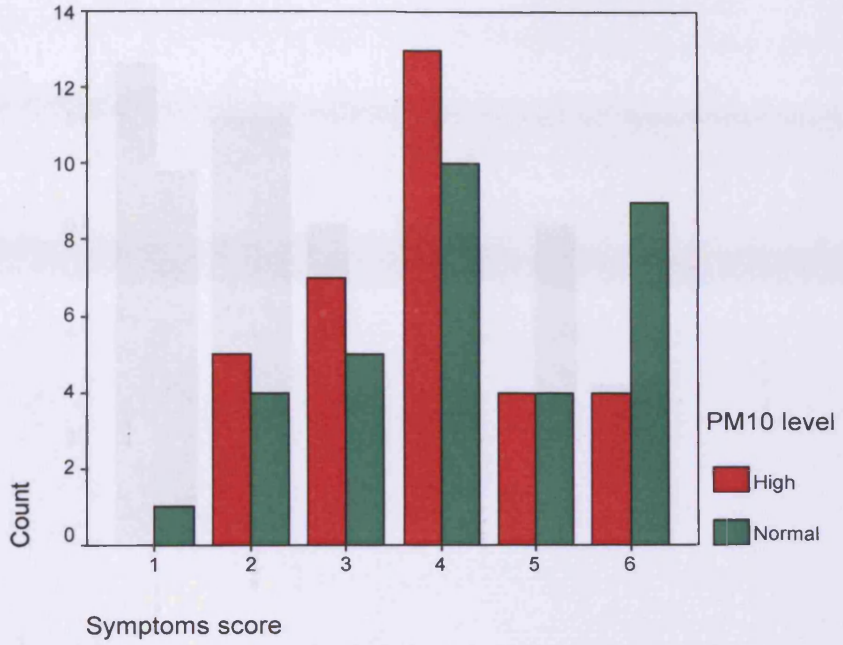

Figure 12a: Breakdown of cardiac symptoms score of question 12 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

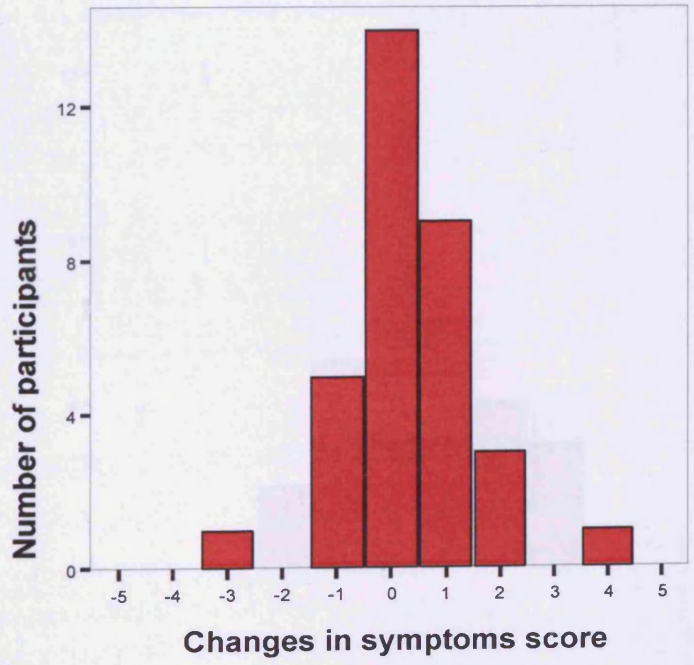

Figure 12b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 12.

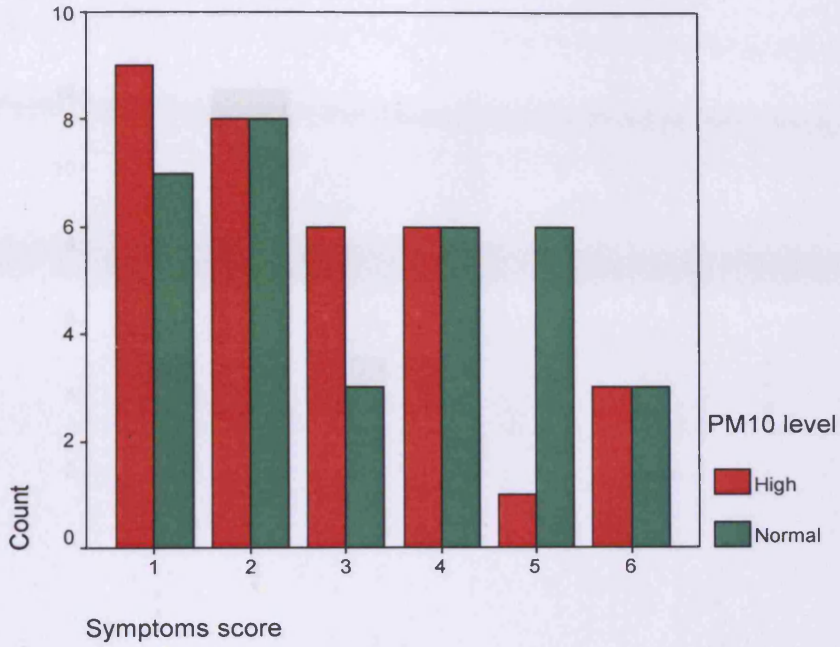

Figure 13a: Breakdown of cardiac symptoms score of question 13 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

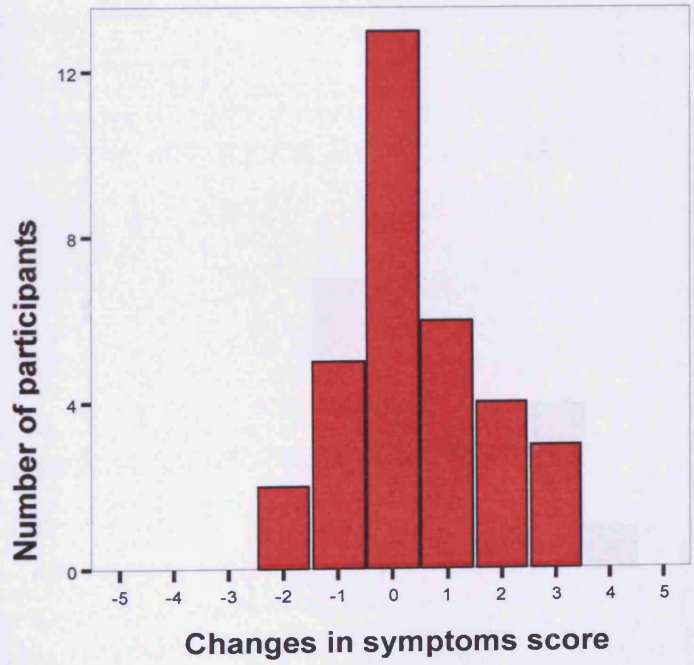

Figure 13b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 13.

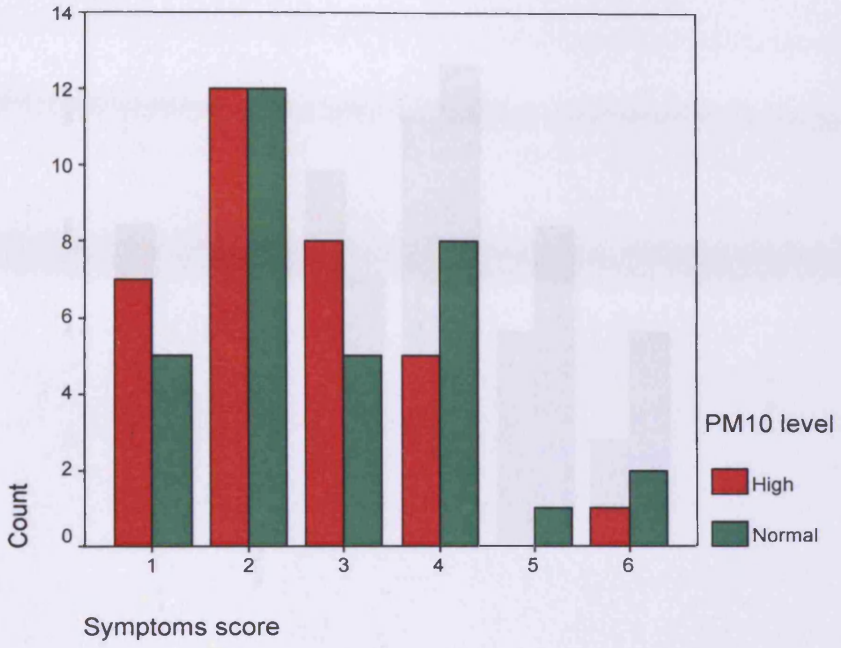

Figure 14a: Breakdown of cardiac symptoms score of question 14 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

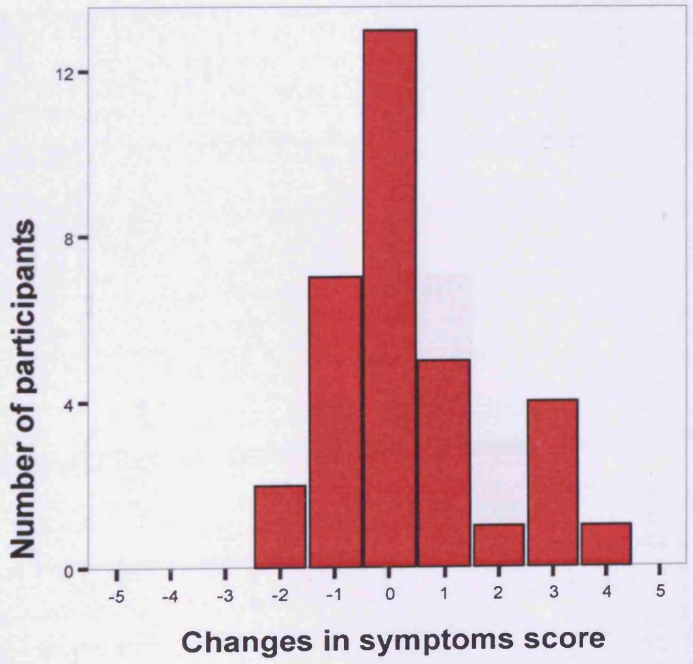

Figure 14b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 14.

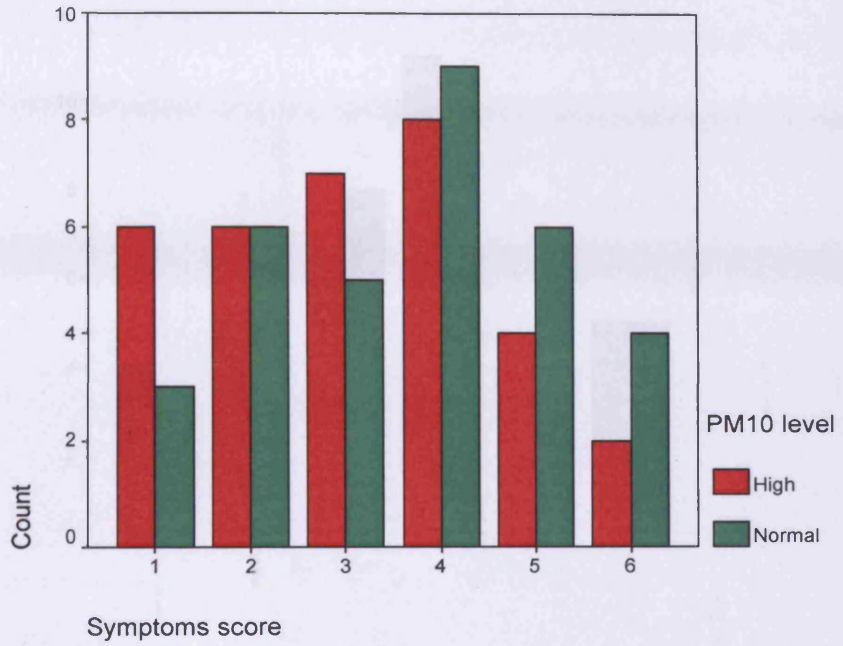

Figure 15a: Breakdown of cardiac symptoms score of question 15 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

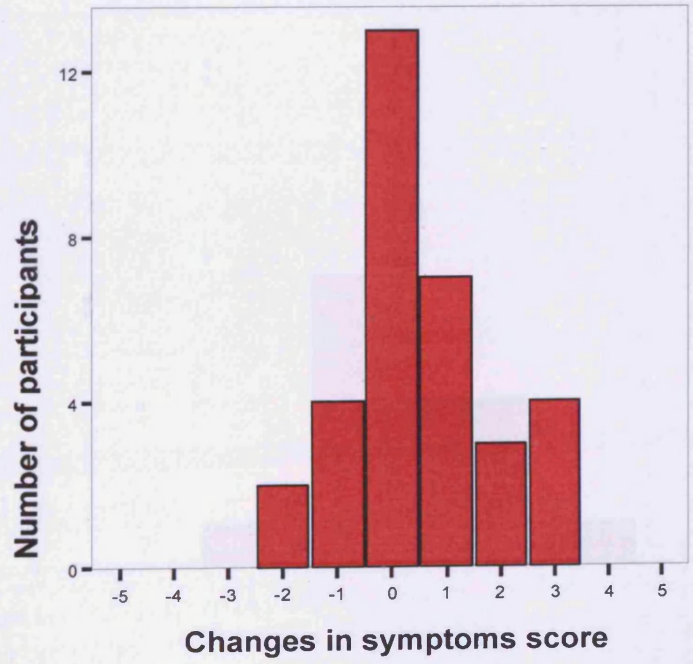

Figure 15b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 15.

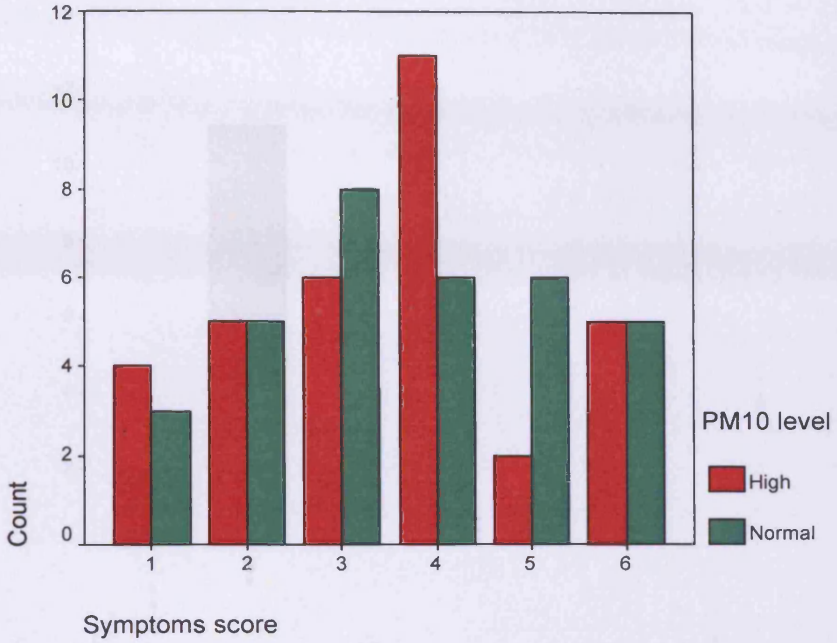

Figure 16a: Breakdown of cardiac symptoms score of question 16 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

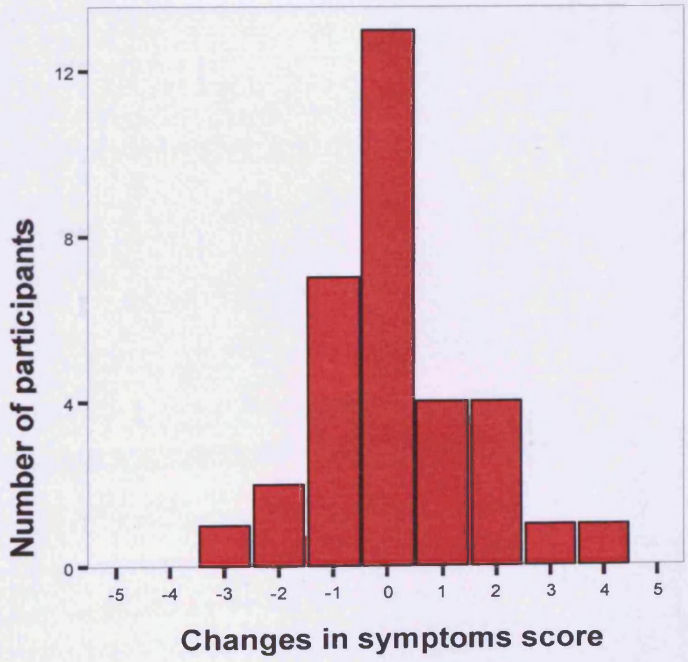

Figure 16b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 16.

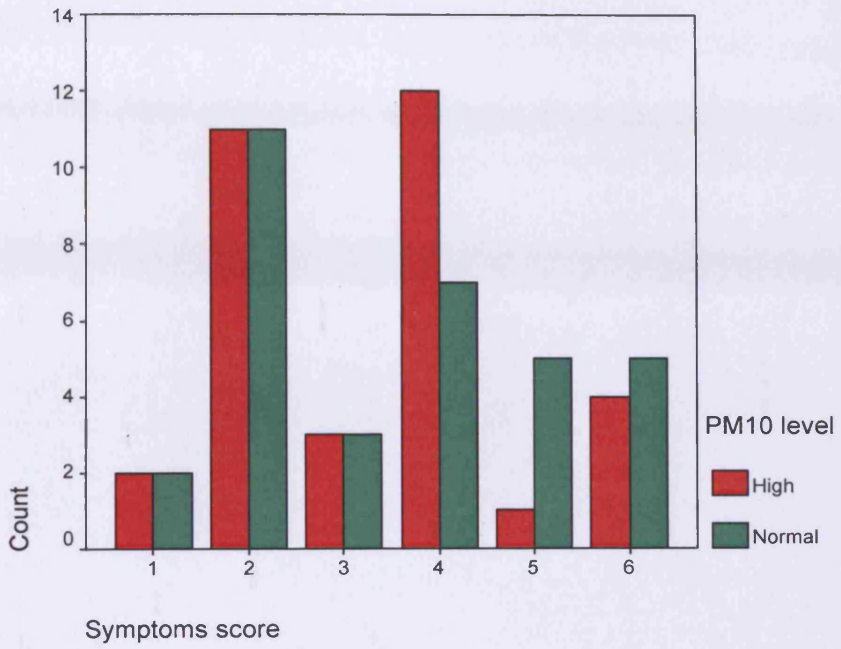

Figure 17a: Breakdown of cardiac symptoms score of question 17 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

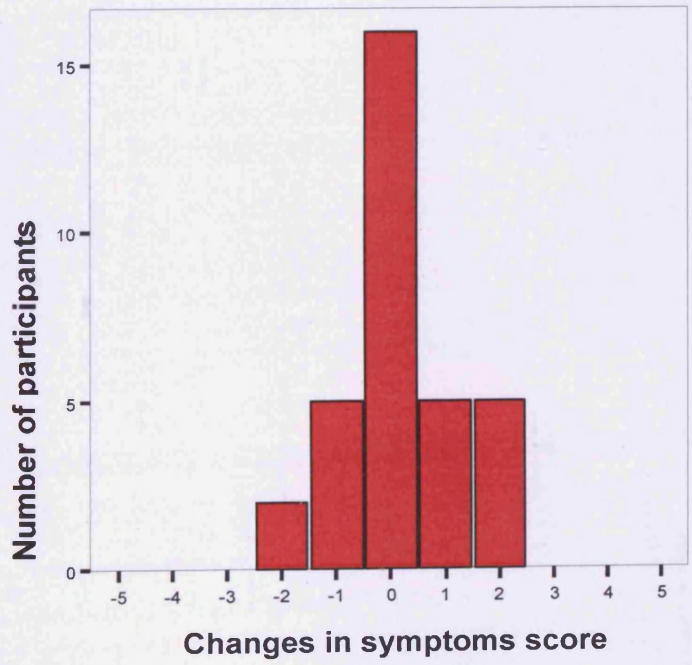

Figure 17b: Changes in cardiac symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 17.

APPENDIX 10.1

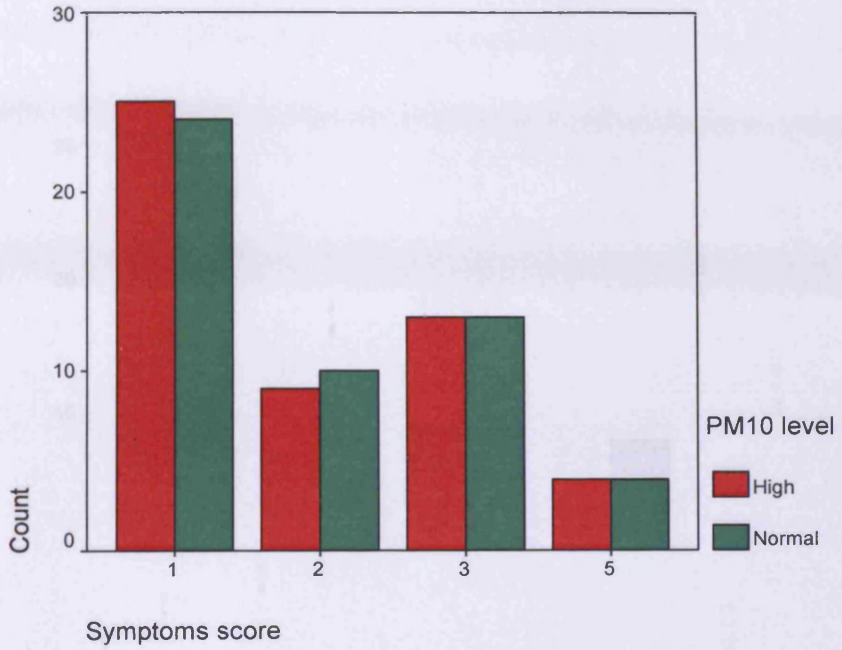

Figure 1a: Breakdown of respiratory symptoms score of question 1 and count of participant number, high v normal levels of PM_{10}.

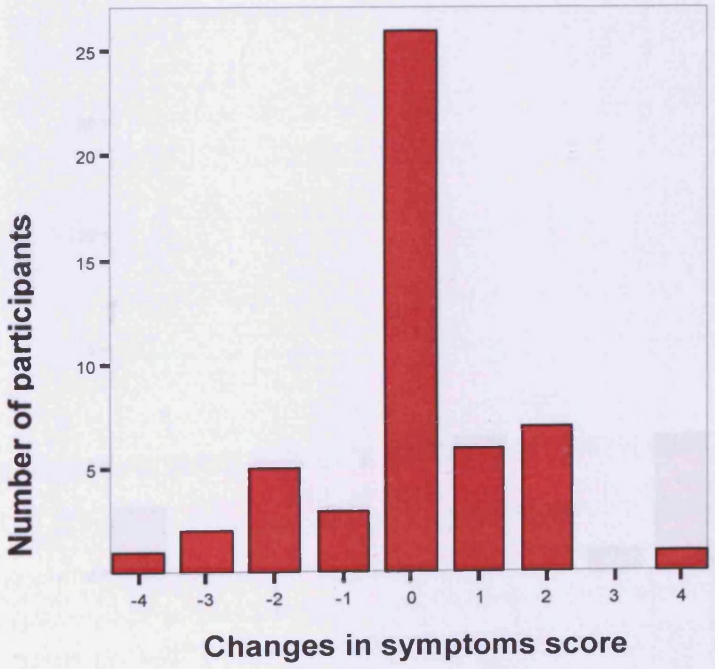

Figure 1b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 1.

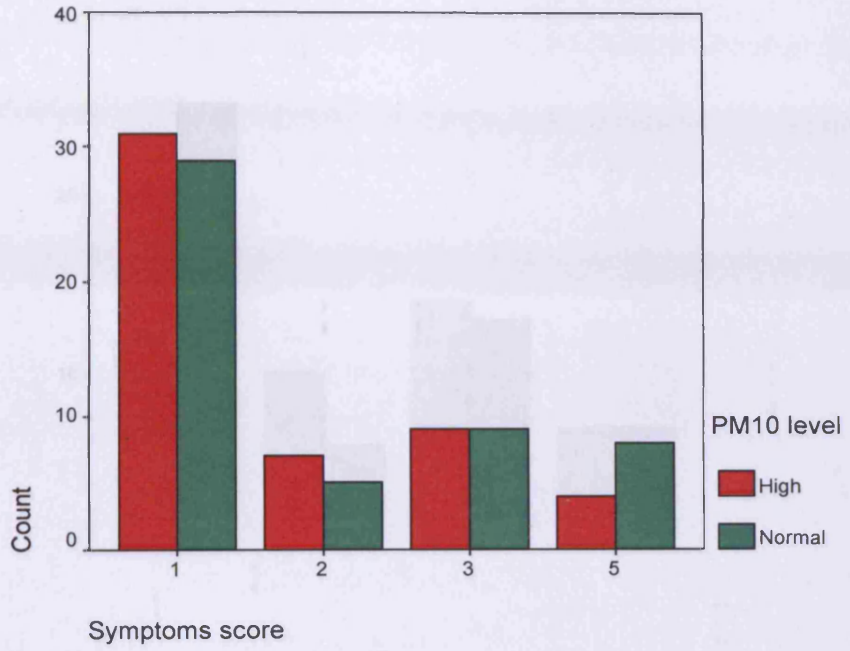

Figure 2a: Breakdown of respiratory symptoms score of question 2 and count of participant number, high v normal levels of PM_{10}.

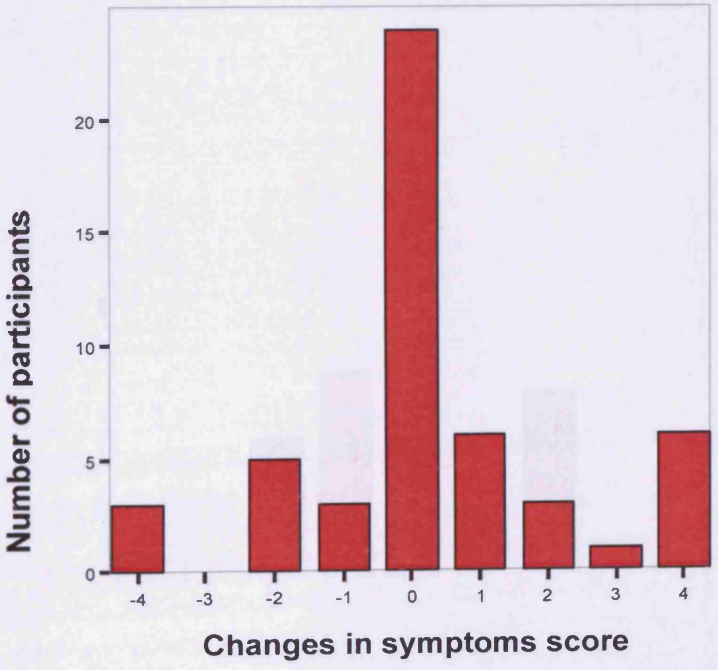

Figure 2b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 2.

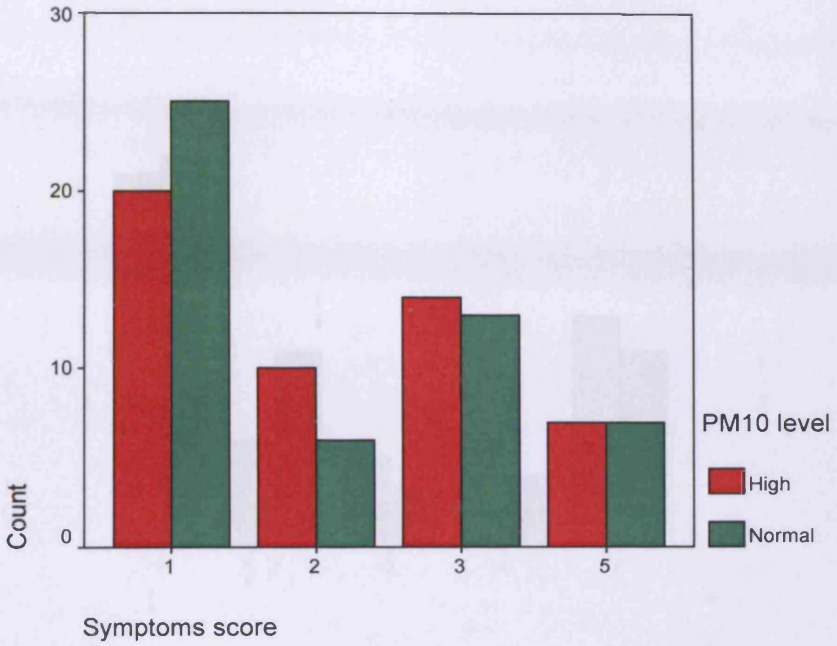

Figure 3a: Breakdown of respiratory symptoms score of question 3 and count of participant number, high v normal levels of PM_{10}.

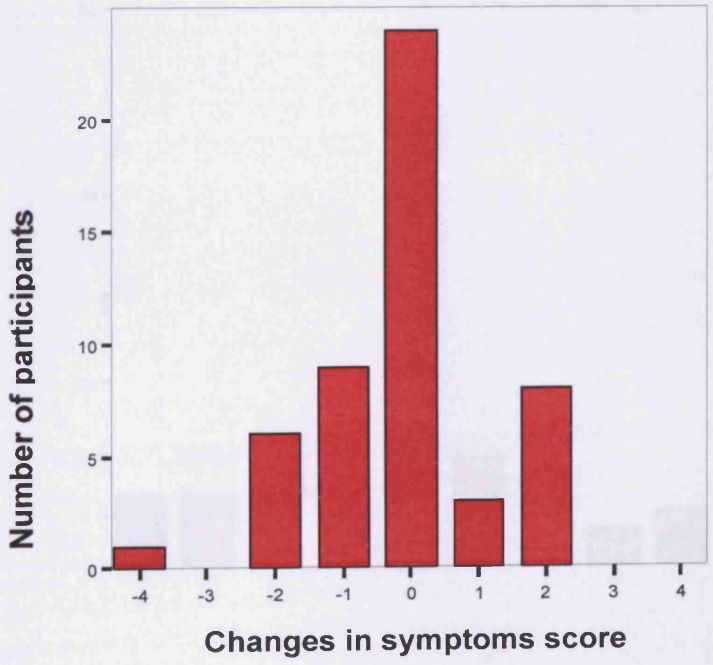

Figure 3b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 3.

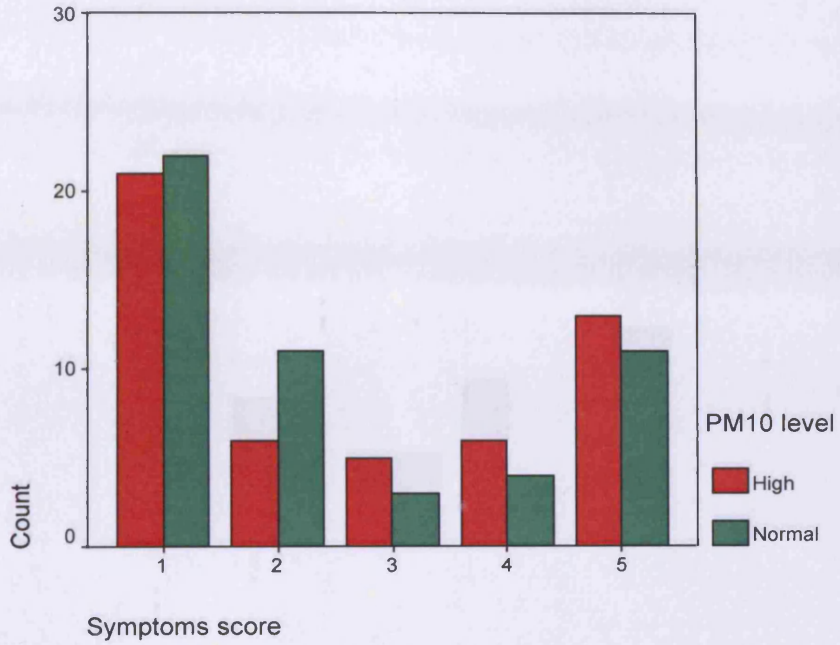

Figure 4a: Breakdown of respiratory symptoms score of question 4 and count of participant number, high v normal levels of PM_{10}.

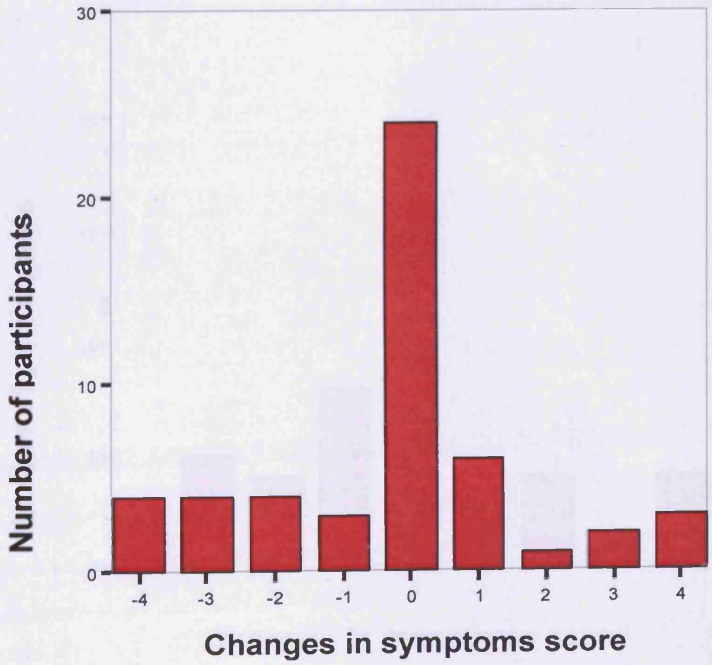

Figure 4b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 4.

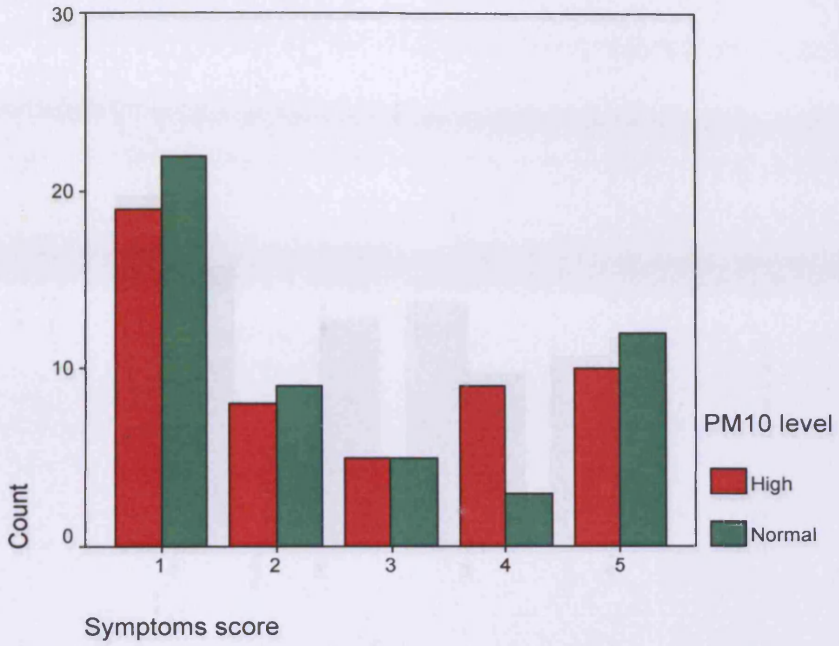

Figure 5a: Breakdown of respiratory symptoms score of question 5 and count of participant number, high v normal levels of PM_{10}.

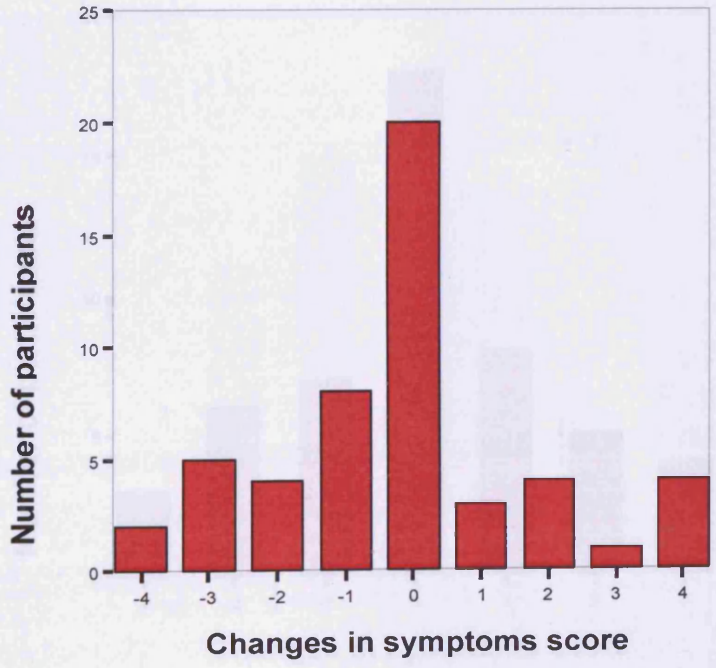

Figure 5b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 5.

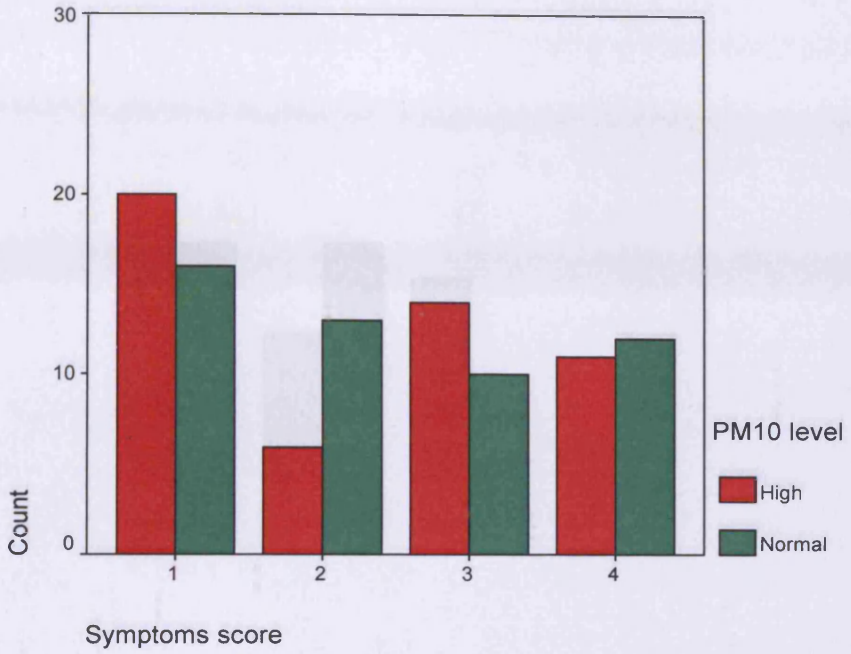

Figure 6a: Breakdown of respiratory symptoms score of question 6 and count of participant number, high v normal levels of PM_{10}.

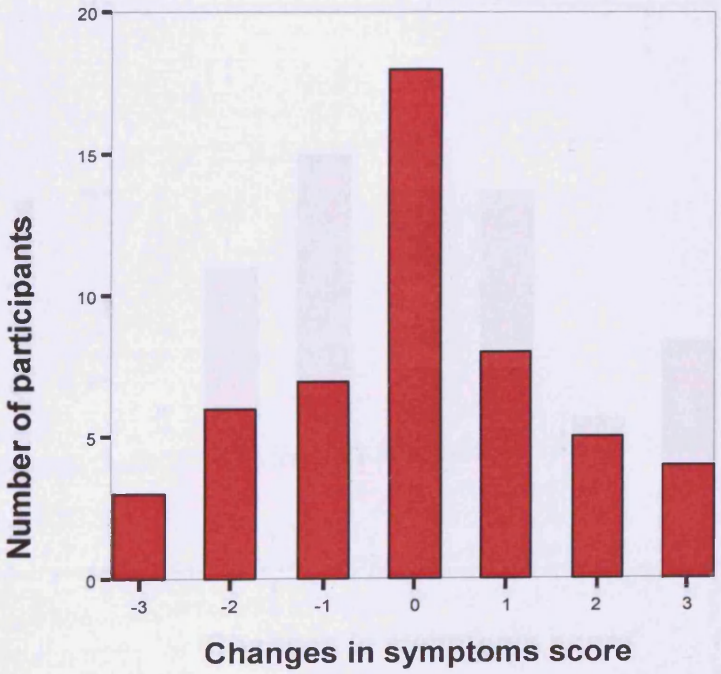

Figure 6b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 6.

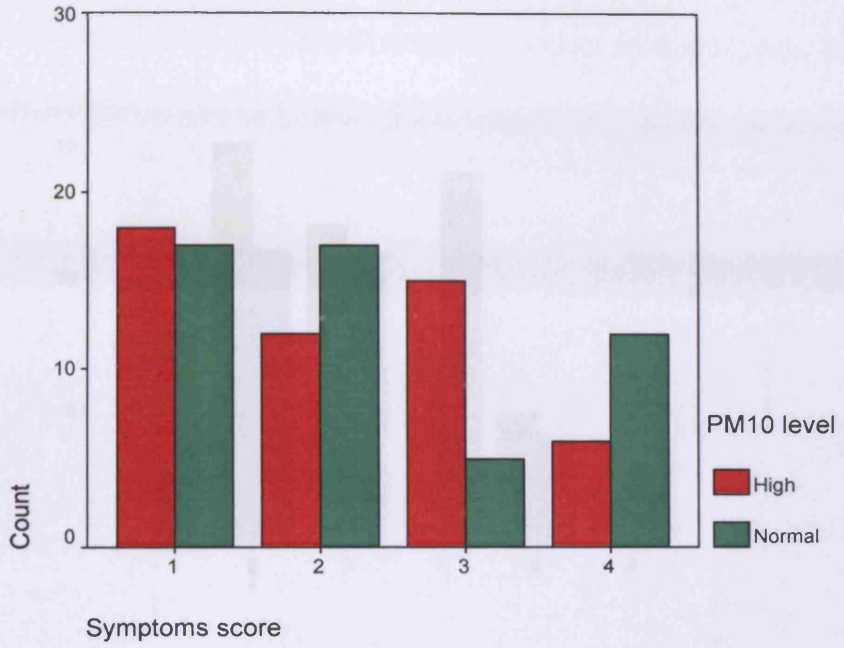

Figure 7a: Breakdown of respiratory symptoms score of question 7 and count of participant number, high v normal levels of PM_{10}.

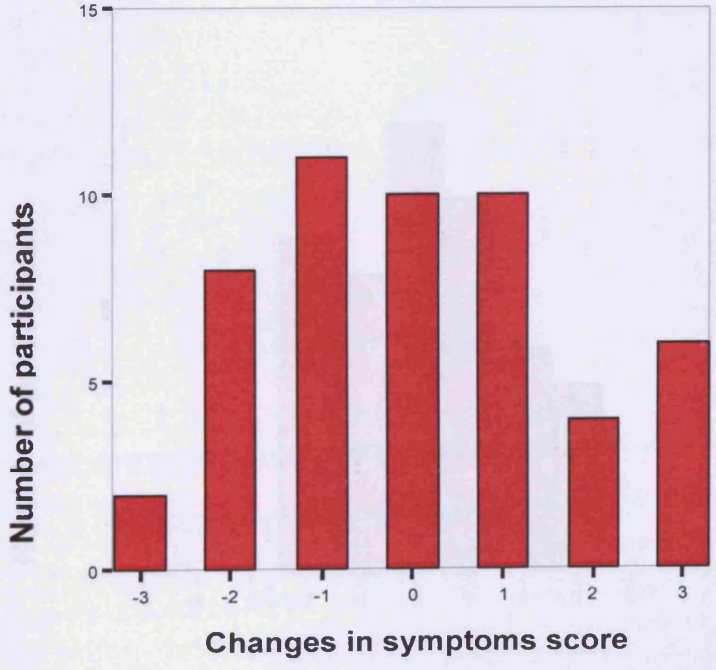

Figure 7b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 7.

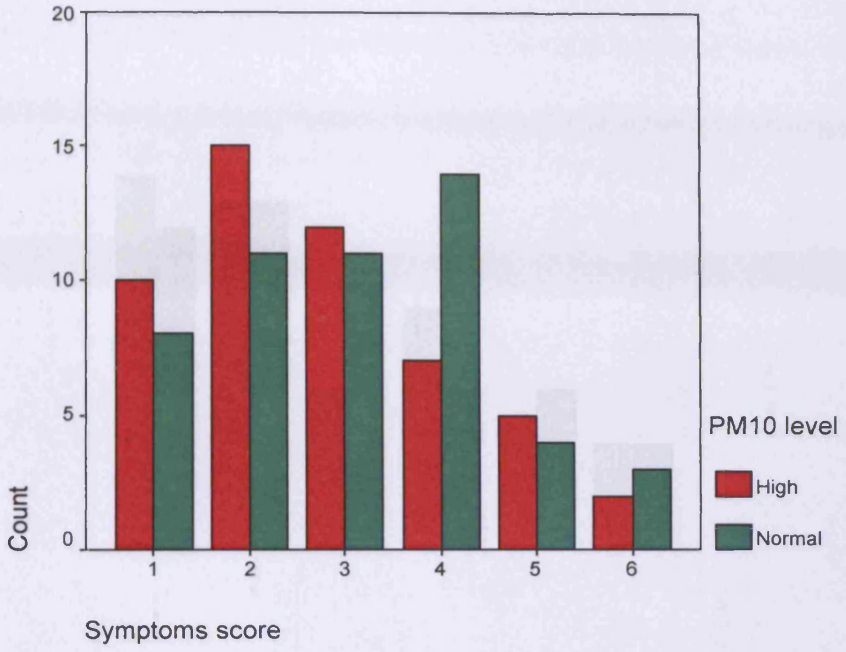

Figure 8a: Breakdown of respiratory symptoms score of question 8 and count of participant number, high v normal levels of PM_{10}.

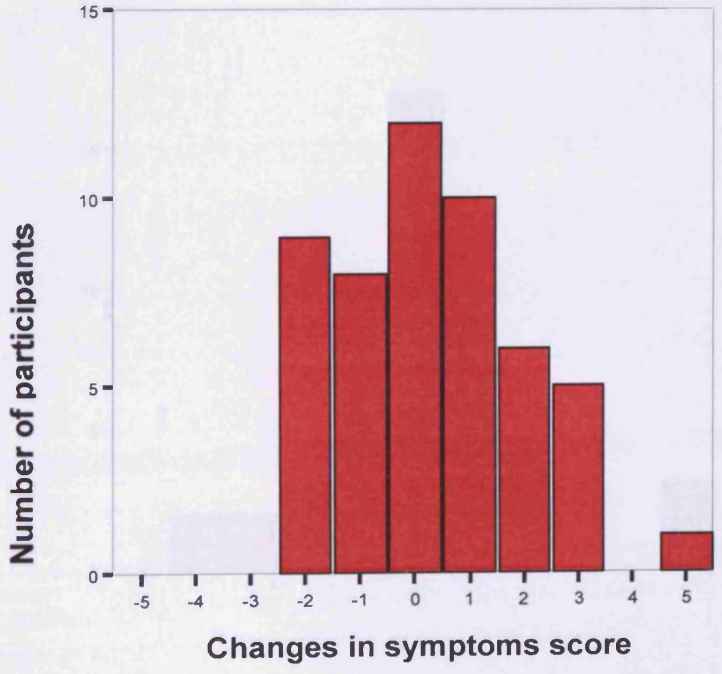

Figure 8b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 8.

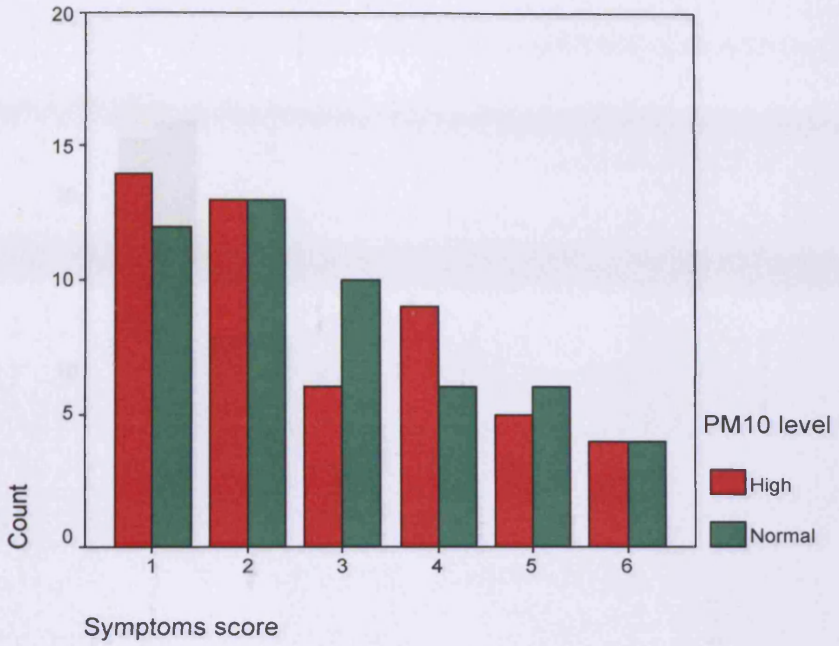

Figure 9a: Breakdown of respiratory symptoms score of question 9 and count of participant number, high v normal levels of PM_{10}.

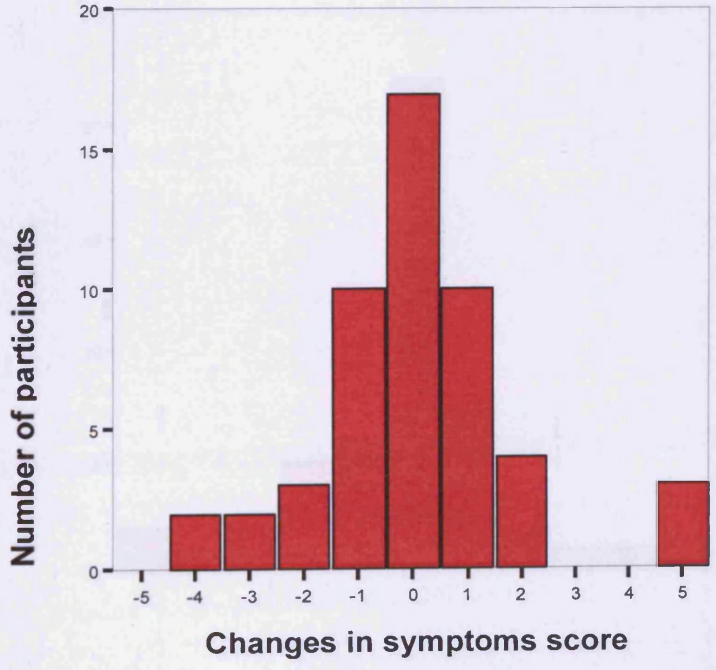

Figure 9b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 9.

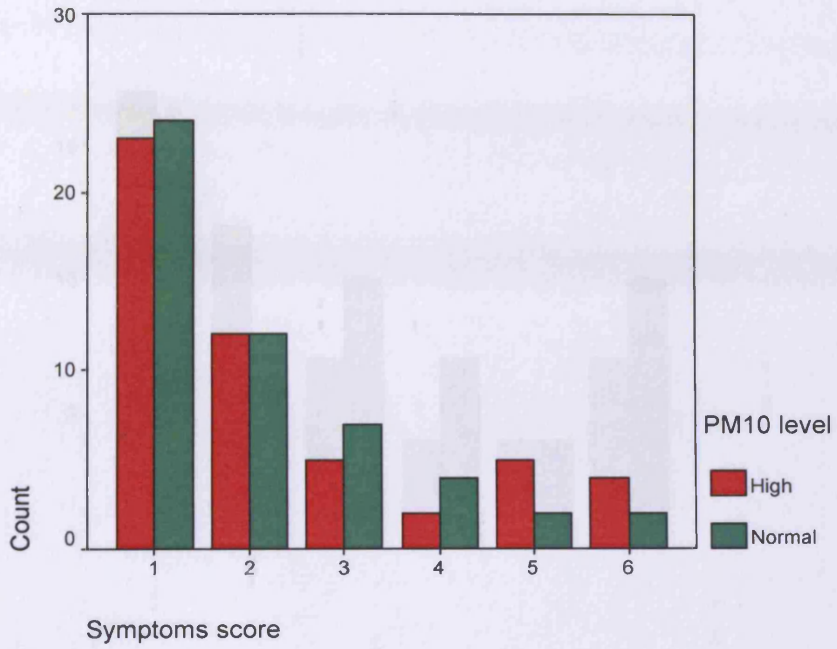

Figure 10a: Breakdown of respiratory symptoms score of question 10 and count of participant number, high v normal levels of PM_{10}.

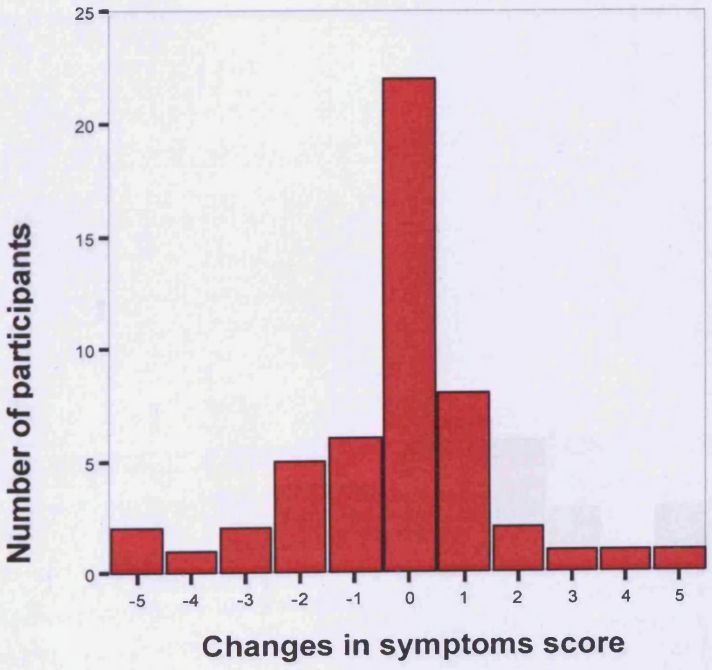

Figure 10b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 10.

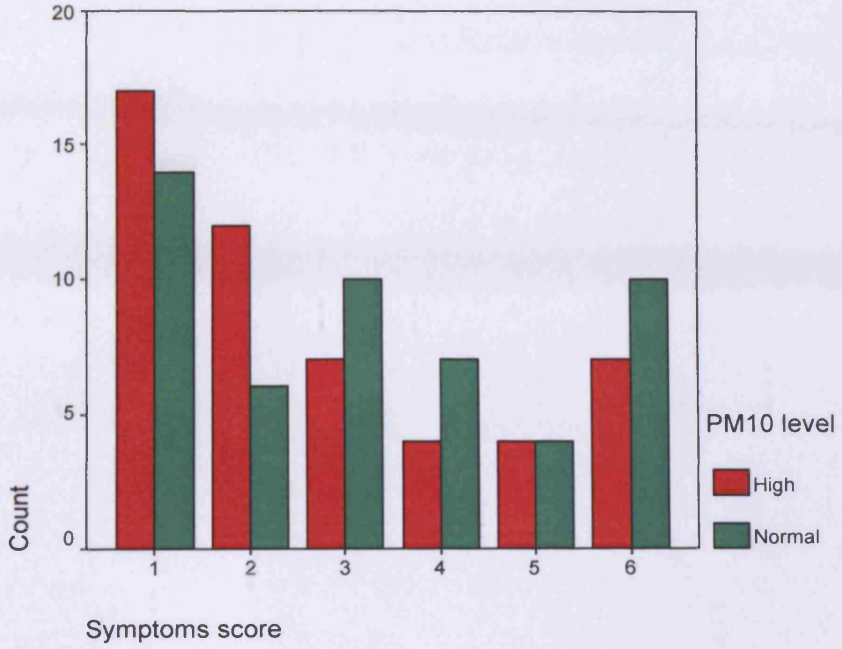

Figure 11a: Breakdown of respiratory symptoms score of question 11 and count of participant number, high v normal levels of PM_{10}.

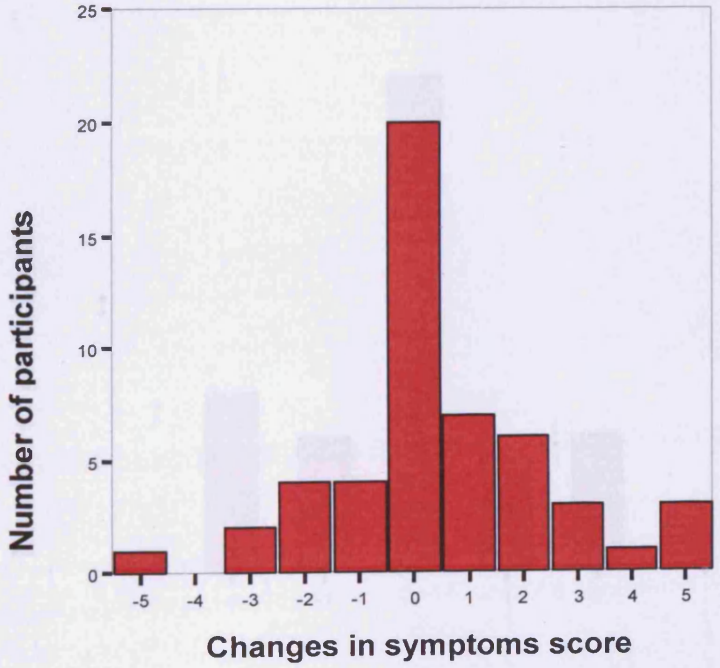

Figure 11b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 11.

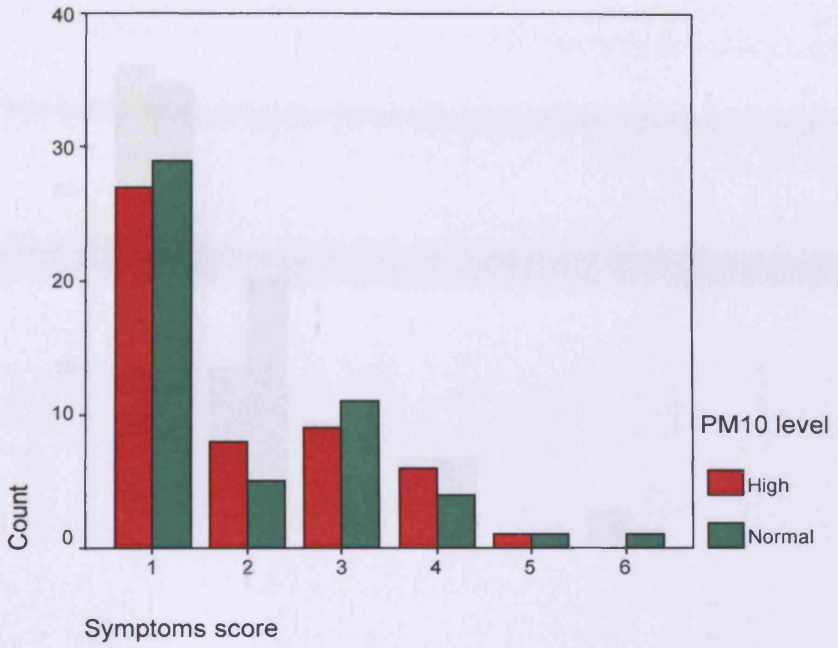

Figure 12a: Breakdown of respiratory symptoms score of question 12 and count of participant number, high v normal levels of PM_{10}.

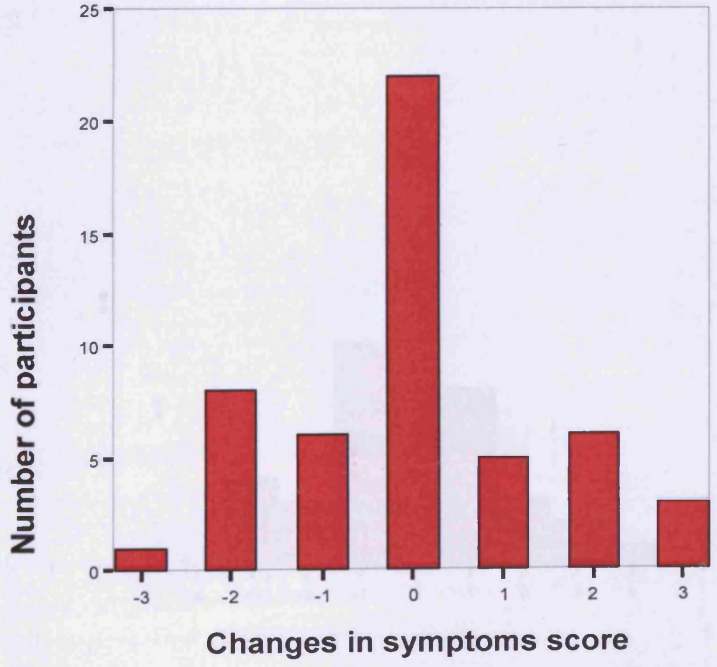

Figure 12b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 12.

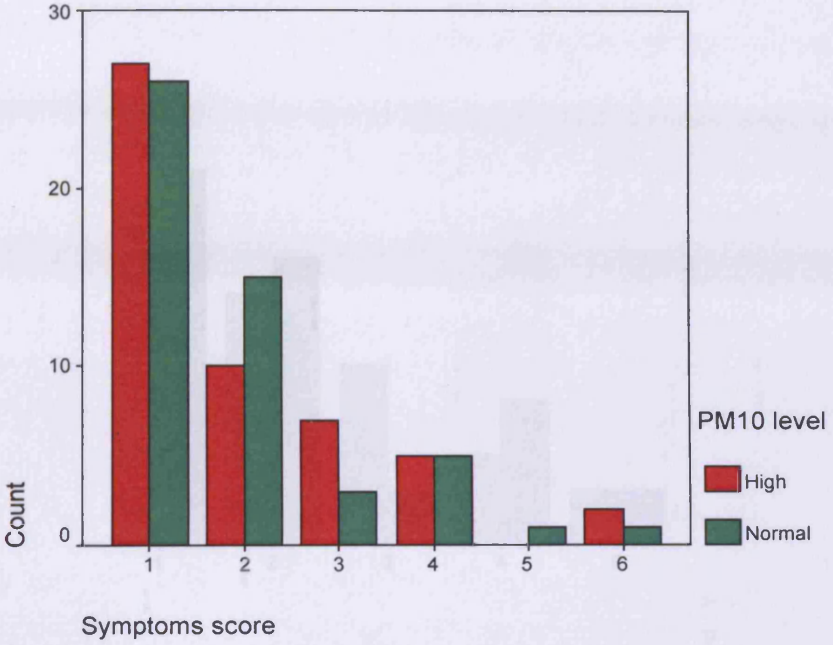

Figure 13a: Breakdown of respiratory symptoms score of question 13 and count of participant number, high v normal levels of PM_{10}.

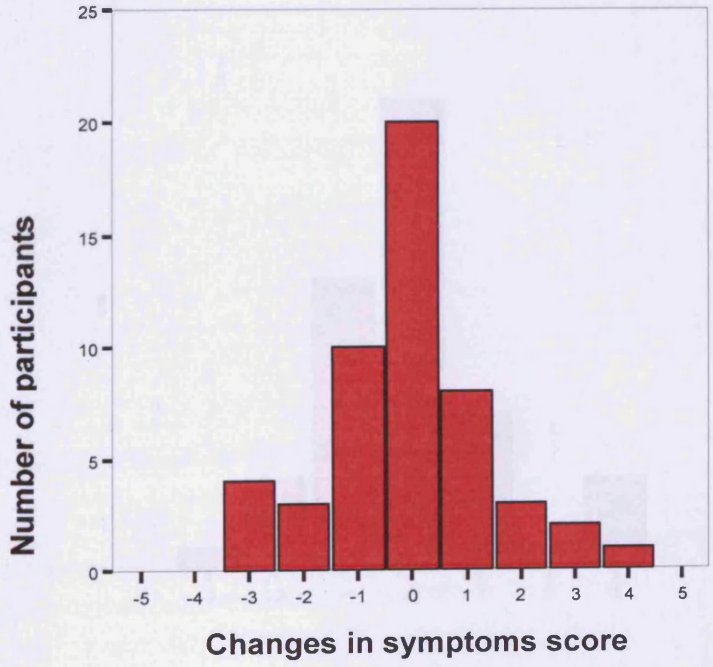

Figure 13b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 13.

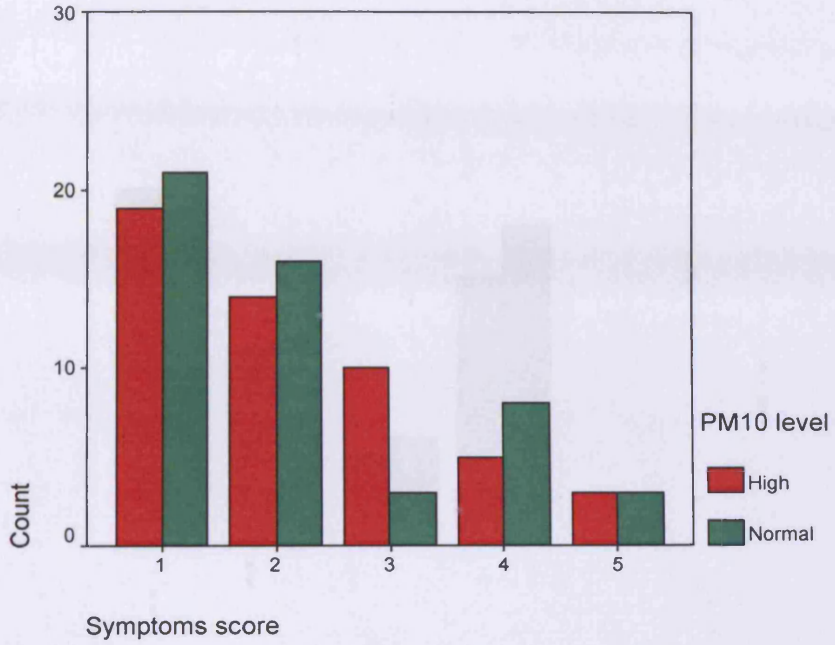

Figure 14a: Breakdown of respiratory symptoms score of question 14 and count of participant number, high v normal levels of PM_{10}.

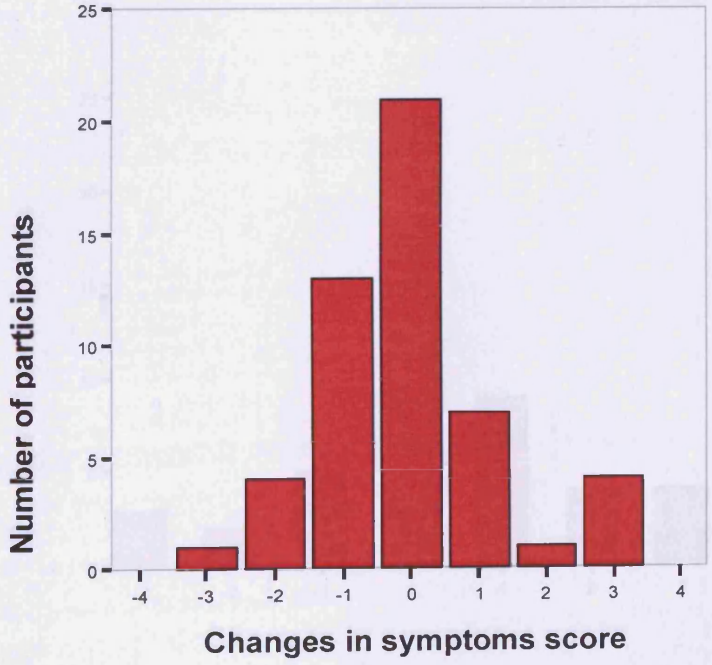

Figure 14b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 14.

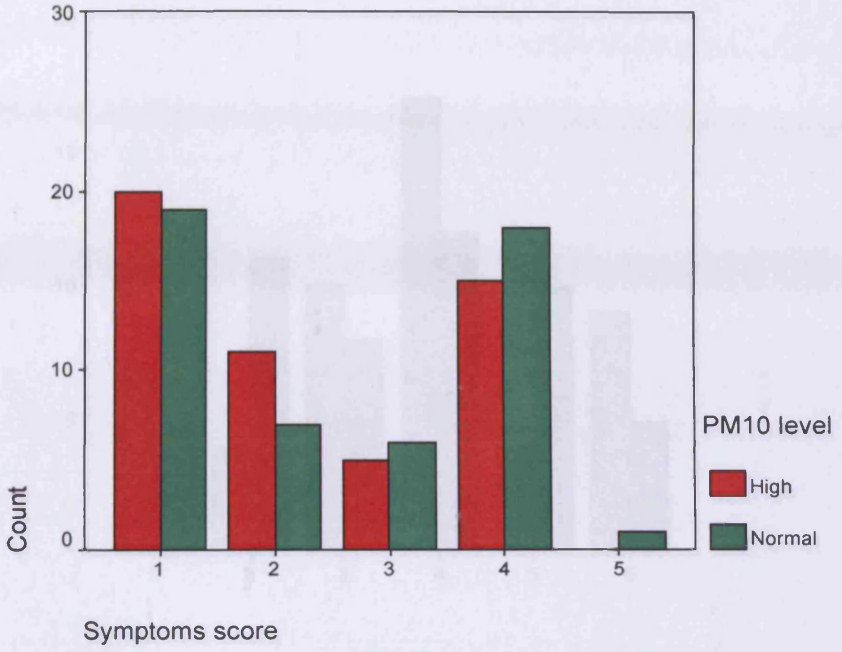

Figure 15a: Breakdown of respiratory symptoms score of question 15 and count of participant number, high v normal levels of PM_{10}.

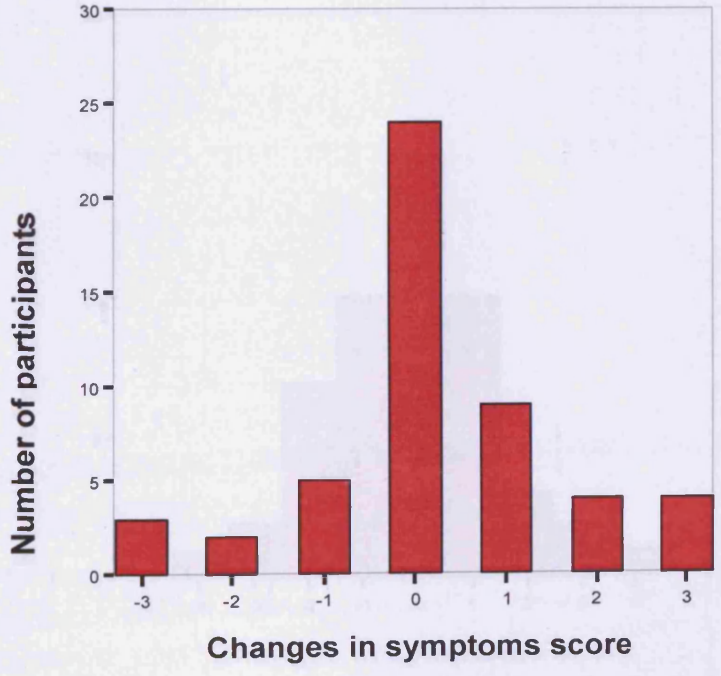

Figure 15b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 15.

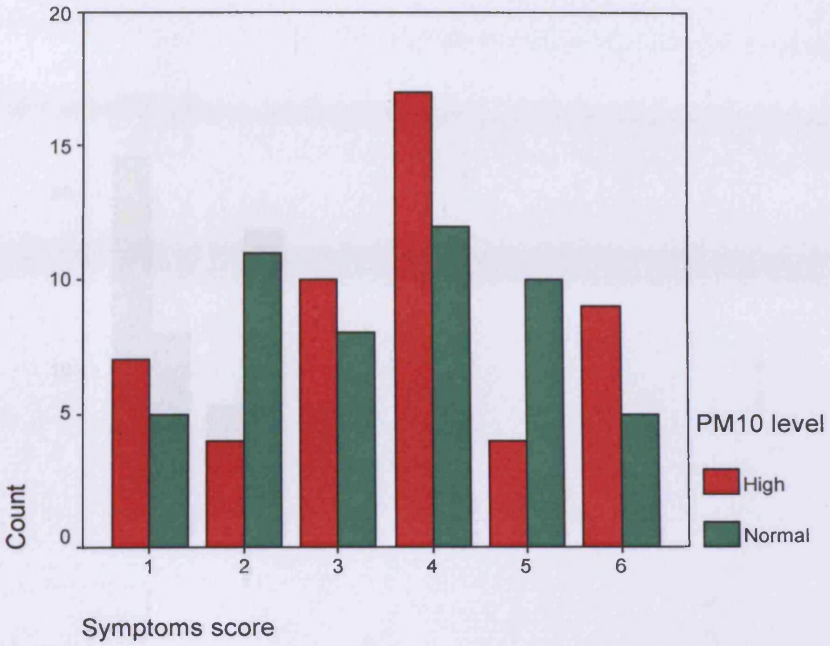

Figure 16a: Breakdown of respiratory symptoms score of question 16 and count of participant number, high v normal levels of PM_{10}.

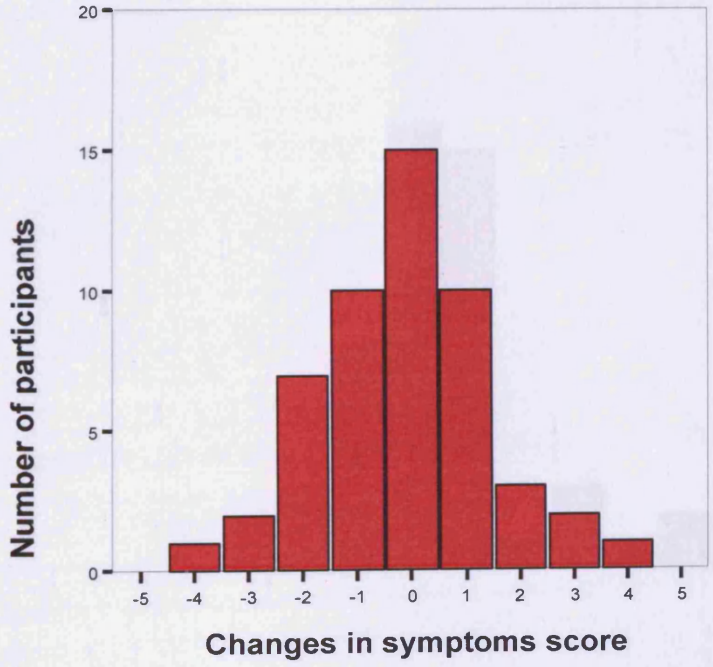

Figure 16b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 16.

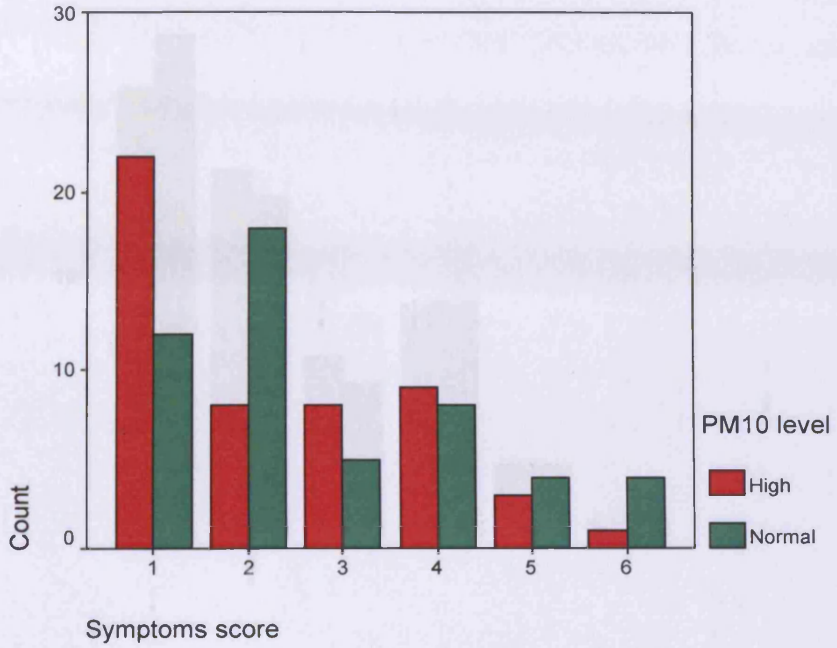

Figure 17a: Breakdown of respiratory symptoms score of question 17 and count of participant number, high v normal levels of PM_{10}.

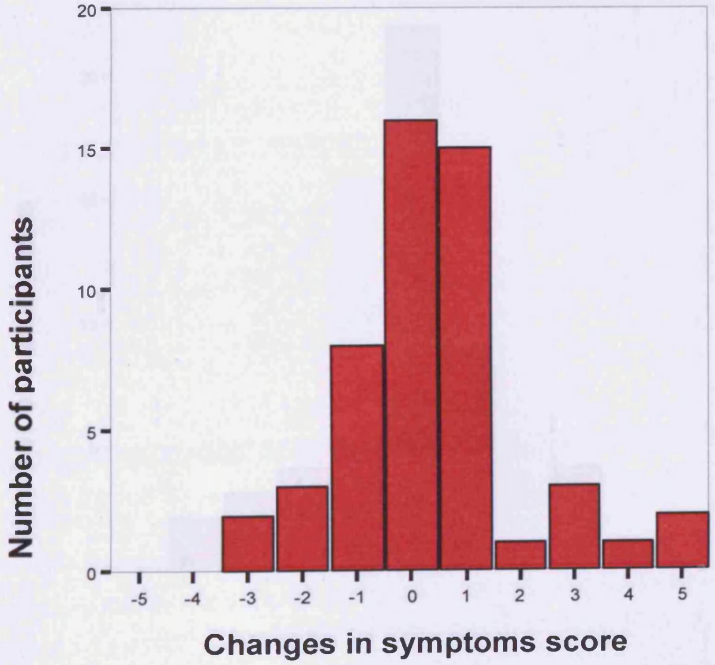

Figure 17b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 17.

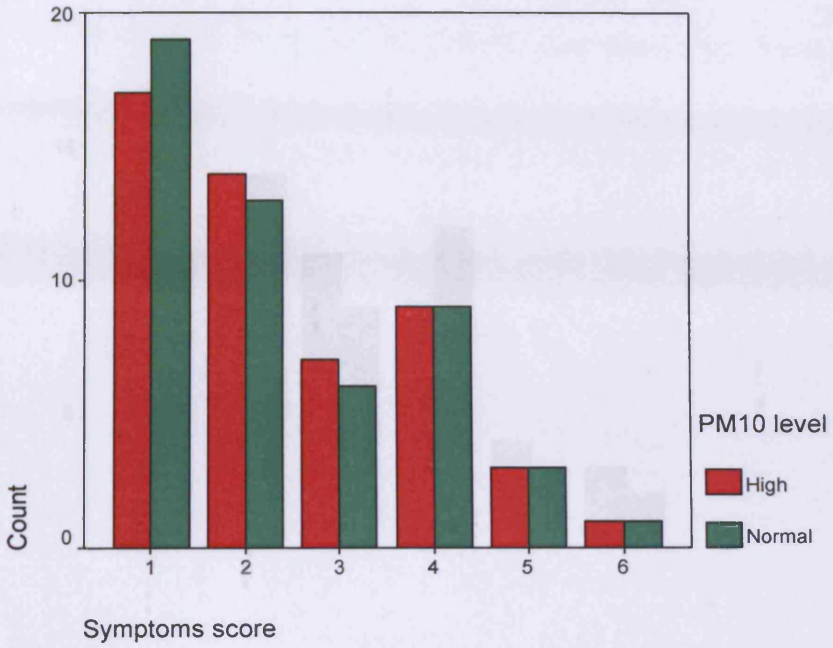

Figure 18a: Breakdown of respiratory symptoms score of question 18 and count of participant number, high v normal levels of PM_{10}.

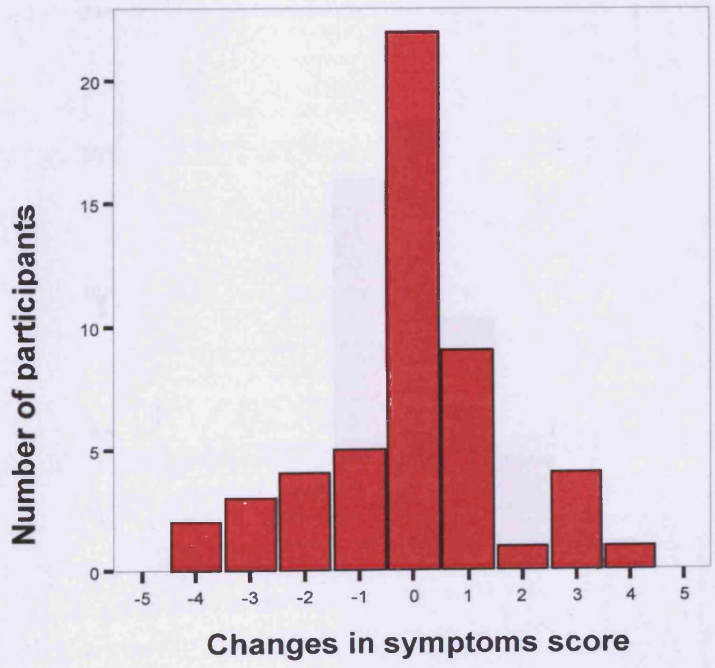

Figure 18b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 18.

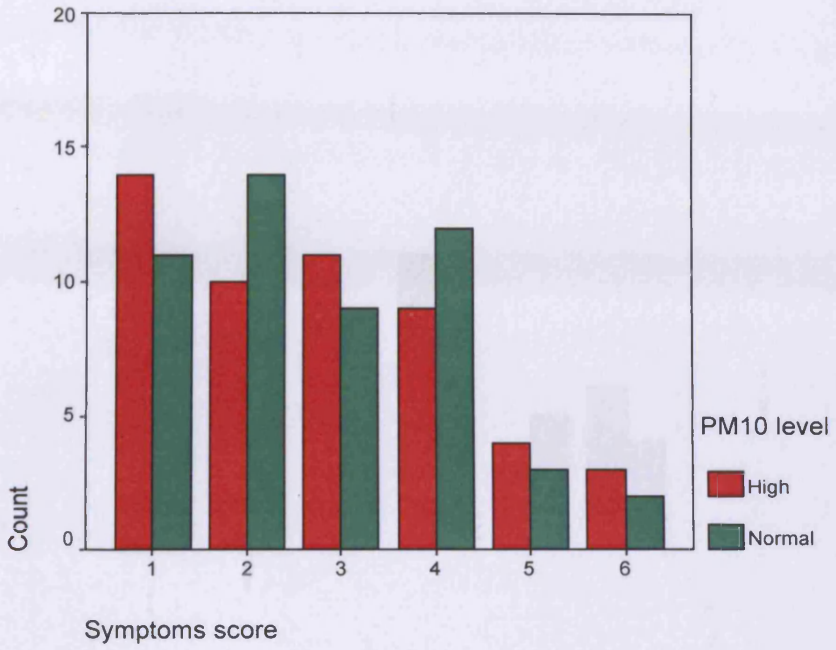

Figure 19a: Breakdown of respiratory symptoms score of question 19 and count of participant number, high v normal levels of PM_{10}.

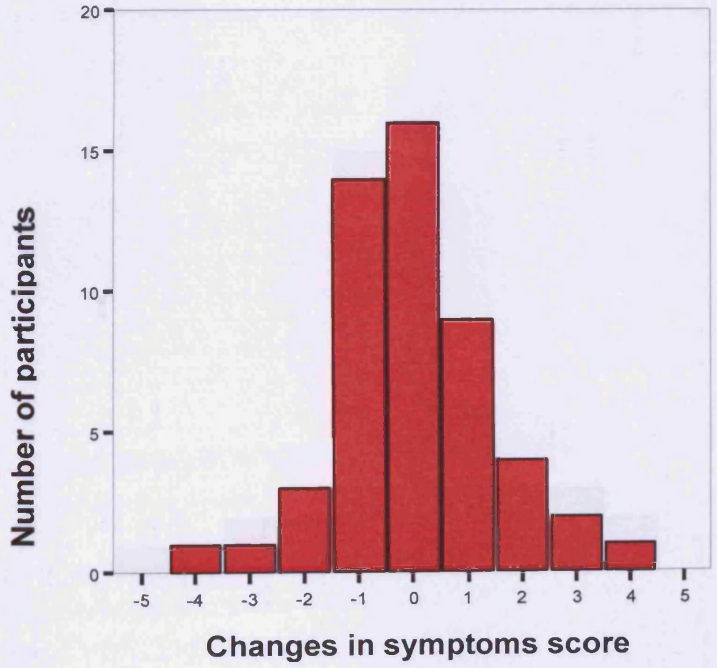

Figure 19b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 19.

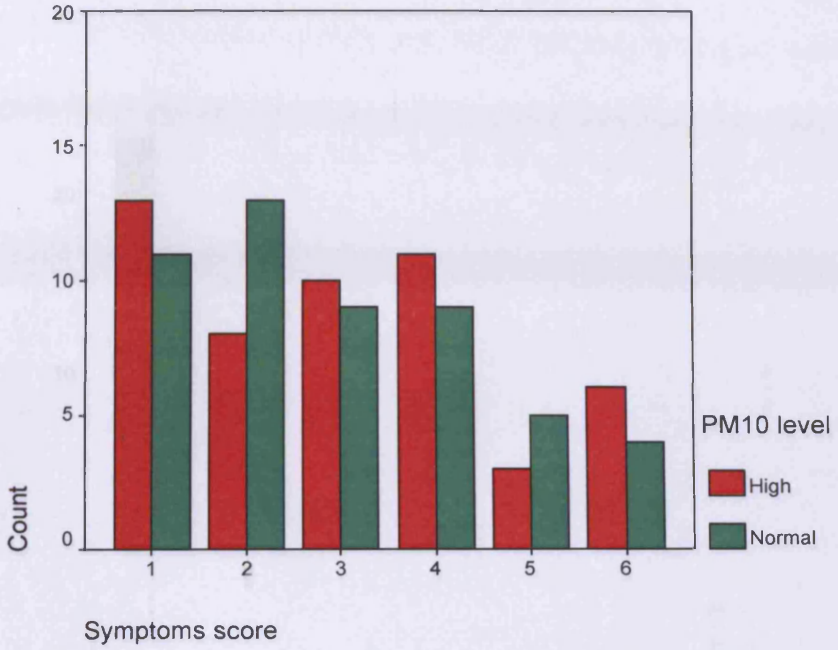

Figure 20a: Breakdown of respiratory symptoms score of question 20 and count of participant number, high v normal levels of PM_{10}.

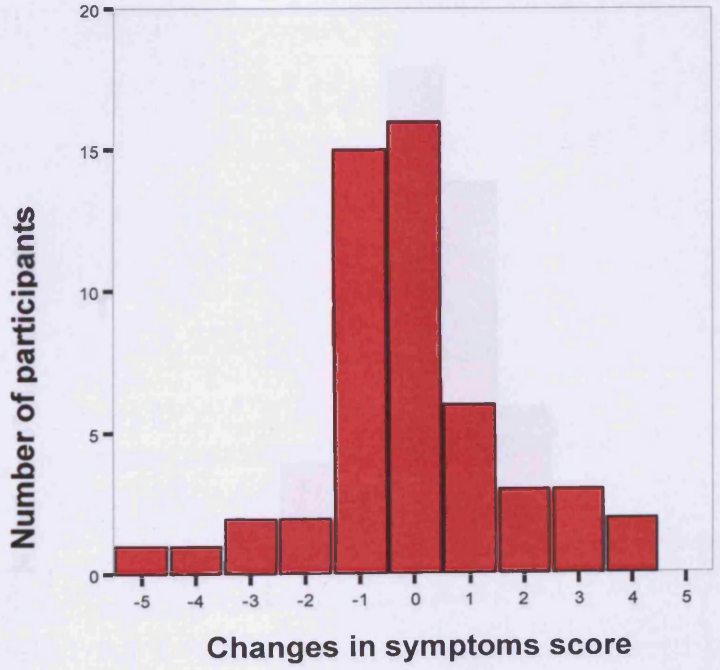

Figure 20b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 20.

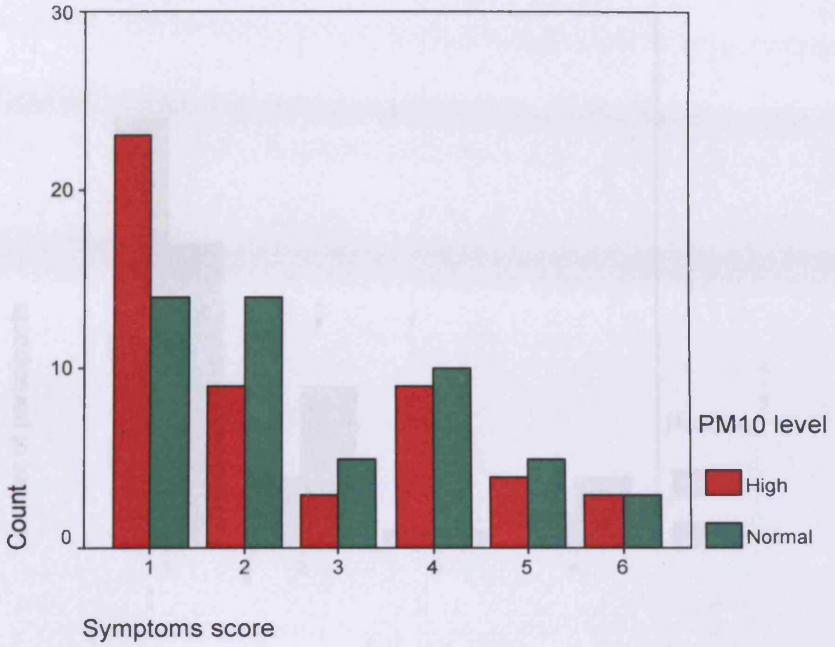

Figure 21a: Breakdown of respiratory symptoms score of question 21 and count of participant number, high v normal levels of PM_{10}.

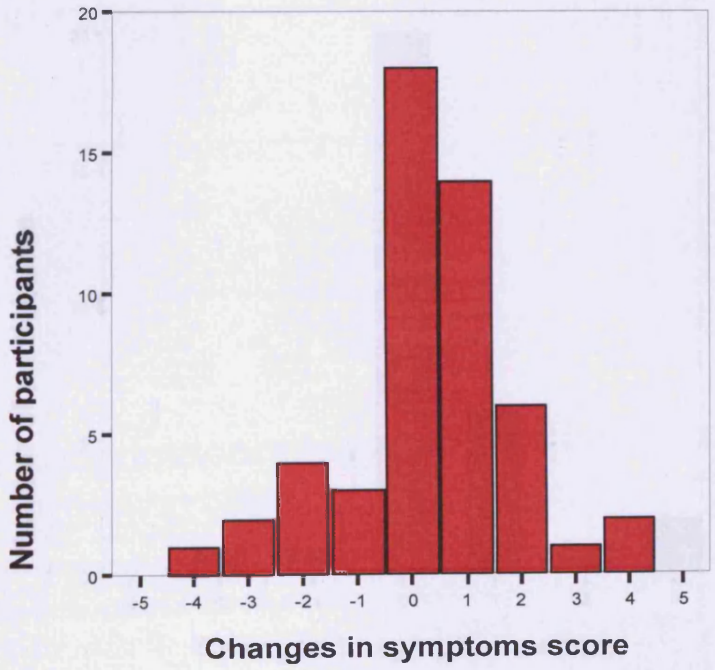

Figure 21b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 21.

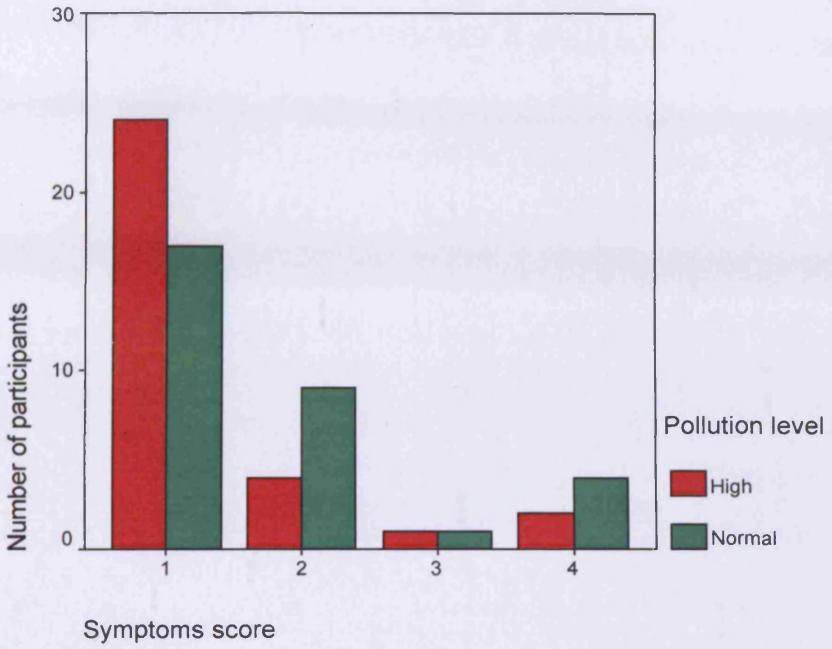

Figure 22a: Breakdown of respiratory symptoms score of question 22 and count of participant number, high v normal levels of PM_{10} (n=31)

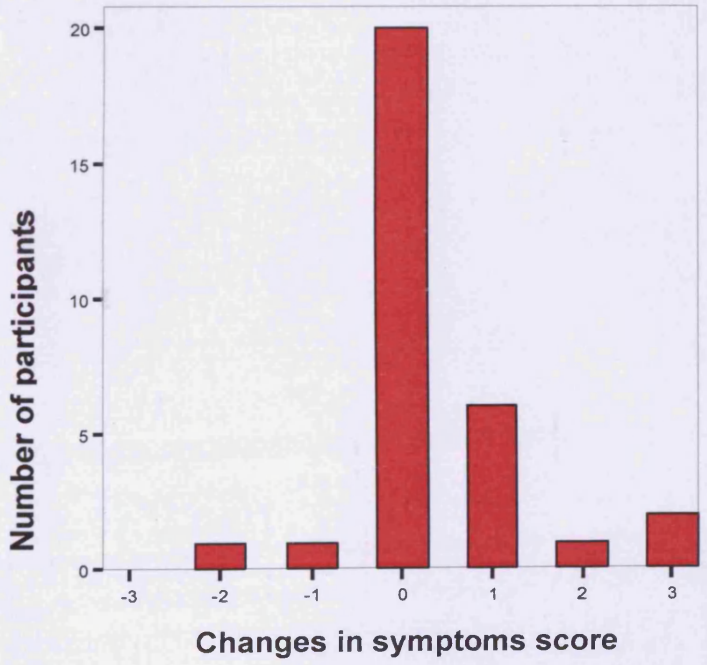

Figure 22b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution, question 22 (n=31).

APPENDIX 10.2

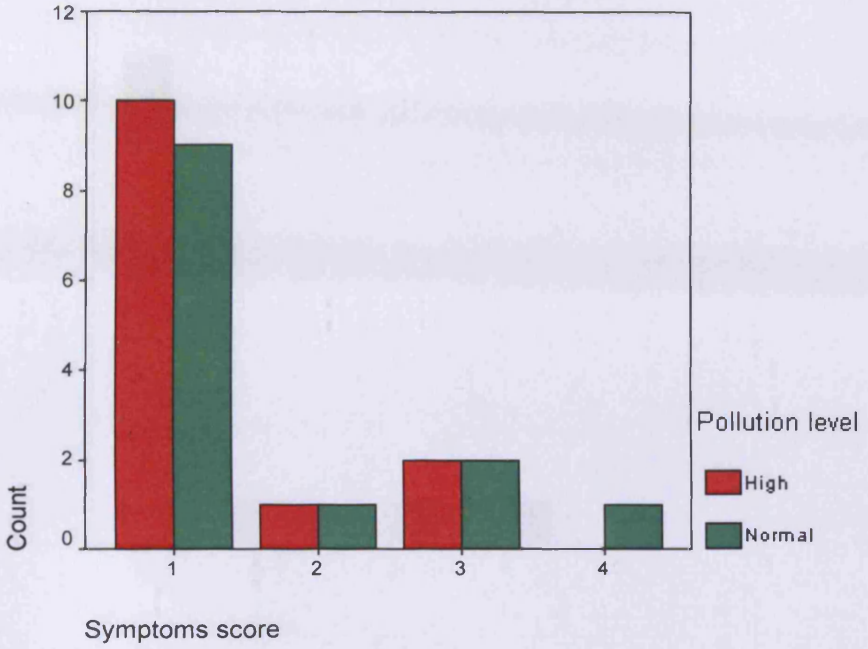

Figure 1a: Breakdown of respiratory symptoms score of question 1 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

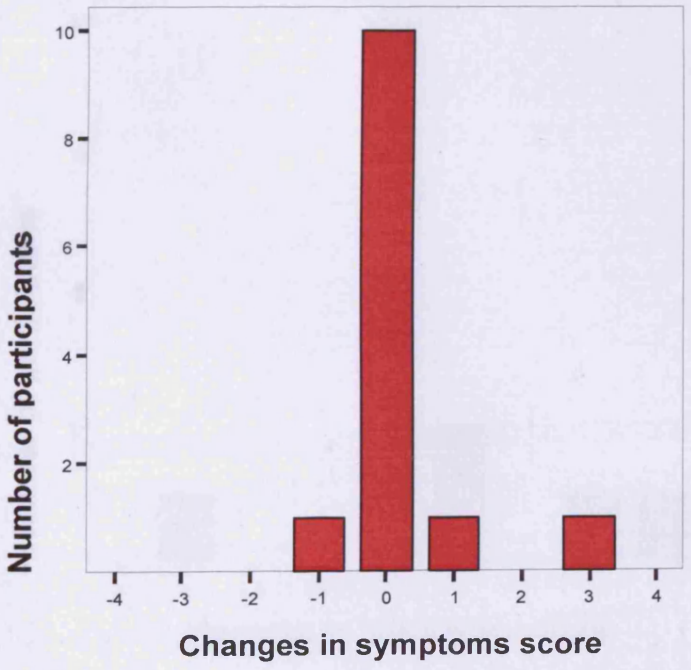

Figure 1b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 1.

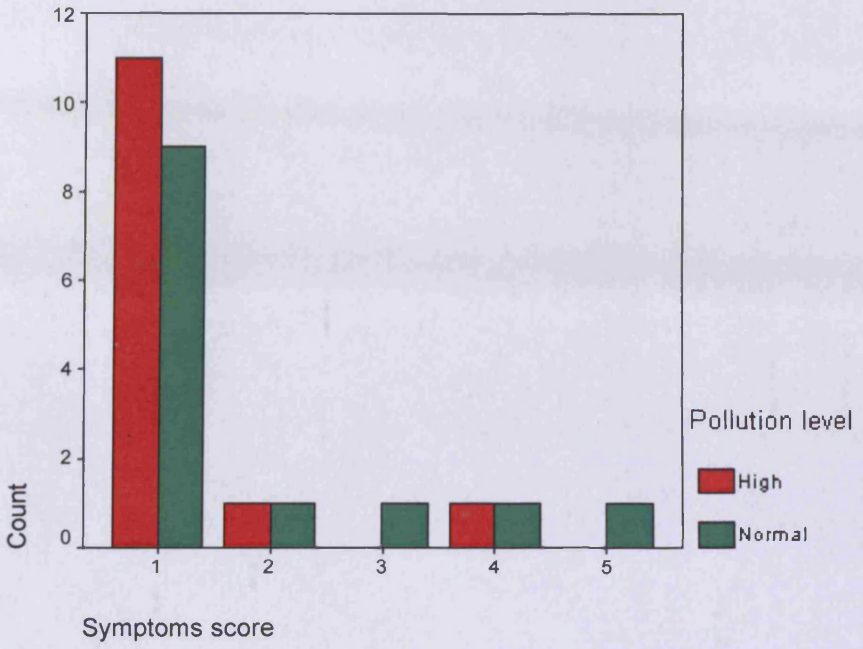

Figure 2a: Breakdown of respiratory symptoms score of question 2 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

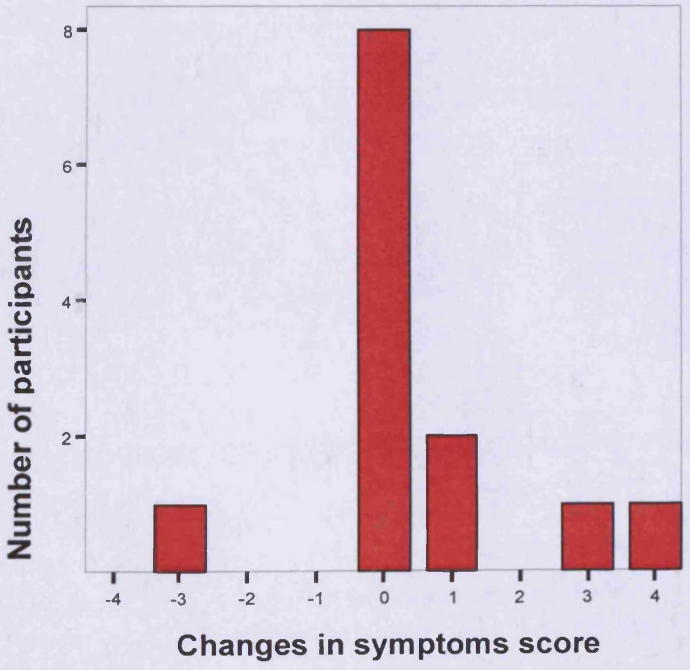

Figure 2b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 2.

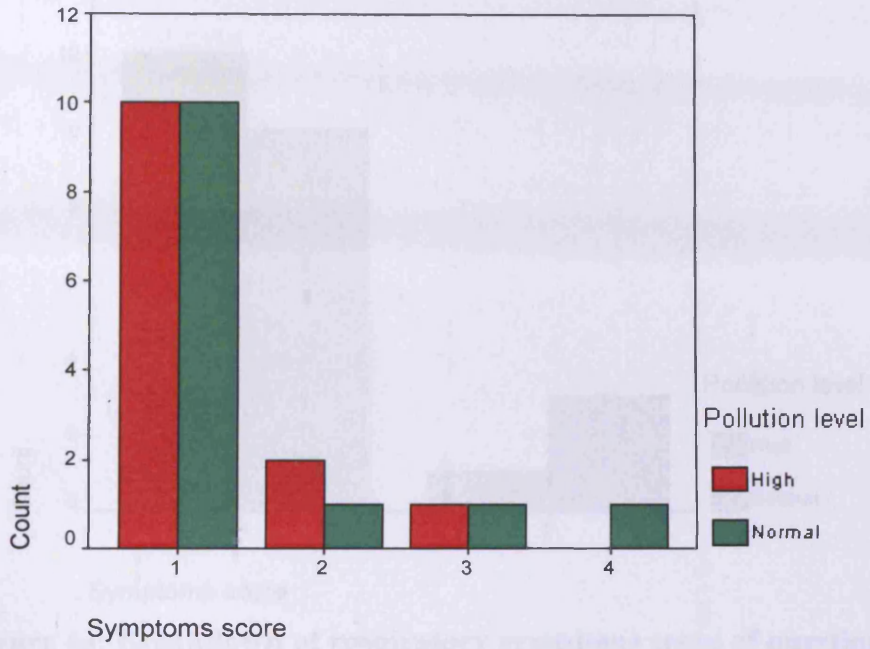

Figure 3a: Breakdown of respiratory symptoms score of question 3 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

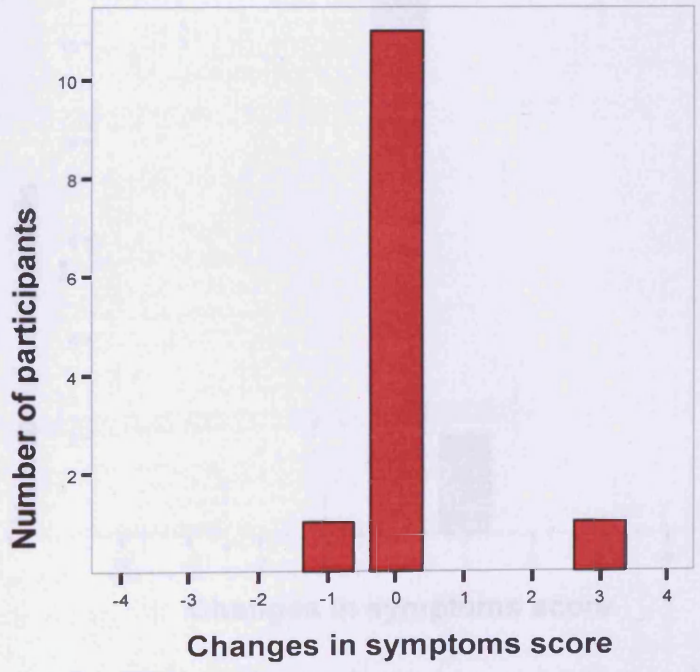

Figure 3b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 3.

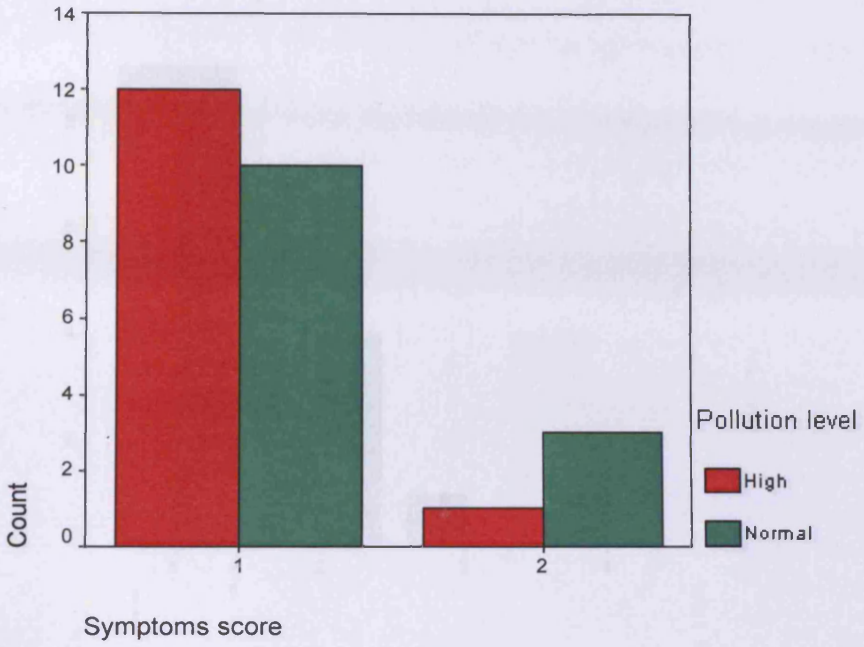

Figure 4a: Breakdown of respiratory symptoms score of question 4 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

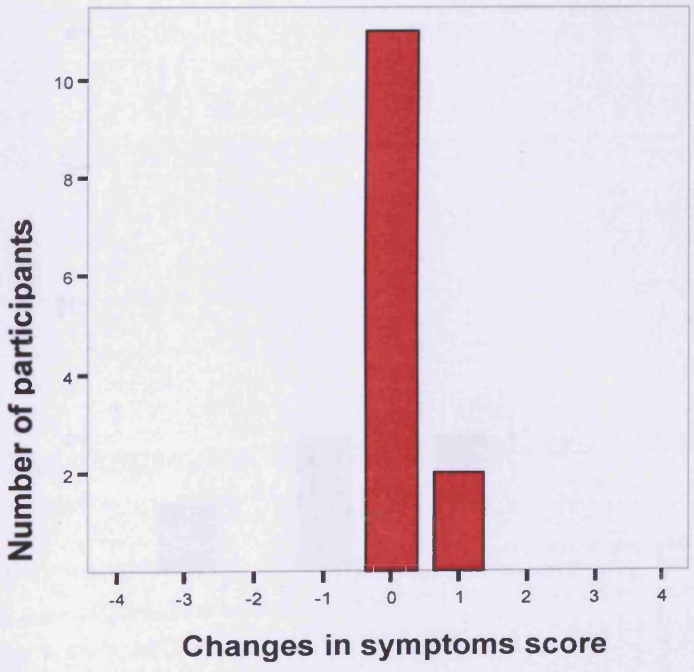

Figure 4b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 4.

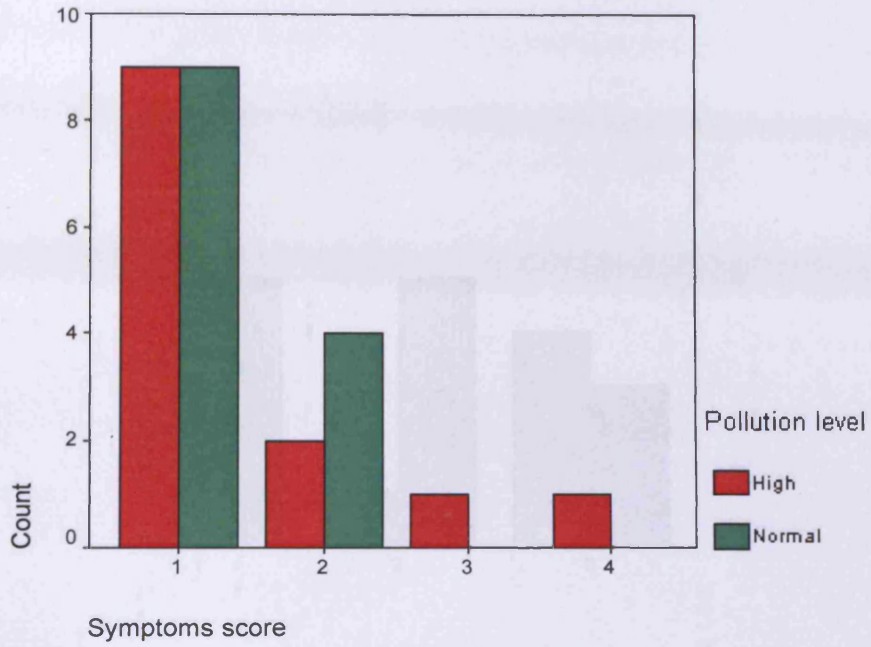

Figure 5a: Breakdown of respiratory symptoms score of question 5 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

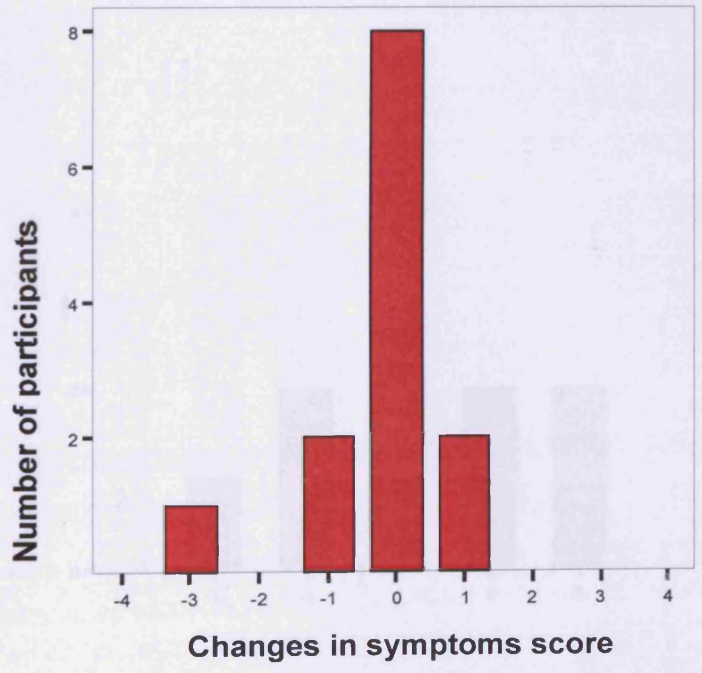

Figure 5b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 5.

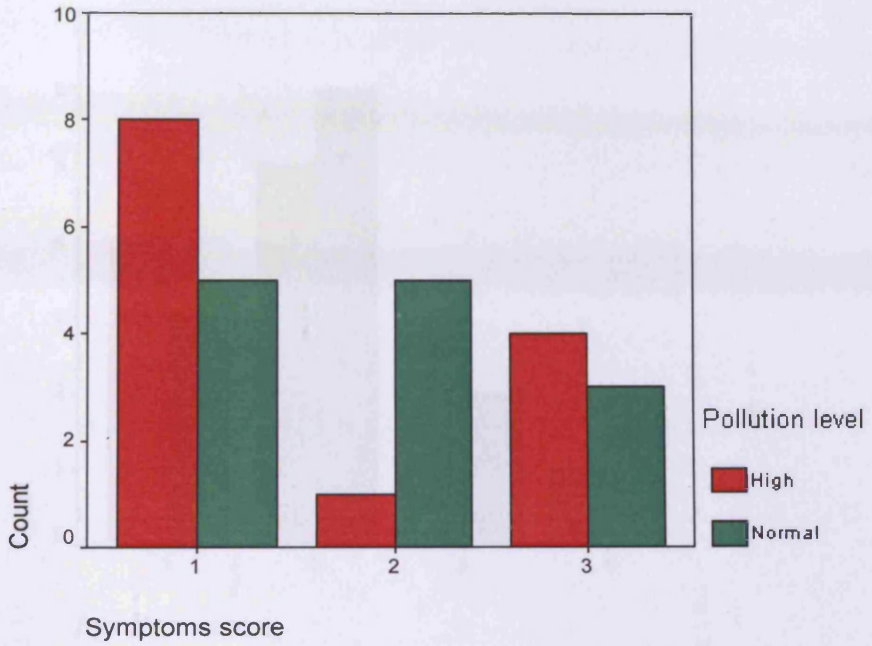

Figure 6a: Breakdown of respiratory symptoms score of question 6 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

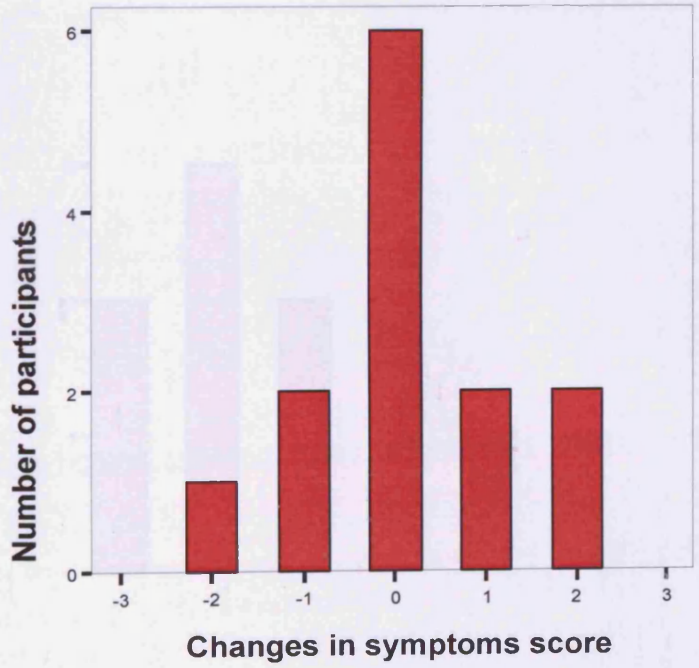

Figure 6b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 6.

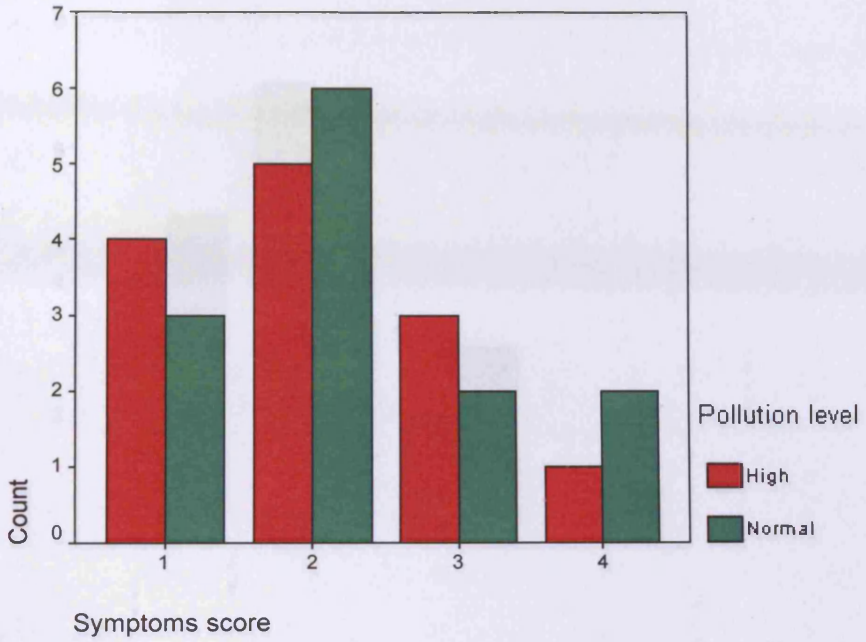

Figure 7a: Breakdown of respiratory symptoms score of question 7 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

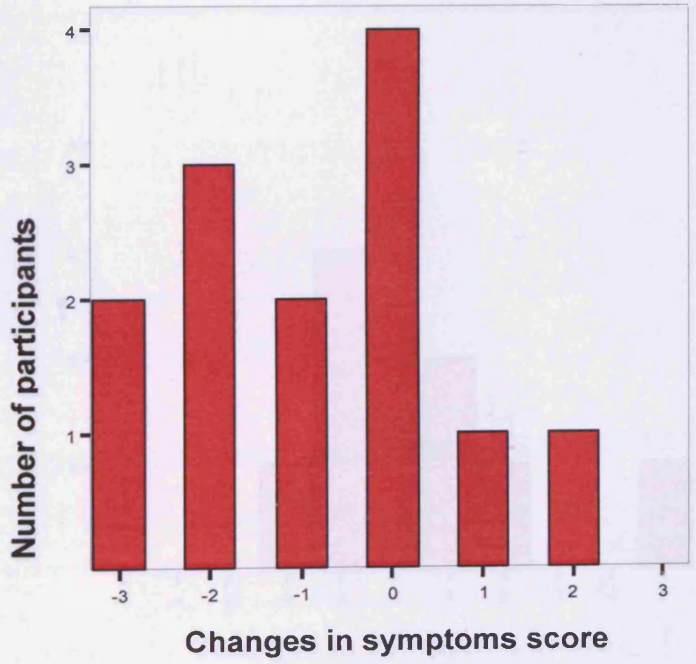

Figure 7b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 7.

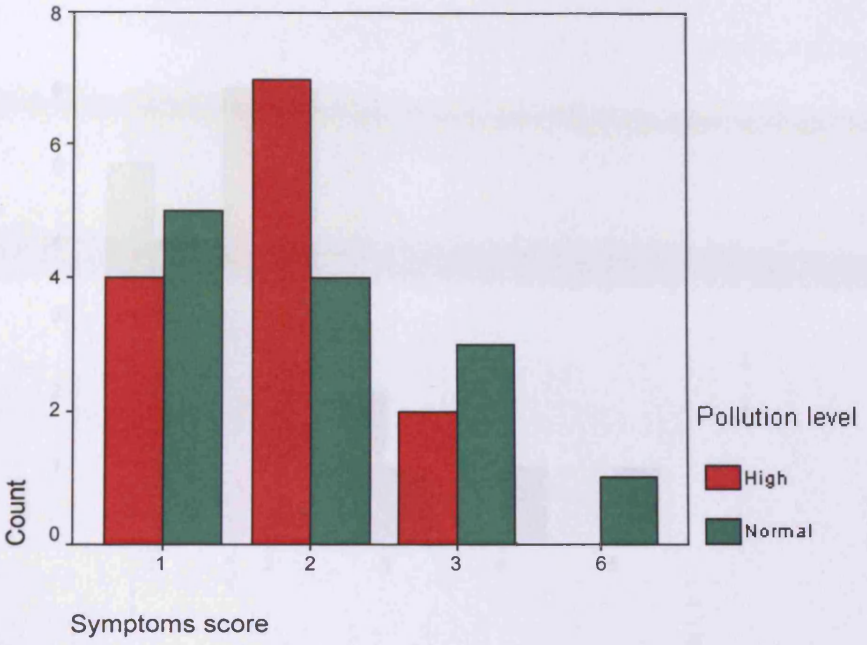

Figure 8a: Breakdown of respiratory symptoms score of question 8 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

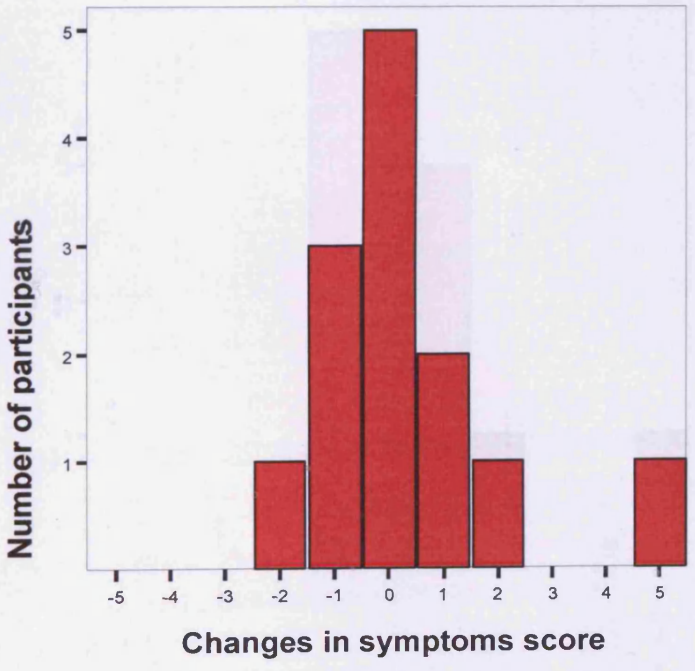

Figure 8b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 8.

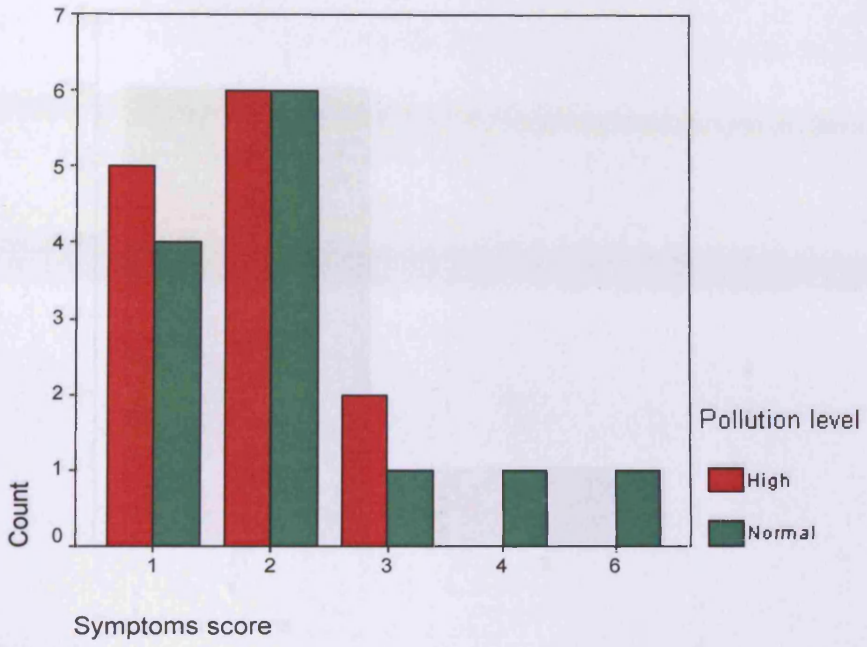

Figure 9a: Breakdown of respiratory symptoms score of question 9 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

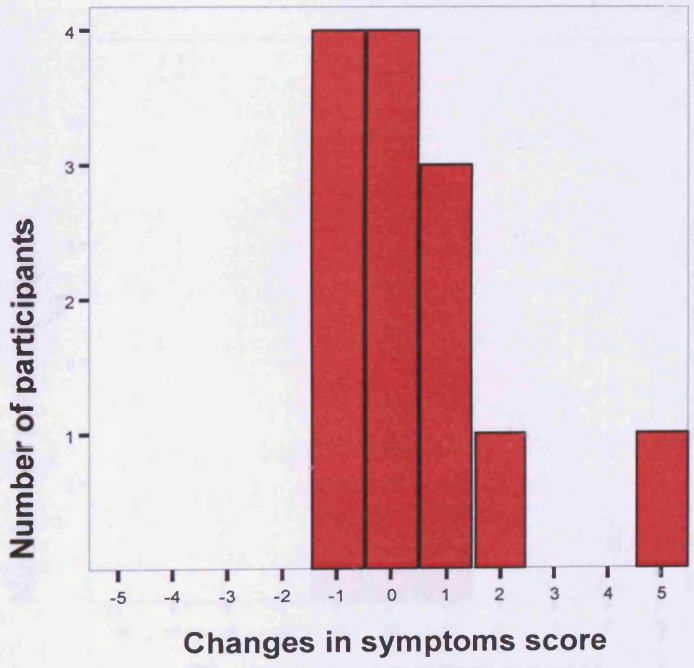

Figure 9b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 9.

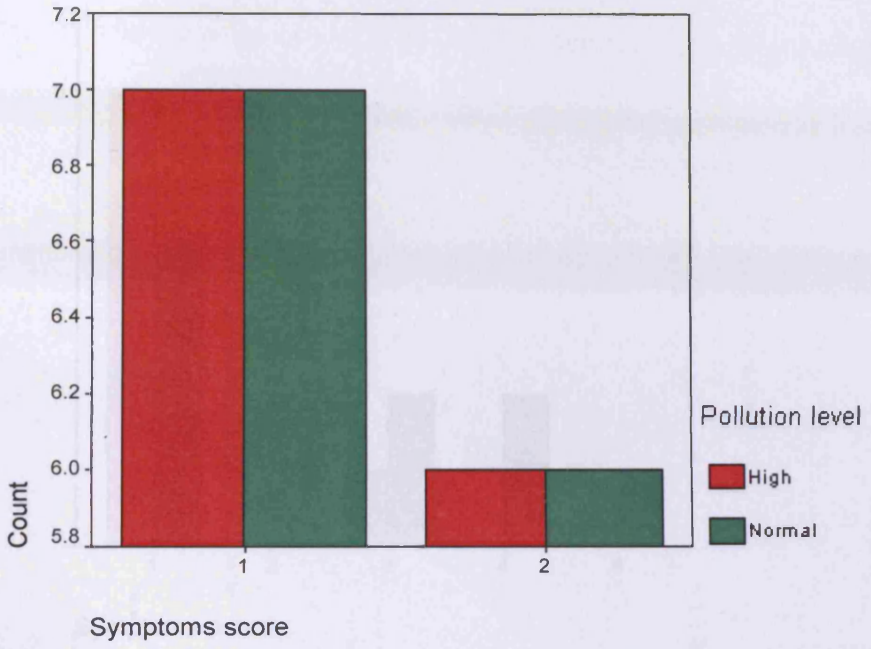

Figure 10a: Breakdown of respiratory symptoms score of question 10 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

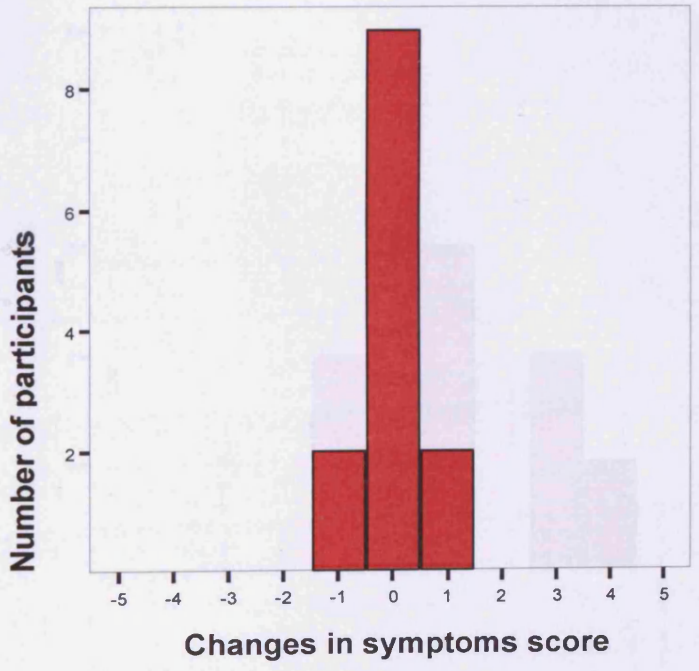

Figure 10b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 10.

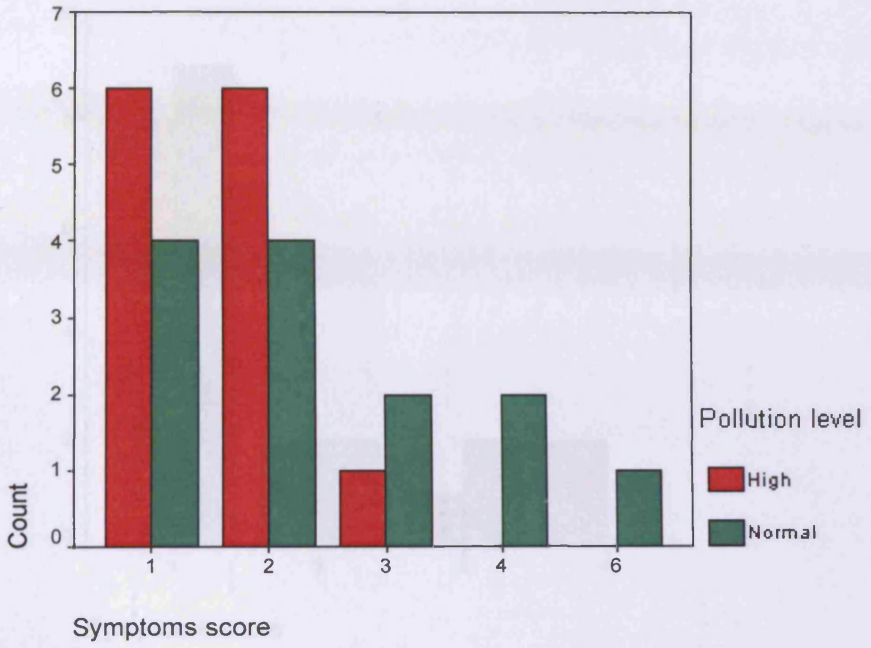

Figure 11a: Breakdown of respiratory symptoms score of question 11 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

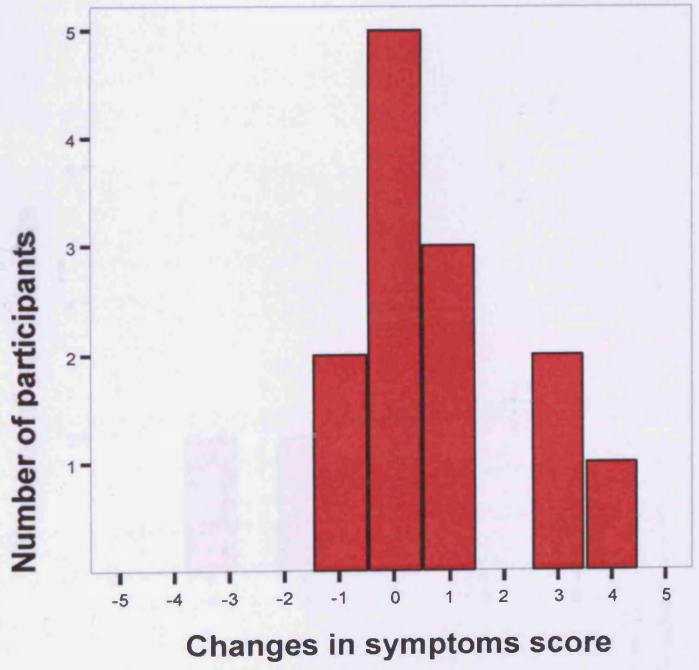

Figure 11b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 11.

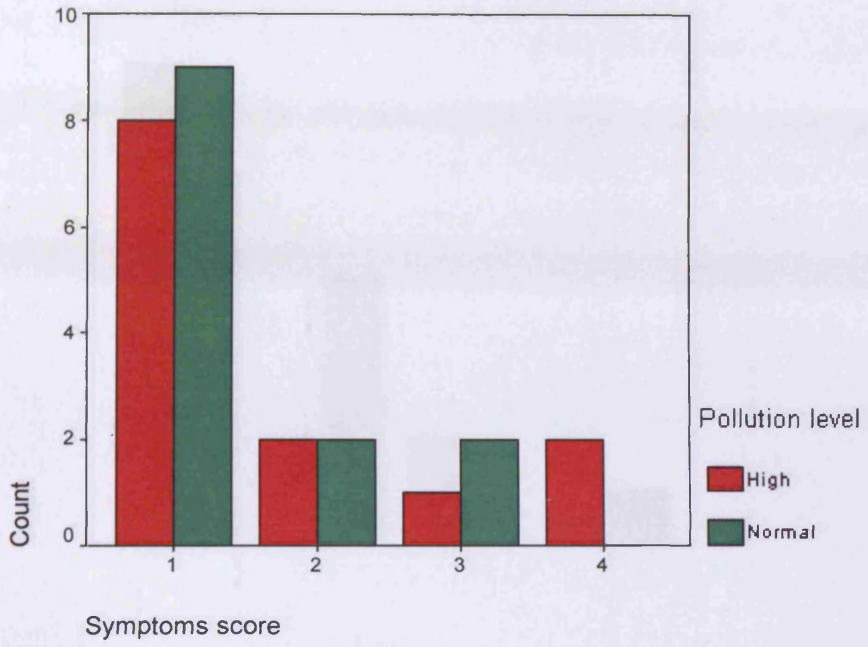

Figure 12a: Breakdown of respiratory symptoms score of question 12 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

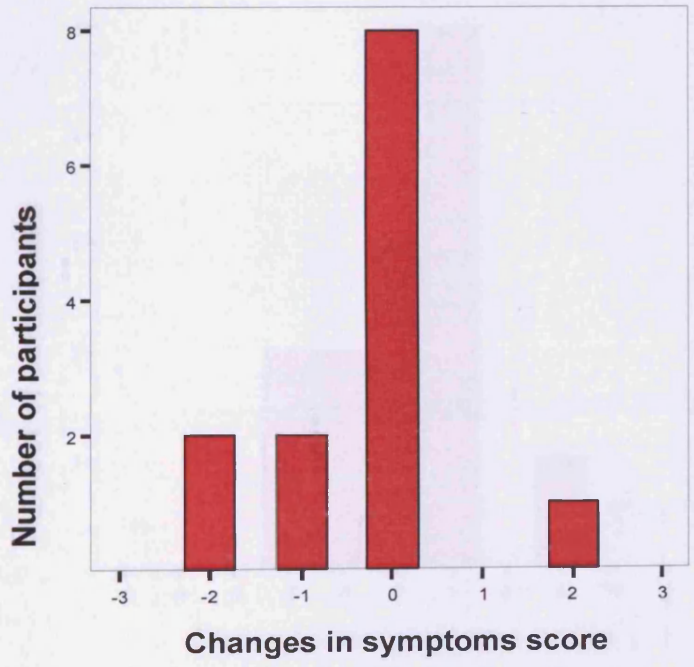

Figure 12b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 12.

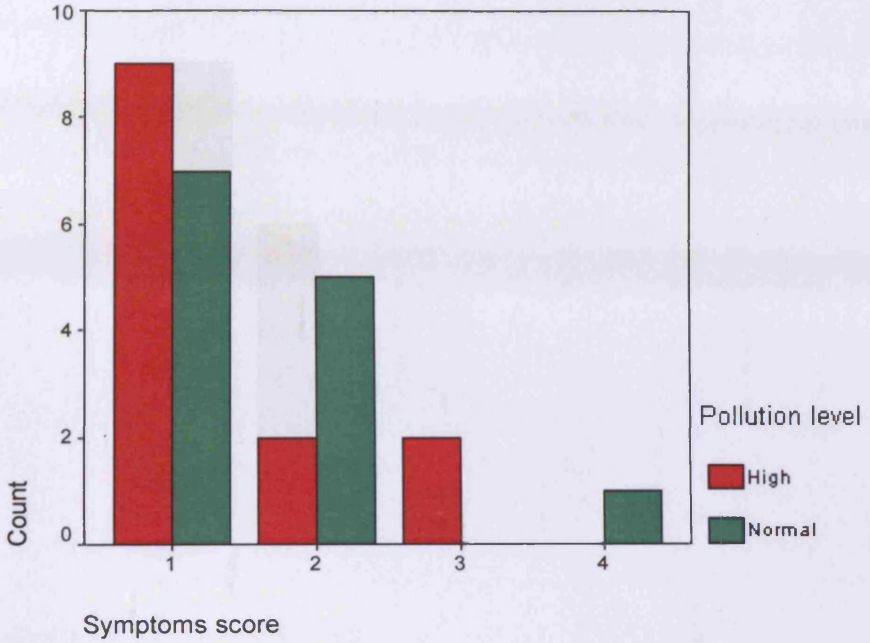

Figure 13a: Breakdown of respiratory symptoms score of question 13 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

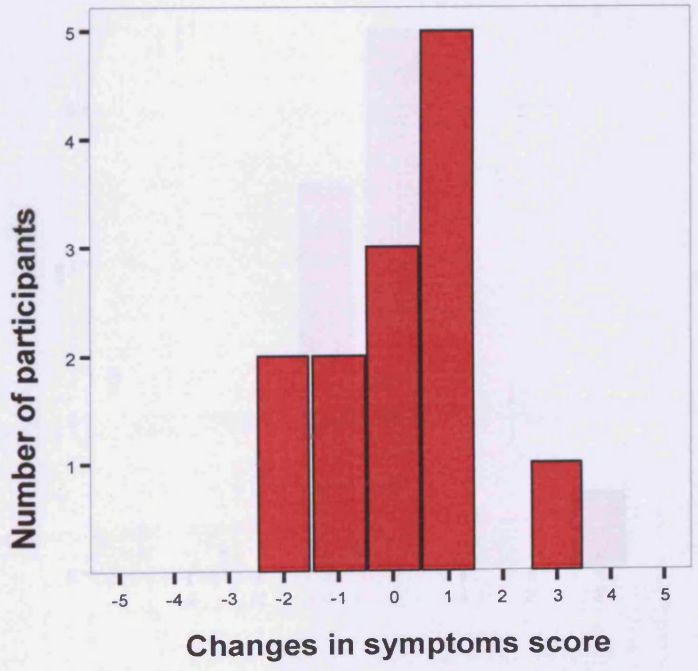

Figure 13b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 13.

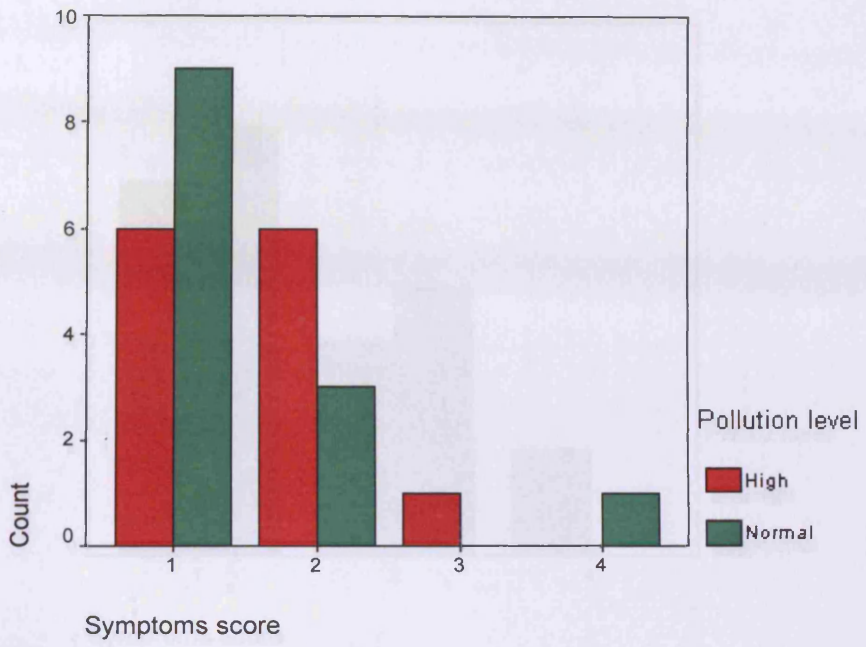

Figure 14a: Breakdown of respiratory symptoms score of question 14 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

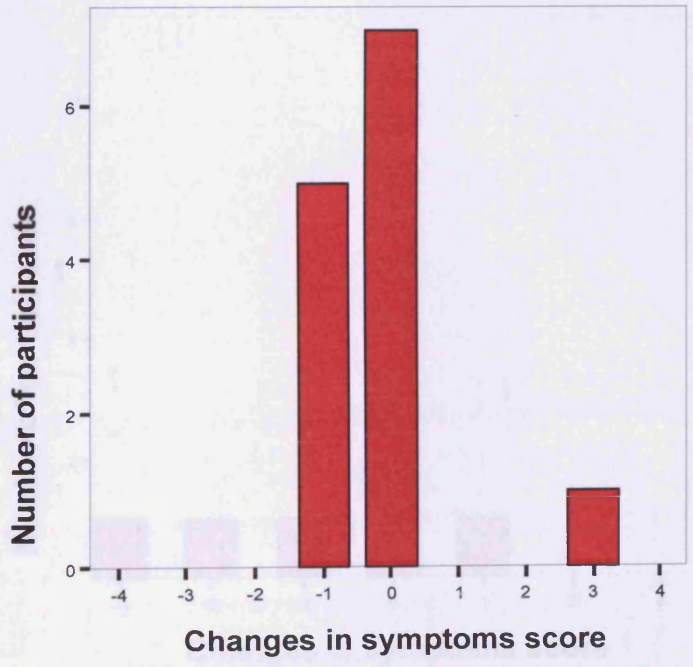

Figure 14b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 14.

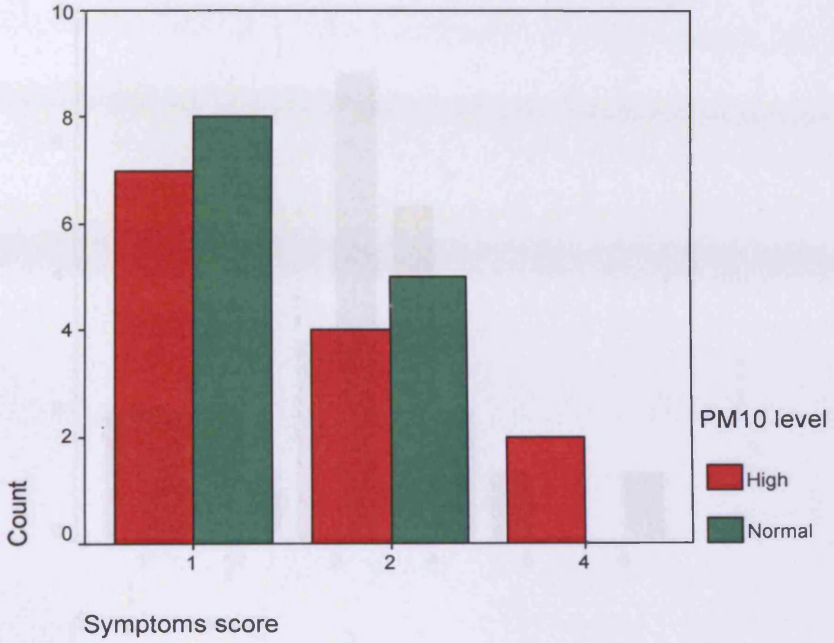

Figure 15a: Breakdown of respiratory symptoms score of question 15 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

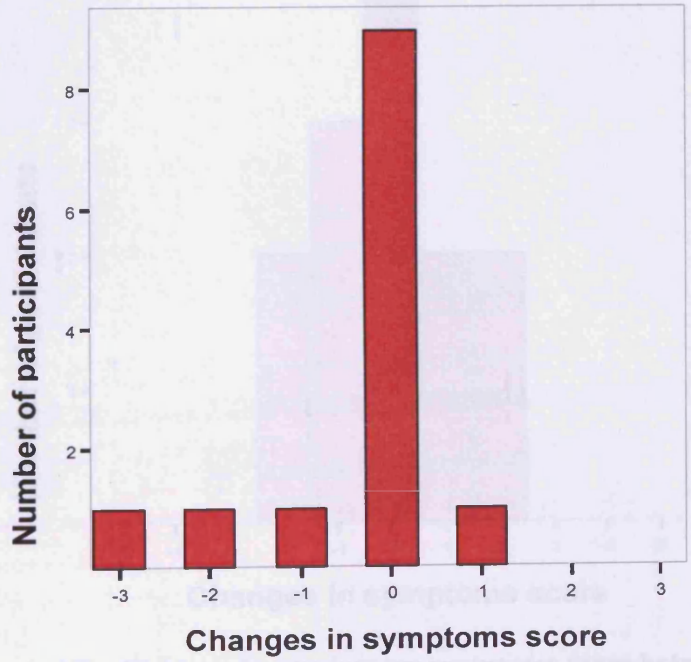

Figure 15b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 15.

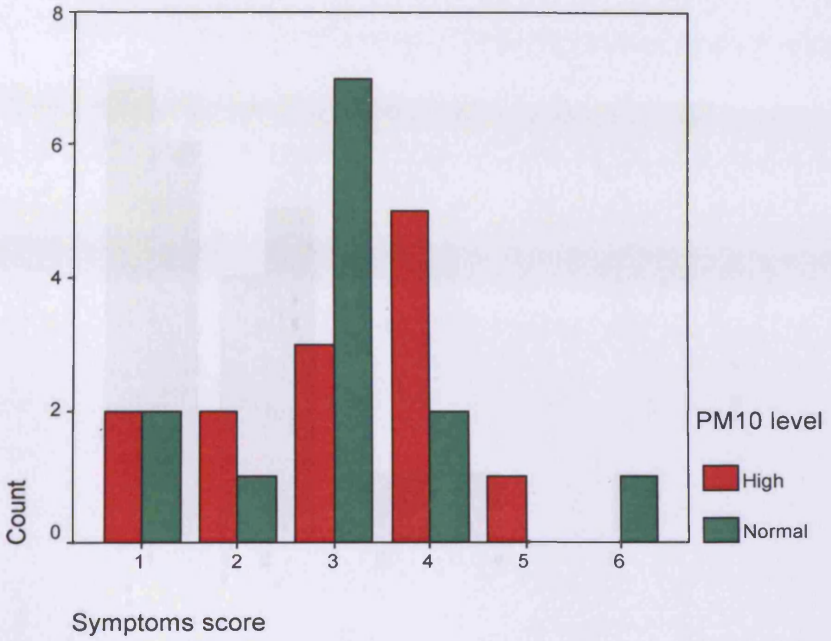

Figure 16a: Breakdown of respiratory symptoms score of question 16 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

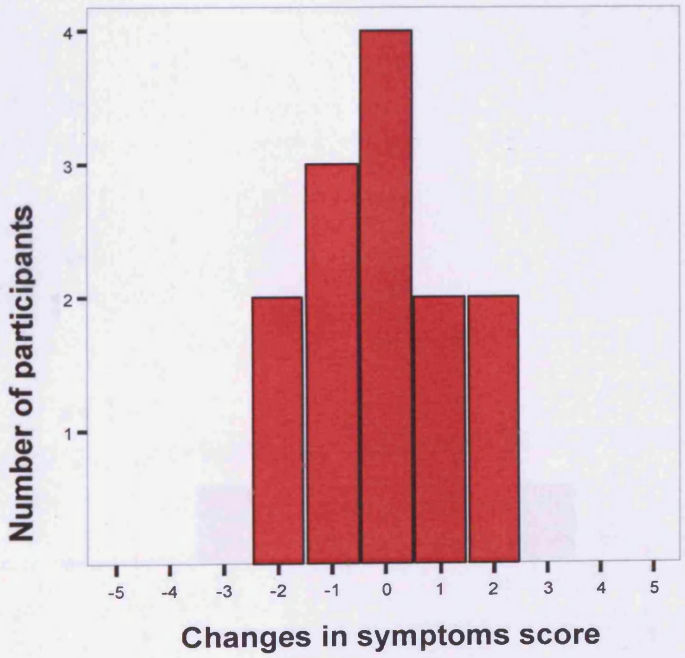

Figure 16b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 16.

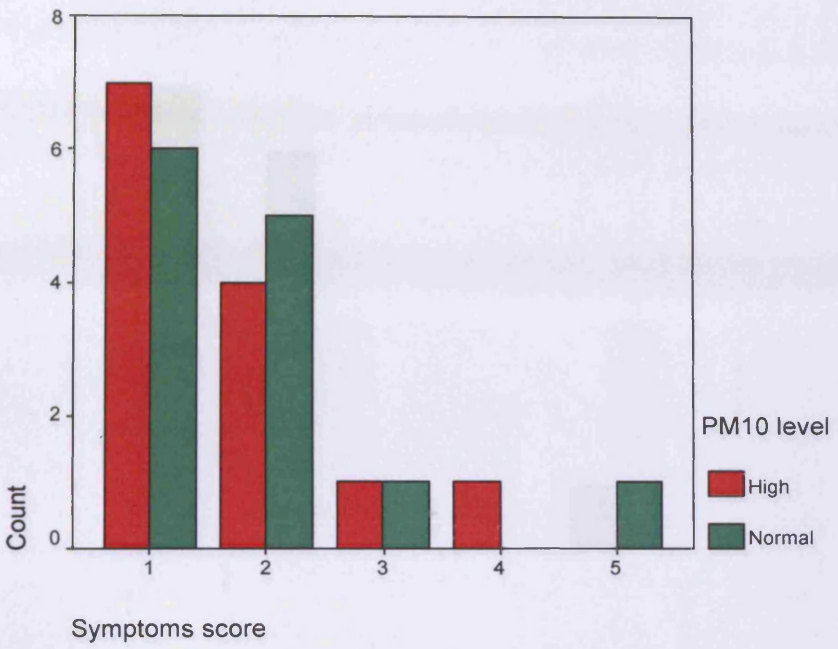

Figure 17a: Breakdown of respiratory symptoms score of question 17 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

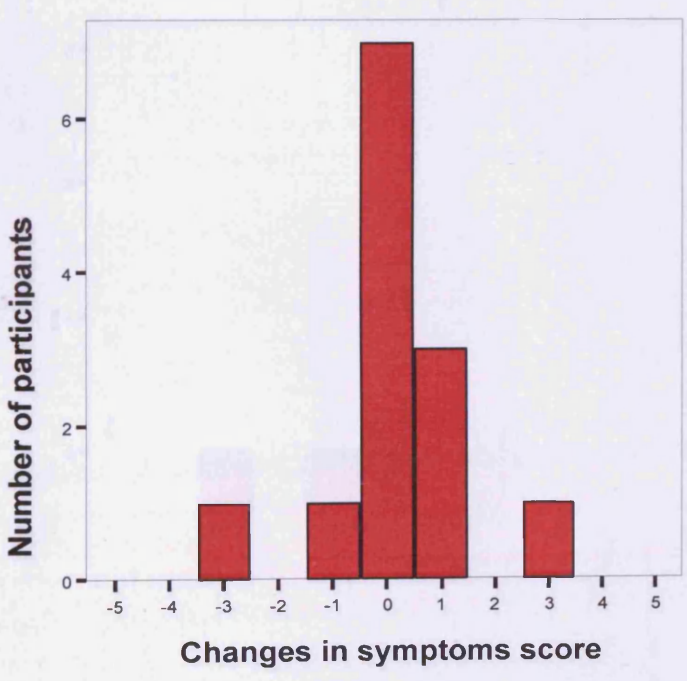

Figure 17b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 17.

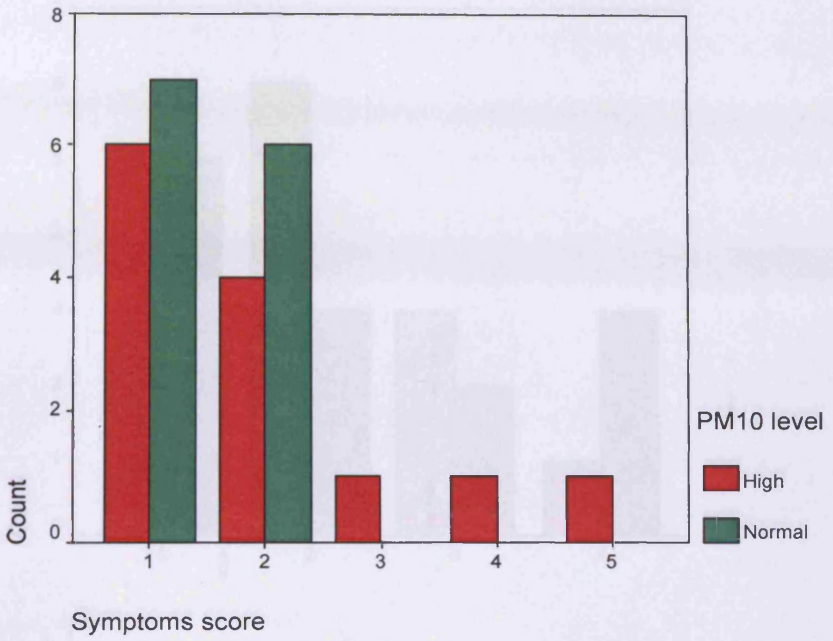

Figure 18a: Breakdown of respiratory symptoms score of question 18 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

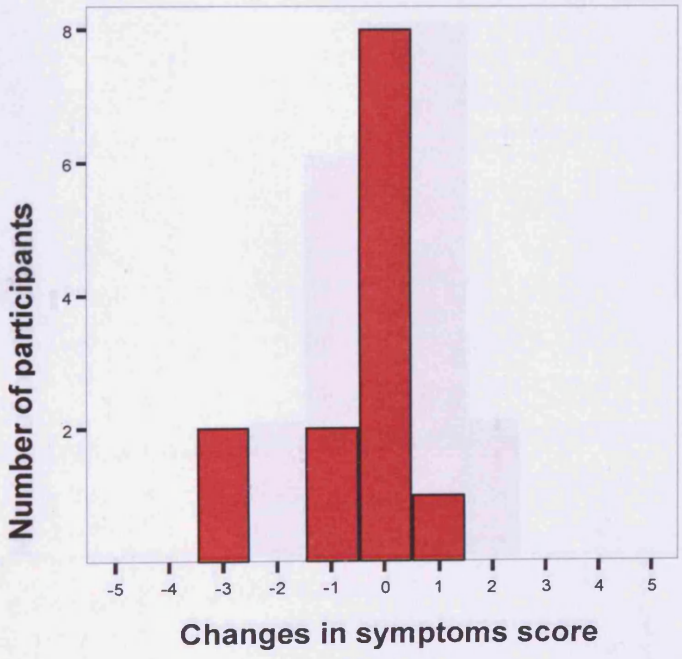

Figure 18b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 18.

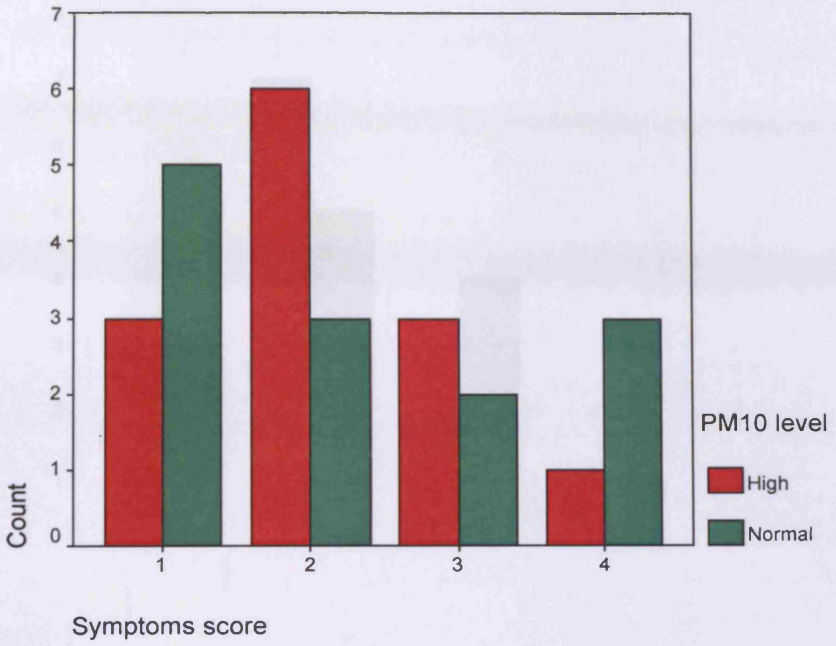

Figure 19a: Breakdown of respiratory symptoms score of question 19 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

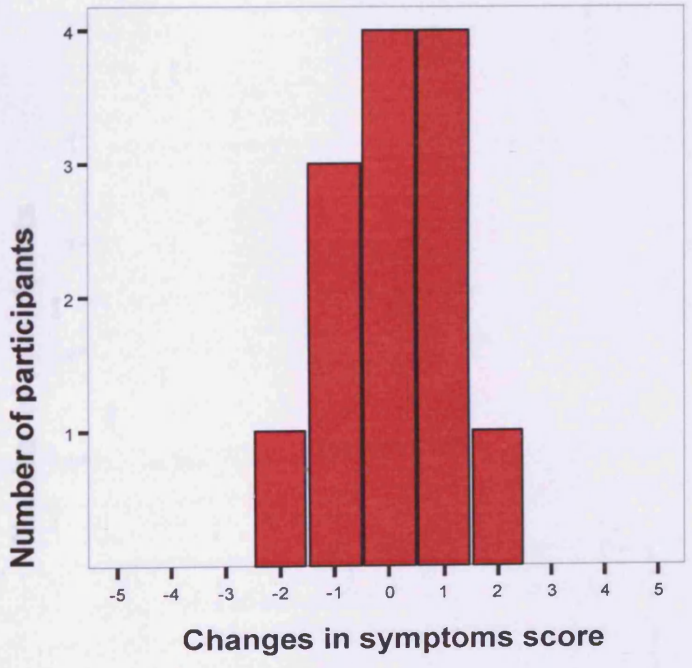

Figure 19b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 19.

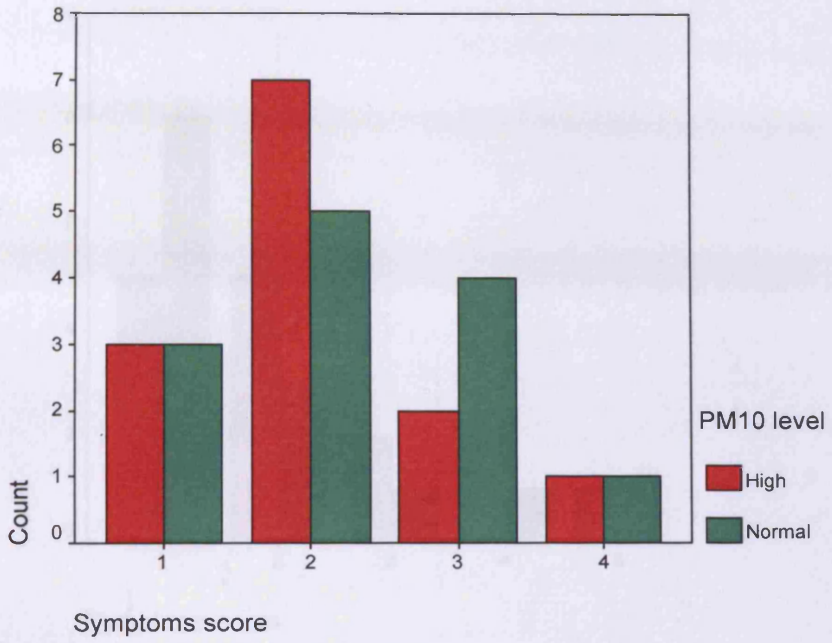

Figure 20a: Breakdown of respiratory symptoms score of question 20 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

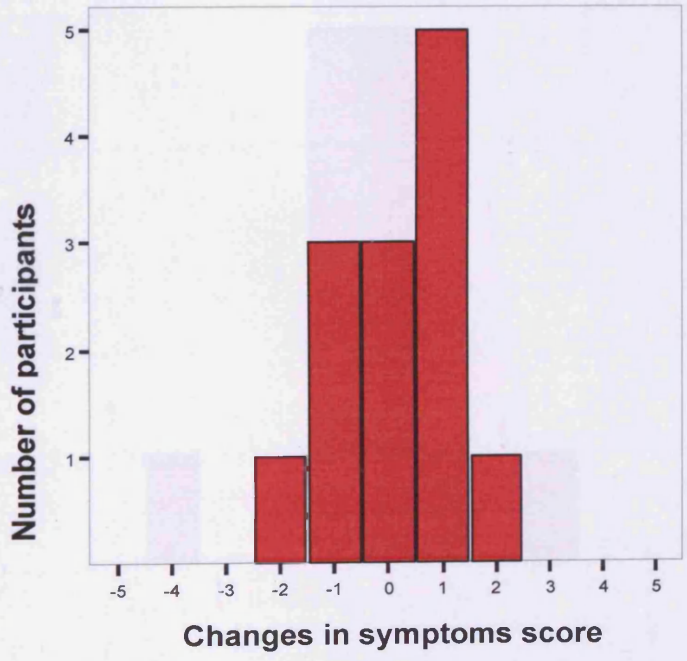

Figure 20b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 20.

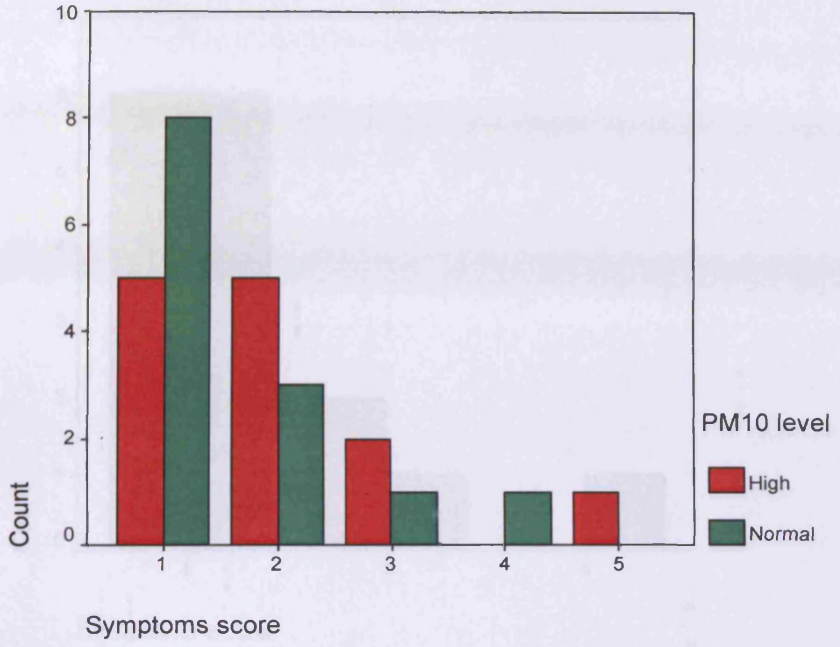

Figure 21a: Breakdown of respiratory symptoms score of question 21 and count of participant number amongst the more severe cases, high v normal levels of PM_{10}.

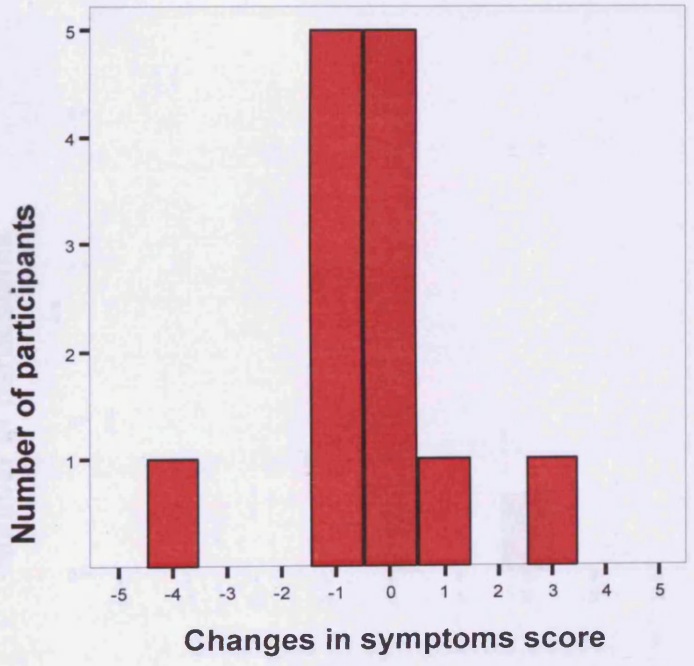

Figure 21b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 21.

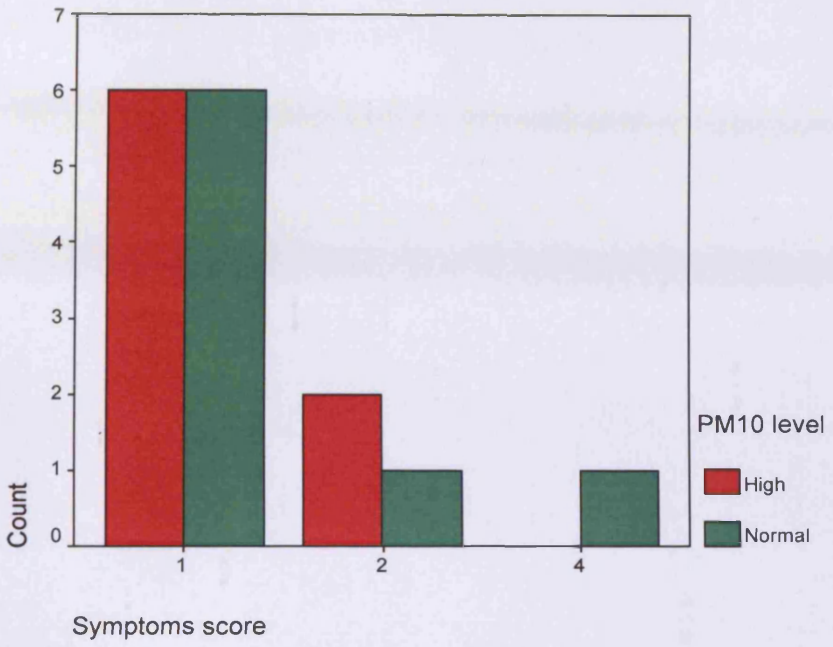

Figure 22a: Breakdown of respiratory symptoms score of question 22 and count of participant number amongst the more severe cases, high v normal levels of PM_{10} (n=8).

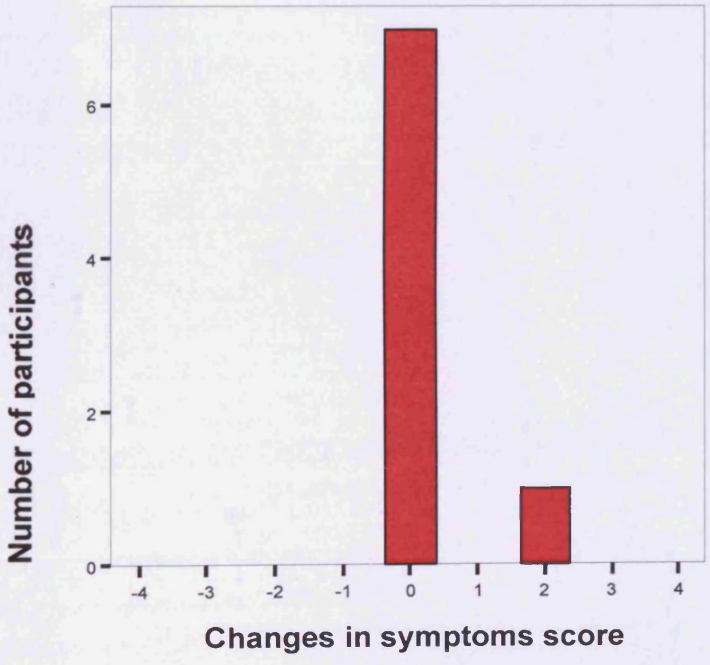

Figure 22b: Changes in respiratory symptoms score between occasions of high and normal PM_{10} pollution amongst the more severe cases, question 22 (n=8).

APPENDIX 11

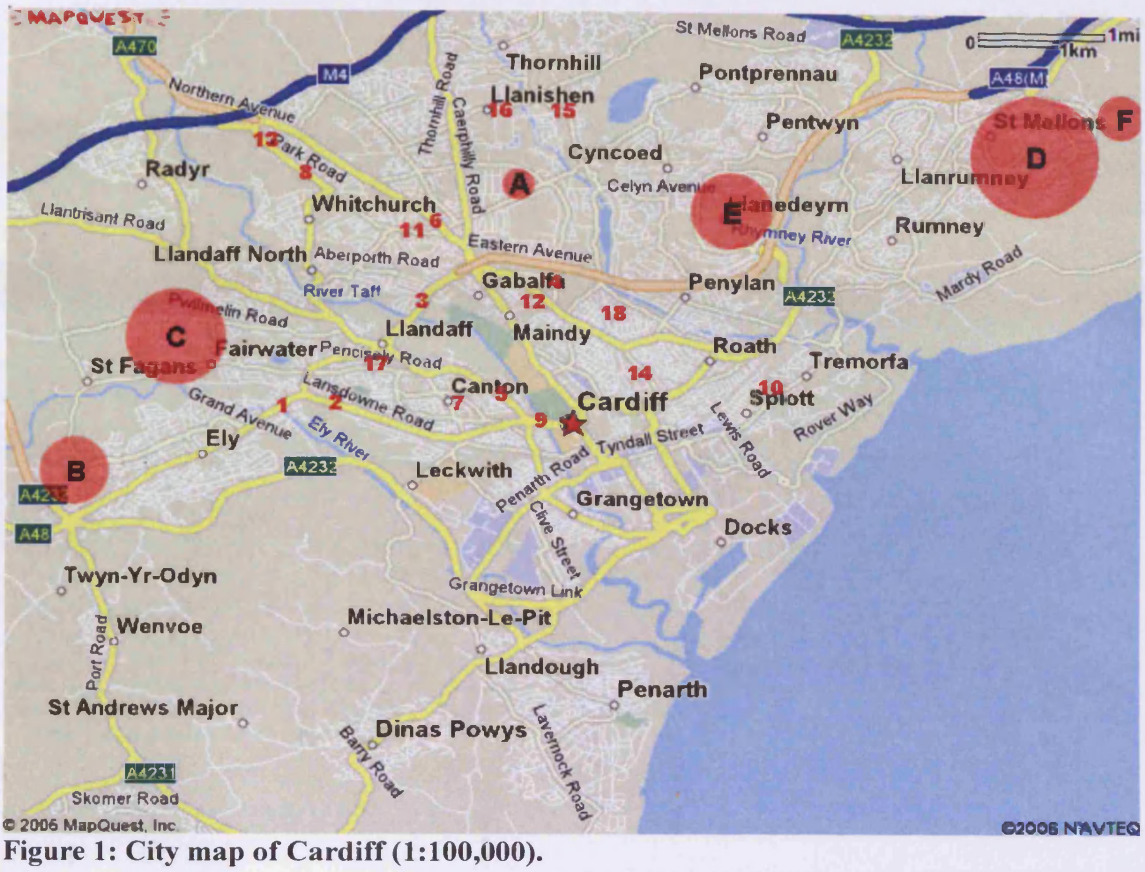

Figure 1: City map of Cardiff (1:100,000).

	Exposed group		Control group
1	Cowbridge Road West	*A*	Llanishen
2	Cowbridge Road East	*B*	Michaelston-Super-Ely
3	Western Avenue	*C*	Fairwater
4	Ninian Road	*D*	St Mellons
5	Cathedral Road	*E*	Llanedeyrn
6	Manor Way	*F*	Marshfield
7	Llandaff Road		
8	Park Road		
9	Tudor Street		
10	Moorland Road		
11	The Philog		
12	Whitchurch Road		
13	Pendwyallt Road		
14	Richmond Road		
15	Fidlas Road		
16	Ty-Glas Road		
17	Pencisely Road		
18	Mackintosh Place		