ASSOCIATION OF PARTICULATE MATTER WITH

CARDIOVASCULAR DISEASES IN BANGKOK

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A Dissertation Submitted in Partial Fulfillment of the Requirements

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ความสัมพันธ์ของฝุ่นละอองกับโรคระบบหลอดเลือดหัวใจในกรุงเทพมหานคร

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ดวงฤทัย บัวด้วง : ความสัมพันธ์ของฝุ่นละอองกับโรคระบบหลอดเลือดหัวใจในกรุงเทพมหานคร (ASSOCIATION OF PARTICULATE MATTER WITH CARDIOVASCULAR DISEASES IN BANGKOK) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: รศ.ดร. วนิดา จีนศาสตร์, อ. ที่ปรึกษาวิทยานิพนธ์ร่วม: ศ.นพ. อิจิ ยาโนะ, 136 หน้า

การศึกษาความสัมพันธ์ระหว่างฝุ่นละอองที่มีเส้นผ่านศูนย์กลางน้อยกว่า 10 ไมครอน (PM_{10}) กับโรคระบบหลอดเลือดหัวใจในกรุงเทพมหานคร โดยวิเคราะห์ความสัมพันธ์ของจำนวนผู้ป่วยรายวันที่มารักษาตัวในสามโรงพยาบาลใหญ่ของรัฐบาล แบ่งออกตามช่วงอายุและกลุ่มย่อยของโรค ข้อมูลฝุ่นละอองรายวันจากกรมควบคุมมลพิษและข้อมูลคุณภาพอากาศจากกรมอุตุนิยมวิทยาตั้งแต่เดือนเมษายน 2545 ถึงเดือนธันวาคม 2549 (1,736 วัน) คำนวณอนุกรมเวลารูปแบบจีเอ็มโมเดล (GAM) โดย SAS โปรแกรม ผลการศึกษาพบว่าปริมาณฝุ่นละอองในหนึ่งวันที่ผ่านมา (lag1) มีผลต่อเปอร์เซ็นต์การเพิ่มจำนวนของผู้ป่วยที่เข้ารับรักษาตัวในโรงพยาบาลด้วยโรคหลอดเลือดหัวใจในกลุ่มผู้สูงอายุ ($\geq$ 65 ปี) โดยเพิ่มขึ้น 0.10% (95% CI: 0.03, 0.19) เมื่อปริมาณฝุ่นละอองเฉลี่ยเพิ่มขึ้นระดับ 10 ไมโครกรัมต่อลูกบาศก์เมตร และทั้งนี้ได้ศึกษาอาการของระบบหลอดเลือดหัวใจ ใช้แบบสอบถามรูปแบบมาตรฐาน ATS-DLD and CDQ ในช่วงเดือนมิถุนายนถึงเดือนตุลาคม พ.ศ. 2550 โดยเก็บตัวอย่างผู้ป่วยสูงอายุโรคระบบหลอดเลือดหัวใจ ที่มารักษาตัวใน โอพีดี โรงพยาบาลรามาธิบดี จำนวนทั้งสิ้น 330 ตัวอย่าง แบบสอบถามและการสัมภาษณ์ถูกใช้เป็นเครื่องมือลดปัจจัยแทรกซ้อน โดยตรวจ การเปลี่ยนแปลงของคลื่นหัวใจ จากจำนวนตัวอย่างที่ผ่านการคัดกรองจำนวนทั้งสิ้น 8 ใน 20 คนที่อาศัยเฉพาะในกรุงเทพชั้นใน และไม่มีปัจจัยแทรกซ้อนโดยผ่านการยินดีรับรองเข้าร่วมการวิจัยตามจริยธรรมการวิจัย ตรวจวัดคลื่นหัวใจโดยผู้เชี่ยวชาญ พร้อมกับศึกษาความสัมพันธ์ข้อมูลรายชั่วโมงของค่าฝุ่นละอองและคุณภาพอากาศจากกรมควบคุมมลพิษและกรมอุตุนิยมวิทยา ณ.จุดใกล้เคียงที่พักในช่วงเวลาเดียวกัน โดยใช้สถิติความถดถอยโลจิสติก วิเคราะห์ความสัมพันธ์ระหว่างการได้รับสัมผัสฝุ่นละอองและการเปลี่ยนแปลงค่าของคลื่นหัวใจ การ ศึกษาพบว่าอัตราการเต้นของหัวใจ (HR) เพิ่มขึ้น 0.37%(95% CI; -0.01, 0.73) ในขณะที่ค่า SDNN และ r-MSSD การทำงานของคลื่นหัวใจลดลง -1.7% (95% CI; -2.6, -1.2) และ -2.8 % (95% CI; -4.6, -1.0) ตามลำดับ เมื่อปริมาณฝุ่นละอองในอากาศเฉลี่ยมีค่าเพิ่มขึ้น 10 ไมโครกรัมต่อลูกบาศก์เมตร ทั้งนี้กล่าวได้ว่ากลุ่มผู้สูงอายุ ($\geq$ 65 ปี) โรคหลอดเลือดหัวใจที่อาศัยอยู่ในพื้นที่ชั้นในกรุงเทพมหานครนั้นเป็นกลุ่มเสี่ยงสำคัญที่ได้รับผลกระทบจากมลพิษทางอากาศจากปัญหาฝุ่นละออง

สาขาวิชา วิทยาศาสตร์สิ่งแวดล้อม ลายมือชื่อนิสิต...

ปีการศึกษา 2551   ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก....................................

            ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์ร่วม..

4789658520: MAJOR ENVIRONMENTAL SCIENCE

DONGRUETHAI BUADONG: ASSOCIATION OF PARTICULATE MATTER WITH CARDIOVASCULAR DISEASES IN BANGKOK: ADVISOR: ASSOC. PROF. WANIDA JINSART, Ph.D., CO-ADVISOR: PROF. EIJI YANO, M.D., 136 pp.

The association between air pollution and cardiovascular diseases is well known, but previous studies only assessed in America and Europe. Few studies have been conducted in less-developed countries in regions with a tropical climate. This study aimed to evaluate the association between short-term exposures to fine particulate matter (PM_{10}) in relation to hospital visits for CVD (I00–I99) in inner Bangkok. Data from hospital records were obtained from three major government hospitals. All hospital visits were stratified by age group and category of CVD. Daily PM_{10} levels and the weather reported by the Pollution Control Department (PCD) and the Meteorology Department from April 2002 to December 2006 (1,736 days) were used in time series analysis with GAM procedure in the Statistical Analysis Software (SAS). Exposures on the previous day (lag1) to PM_{10} had positive association with hospital visits for CVD in the elderly ($\geq$ 65 years). The increase in CVD hospital visits in this age group was 0.10% (95% CI: 0.03, 0.19) with increase in PM_{10} by 10 $\mu g\ m^{-3}$. This research, also study the incidence of CVD by standards cardio-respiratory questionnaires (ATS-DLD and CDQ). 330 elderly existing CVD patients visit Ramathibodi hospital from June to October 2007 was investigated. After adjusting all confounding by questionnaires and interviewed, there were 8 qualified subjects conducted HRV measurement for 24 hours. The hourly PM_{10} concentration and meteorology data were assessed from nearby PCD monitoring stations. The multiple logistic regression analysis was carried out to evaluate the relationships between PM_{10} and HRV. The percentage change of heart rate (HR) increasing was 0.37 % (95% CI; -0.01, 0.73) while SDNN and r-MSSD parameter of HRV were decreasing by -1.7% (95% CI; -2.6, -1.2) and -2.8 % (95% CI; -4.6, -1.0) respectively. The magnitude association change per 10 $\mu g\ m^{-3}$ increase in PM_{10}. Elevated levels of ambient PM_{10} may adversely affect HRV functions in elderly subjects with existing CVD patients in inner Bangkok.

Field of Study: <u>Environmental Science</u> Student's Signature………..…………………

 Academic Year: <u> 2008 </u> Advisor's Signature……………..…………

Co-Advisor's Signature………..………………

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Finally, Dedicated to my loving family and my closed friends such as Miss Pattamaporn Yodsanti and Miss Chuenjit Junsawang in PICU of Ramathibodi Hospital, Mahidol University for their whole hearted understanding, encouragement and patient support throughout my entire study.

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CHAPTER I

INTRODUCTION

1.1 Statement of Problem

Epidemiological studies conducted worldwide during the last decade have shown a consistent, increased risk for respiratory and cardiovascular events, including heart and stroke deaths, in relation to short and long term exposures to air pollutants, especially particulate matter. (Zanobetti et al., 2000; Anderson et al., 2001; Dominici et al., 2006; and Zanobetti et al., 2006) Bangkok is the metropolitan area with a very high density (4,051 persons per km^2) and 6.12 millions of registered vehicles. Air pollution causes an important environmental health problem in Bangkok, because of a limited number of roads and the rapidly increasing number of vehicles traveling on the roads. The high concentration of particulate matter those diameters less than 10 microns; (PM_{10}) in ambient air are of the serious environmental problems. The Thai Government has been operating a monitoring system for air pollution at 32 Pollution Control Department (PCD) monitoring stations for several years. There were many areas that annual average PM_{10} concentrations were found higher than the National Ambient Air Quality Standards (NAAQS) in 2004-2006.

Recent studies have reported that air pollution is a risk factor for heart and lung disease by associated with reduced Heart Rate Variability (HRV) and increased fibrinogen levels in animals.(Kodanvanti et al., 2003) There were known risk factors for arrhythmia and Ischemic events, which were the major sources of hospital admission for heart disease. Human studies also have reported airborne particles were associated with increased plasma viscosity (Peter et al., 2001, Bhatnager et al., 2004, and Bhatnager et al., 2006) decrease heart rate variability (Pope et al., 1999; Gold et al., 2000; and Magari et al., 2001) and triggering of Myocardial Infarction (MI). (Zanobetti et al., 2000; and Peter et al., 2001) Cardiovascular diseases (CVD) are one of the most important causes of poor health and death in the developed world. An increasing amount of evidence shows that the contribution of air pollution to increasing cardiovascular damage is not negligible and experimental studies provided

information on the potential mechanisms involved in this time. (Arito et al., 1990, Chang et al., 1992 and Magari et al., 2001) There have been several studies on the short term effects of air pollution associated with increased risk of hospital admission or death for CVD around the world (Anderson et al., 2001, Koken et al., 2003 and Dominici et al., 2006), however most have examined in Europe (Brook et al., 2004) and America. (Anderson et al., 2001)

Among traffic-related air pollutants, PM_{10} becomes one of the greatest concerns in terms of health and regulatory in Thailand. It was found that PM_{10} has been associated with serious health effects, such as increased hospital admissions and mortality in Bangkok. (Ostro et al., 1999) The associations were also reported between air pollution and respiratory health effect among traffic policemen (Karita et al., 2001) and their family. (Karita et al., 2004) Thus, previous studies have found a statistically significant relationship between respiratory effects of ambient PM_{10} in Bangkok, whereas little has been published on association of hospital visit for CVD and daily PM_{10} fluctuations. There have been few studies conducted in developing countries in tropical climate regions, where seasonal patterns of illness and hospital usage are likely to differ from Western countries. This research aims to study what extent such associations of daily PM_{10} concentration would be revealed in daily hospital visit based on the category of CVD and impaired cardiac functions as Heart Rate Variability (HRV) in Bangkok.

1.2 Objectives

The main objective of this study is to reveal the association between the levels of exposure to Air pollution of particulate matter those diameters less than 10 microns; (PM_{10}) concentration and cardiovascular diseases (CVD). This study will also determine the degree of correlation between particulate matter and the impairment of cardiovascular function; Heart Rate Variability (HRV) in inner Bangkok.

This objective can be divided into three sub-objectives:

1. To demonstrate the association between the level of exposure to air pollution (PM_{10}) and cardiovascular diseases (CVD) in Bangkok.

2. To determine if day to day fluctuation in ambient PM_{10} concentration are associated with day to day fluctuation in CVD hospital visit.

3. To determine the degree of correlation between PM_{10} and the impairment of cardiovascular function; Heart Rate Variability (HRV) in pre-existing CVD patients in inner part of Bangkok.

1.3 Hypothesis

1. Higher level of particulate matter (PM_{10}) concentration is associated with higher rate of hospital visit due to cardiovascular diseases (CVD).

2. Higher level of particulate matter (PM_{10}) concentration is associated with decreased Heart Rate Variability (HRV) function among people with pre-existing cardiovascular diseases elderly patients in inner Bangkok.

1.4 Scopes of the study

1.4.1) PM_{10} and hospital visit

1) This study concentrated on cardiovascular effects from respirable particulate mater air pollution (PM_{10}) in inner Bangkok.

2) To reveal the correlation of daily PM_{10} measurement data from Pollution Control Department (PCD) and data of the weather from Bangkok Meteorology Department with daily emergency hospital visit for categories of cardiovascular diseases (CVD) in International Classification of Disease Version 10th; (ICD-10th; I00-I99) in three major government hospitals namely; Ramathibodi, Chulalongkorn and Siriraj from 1 April 2002 to 31 December 2006. (1,736 day)

3) To determine if day-to-day fluctuation in daily ambient PM_{10} concentrations are associated with day-to-day variations in CVD hospital visit in inner Bangkok by consider time lag.

1.4.2) PM$_{10}$ and HRV sampling

1) Screened and adjust confounding by used a modified standard cardiorespiratory (ATS-DLD and CDQ) Thai version questionnaires in pre-existing cardiovascular diseases elderly patients only living in inner Bangkok, high pollutant area.

2) To determine amount of 24 hour fine particulate matter less than 10 micron aerodynamic diameters (PM$_{10}$) in inner Bangkok.

3) Health examination in participation with pre-existing CVD elderly patients who living in inner Bangkok: 24-hour personal HRV sampling (ECG) for monitoring cardiac autonomic function.

1.5 Benefits of the study

This study can lead to contributing scientific information in risk assessment especially about relationships between particulate matter (PM$_{10}$) air pollution and public health. In addition, it is useful for decision makers in setting priorities between many competing environmental and public health issues.

CHAPTER II

BACKGROUNDS AND LITERATURE REVIEW

2.1 Air Quality and Trends in Bangkok

Bangkok is a metropolitan area with a population greater than 6 million. It has a tropical climate, with warm to hot temperatures and humid conditions year-round. The Thai Government has been operating a monitoring system for PM_{10} for several years by Pollution Control Department (PCD) in both general background or ambient areas and roadside areas (Wangwongwatana et al., 2006) as follow:

2.1.1 General ambient air quality monitoring

Continuous general ambient air monitoring stations are placed in residential, commercial, industrial and mixed areas of Bangkok which far away from main road 50 meters. Monitoring locations are carefully selected to ensure that monitoring stations are not directly influenced by any particular major sources so that the quality of the general ambient air in Bangkok is monitored and impacts to general population can then be evaluated. Originally, there were 6 continuous monitoring stations installed in 1983. The air pollutants being measured were only limited to CO, TSP, and Pb. They were subsequently renovated and upgraded and a few new stations were installed in October of 1996 bringing the total number of stations for general ambient air quality monitoring in Bangkok to 10 stations. Every station monitors CO, TSP, PM_{10}, Pb, SO_2, NO_x, O_3 and Hydrocarbons (HC) are also monitored in some monitoring stations. The new stations are equipped with 10 meters meteorological masts measuring wind speed, wind direction, temperature, humidity, and solar radiation.

2.1.2 Roadside street-level ambient air quality monitoring

Since, there are a lot of Thai people living and working in shop houses, which are in close proximity to the street, it is also necessary to monitor the quality of air at street level where these people are exposed to air pollution. Roadside ambient air quality monitoring stations are placed far away from the street 3-5 meters. Roadside ambient air quality monitoring in Bangkok is carried out in two different ways as follows:

a) Long-term continuous roadside ambient air quality monitoring

In 1991, four permanent on-line and real-time continuous roadside ambient air quality-monitoring stations were operated in Bangkok in the areas experiencing traffic congestion. Each station has its own electronic display board to continuously display instantaneous concentrations of CO, PM_{10}, and noise levels to the public. Simultaneously, data are transmitted via a dedicated telephone line and are logged into a central processing computer at PCD. In October of 1996, PCD installed three new on-line roadside ambient air quality monitoring stations continuously measuring CO, TSP, PM_{10}, Pb, SO_2, NO_x, O_3 and HC. These new stations are equipped with 10-metre meteorological masts measuring wind speed and direction, temperature, humidity and solar radiation.

b) Short-term temporary roadside ambient air quality monitoring

In addition to permanent roadside monitoring stations, temporary monitoring of CO, TSP and Pb is carried out annually approximately 21 of the most congested streets in Bangkok at roadsides for a period of 2 to 4 consecutive weeks at each street. Data are collected manually every day.

2.1.3 Current ambient air quality and trend in Bangkok

Results of ambient air quality monitoring for more than 10 years indicate that the greatest concerned air pollutants in Bangkok are SPM, especially PM_{10}. They are mostly emitted by transport sector. The report also concluded that air pollution in Bangkok, due to high concentrations of SPM, is among the highest priority problems. (Figure 2.1)
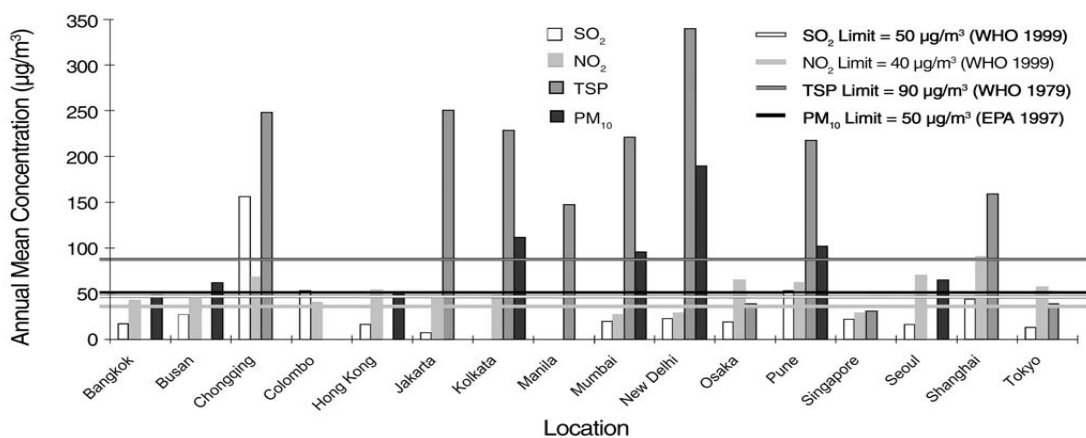
Figure 2.1 Annual mean concentrations of pollutants compared with their guidelines and standards in Asian cities, 2000 and 2001.

Source: Air Pollution in Megacities of Asia 2004.

Table 2.1 Ambient air quality in the general areas of Bangkok in 2006

Pollutants	Concentrations				
	Range	95 percentile	Average	Standard	Frequency of Exceeding Standard (%)
TSP (24-hr), mg m^{-3}	0.02 – 0.43	0.18	0.10	0.33	2/537 (0.37)
PM$_{10}$ (24-hr), µg m^{-3}	15.7 – 124.9	84.2	43.3	120	2/2,147 (0.1)
Pb (1-month), µg m^{-3}	0.01 – 0.78	0.27	0.10	1.5	0/120 (0)
CO (1-hr), ppm	0.0 – 6.1	1.7	0.7	30	0/81,758 (0)
CO (8-hr), ppm	0.0 – 5.2	1.5	0.7	9	0/84,648 (0)
O$_3$ (1-hr), ppb	0.0 – 188.0	55.0	17.0	100	154/65,951 (0.23)
SO$_2$ (1-hr), ppb	0.0 – 150.0	13.0	5.3	300	0/82,073 (0)
SO$_2$ (24-hr), ppb	0.0 – 31.2	10.5	5.3	120	0/3,542 (0)
NO$_2$ (1-hr), ppb	0 – 148.0	53.0	22.9	170	0/82,401 (0)

Source: PCD, 2007

Table 2.2 Ambient air quality at the roadside sites of Bangkok in 2006

	Concentrations				
Pollutants	Range	95 percentile	Average	Standard	Frequency of Exceeding Standard (%)
TSP (24-hr), mg m^{-3}	0.03 – 0.80	0.38	0.16	0.33	43/687 (6.25)
PM$_{10}$ (24-hr), μg m^{-3}	10.4 – 206.2	126.9	63.1	120	146/2,052 (7.1)
Pb (1-month), μg m^{-3}	0.02 – 0.28	0.13	0.07	1.5	0/105 (0)
CO (1-hr), ppm	0.0 – 10.9	3.6	1.4	30	0/62,501 (0)
CO (8-hr), ppm	0.0 – 8.6	3.2	1.4	9	0/63,069 (0.0)
O$_3$ (1-hr), ppb	0.0 – 137.0	43.0	12.4	100	12/24,418 (0.04)
SO$_2$ (1-hr), ppb	0.0 – 56.0	15.0	6.2	300	0/24,359 (0)
SO$_2$ (24-hr), ppb	1.0 – 18.6	11.3	6.2	120	0/1,049 (0)
NO$_2$ (1-hr), ppb	0.0 – 182.0	66.0	31.4	170	1/24,417 (0.004)

Source: PCD, 2007

Table 2.1 and Table 2.2 summarized ambient air quality in Bangkok in 2006 in the general background areas and at roadside sites, respectively. As indicated, the principal concern is along the major roads in Bangkok where pollutant concentrations and frequency of exceeding of the ambient air quality standards (Table 2.3) for TSP, PM$_{10}$, and O$_3$ are high enough to result in significant adverse health impacts on the local population.

Table 2.3 Ambient air standards of Thailand (1995).

Pollutants	1-hr Average		8-hr Average		24-hr Average		1-yr Average		Measurement Method
	$mg\ m^{-3}$	ppm	$mg\ m^{-3}$	ppm	$mg\ m^{-3}$	ppm	$mg\ m^{-3}$	ppm	
1. PM_{10}	-	-	-	-	0.12	-	0.05	-	Gravimetric-High Volume
2. TSP	-	-	-	-	0.33	-	0.10	-	Gravimetric-High Volume
3. CO	34.2	30	10.26	9	-	-	-	-	Non-Dispersive Infrared Detection
4. SO_2	0.78	0.30	-	-	0.30	0.12	0.10	0.04	UV-Fluorescence
5. NO_2	0.32	0.17	-	-	-	-	-	-	Chemiluminescence
6. O_3	0.20	0.10	-	-	-	-	-	-	Chemiluminescence

Source: Notification of National Environmental Board No. 10 (1992) under the Enhancement and Conservation of National Environmental Quality Act B.E. 2535 (1992) published in the Royal Government Gazette No. 112 Part 52 dated May 25, B.E. 2538 (1995)

It was reported that 60 percent of TSP by weight in Bangkok is PM_{10}. Monitoring of PM_{10} began in Bangkok in 1992. In 2004, 24-hour average concentrations of roadside ambient PM_{10} in Bangkok ranged from 21.5-224.8 $\mu g\ m^{-3}$ with the annual average of 78.5 $\mu g\ m^{-3}$. There were 243 out of 2,282 observations representing 10.6 percent of the total observations having concentrations exceeding the standard of 120 $\mu g\ m^{-3}$. The annual average concentration of 78.5 $\mu g\ m^{-3}$ also exceeded the standard of 50 $\mu g\ m^{-3}$. Figure 2.2 showed the increasing trend of roadside and ambient PM_{10} concentrations in Bangkok from 2001 to 2006.
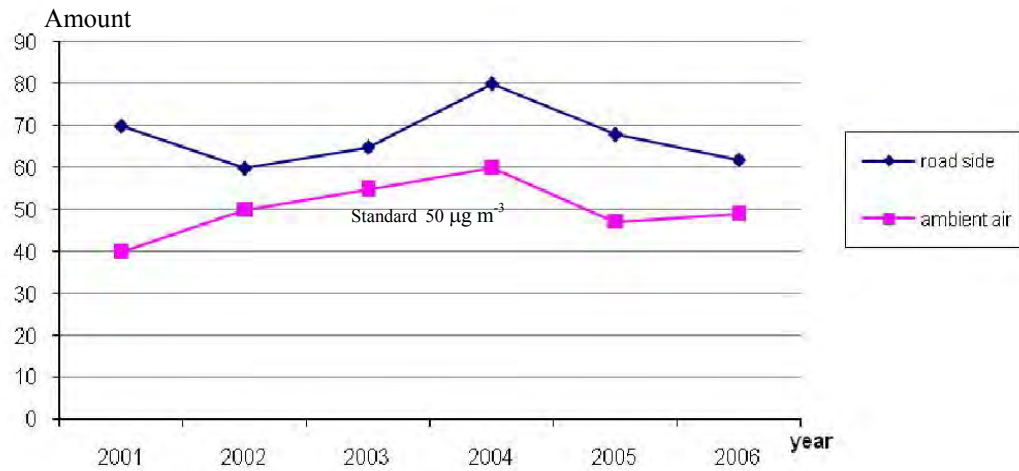
Figure 2.2 Annual PM$_{10}$ concentrations in Bangkok, 2001-2006 (PCD; 2007)

Ozone (O$_3$) posed another significant air pollution problem since they exceeded standards several times in the various areas of Bangkok, and were also increasing continuously (Figure 2.3) Thus, protective and control measures are needed to keep within standards.
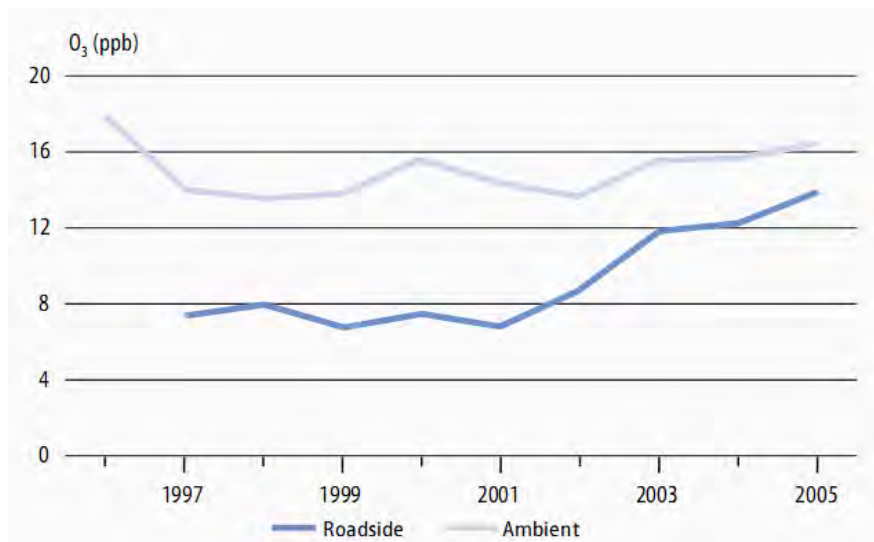
Figure 2.3 Annual Ozone concentrations in Bangkok, 1997-2005 (PCD, 2006)

2.2 Health Effect of Air Pollution

The human health effects of poor air quality are far reaching, but principally affect the body's respiratory system and the cardiovascular system. Individual reactions to air pollutants depend on the type of pollutant a person is exposed to the degree of exposure, the individual's health status and genetics. People who exercise outdoors, for example, on hot, smoggy days increase their exposure to pollutants in the air. The health effects caused by air pollutants may range from subtle biochemical and physiological changes to difficulty breathing, wheezing, coughing and aggravation of existing respiratory and cardiac conditions. (Table 2.4) These effects can result in increased medication use, increased doctor or emergency room visits, more hospital admissions and even premature death.

Table 2.4 Potential Health Effects of Air Pollutants

Pollutant	Pollutants Descriptions	Potential Health Effects
CO	Colorless, odorless gas that is caused by incomplete carbon combustion	CO combined with hemoglobin and interfere the blood's ability to carry oxygen from the lungs to the rest of the body. It can impair the brain's ability to function properly and is a threat especially to individuals with CVD.
NO_2	Reddish-brown, highly reactive gas formed from high temperature combustion through reactions involving N2 and oxygen.	NO_2 can irritate lungs, cause bronchitis and pneumonia, and impair an individual's resistance to infections.
O_3	Gas that is formed by VOCs and NO_X in the presence of heat and sunlight.	Exposure to O_3 can cause chest constrictions and irritations of the mucous membranes.
PM	Particulate matter either solid or liquid usually in the range of 0.005 to 100 um in aerodynamic diameter. Other related terms include aerosols, dust, fumes, soot, etc.	The smaller PM, can penetrate into the respiratory system. Depending on the size and composition, PM can damage lung tissue, aggravate existing respiratory and cardiovascular diseases, and cause cancer.
SO_2	Gas formed when fuels containing sulfur are burned (combusted).	It is highly soluble in water and will likely be trapped in the upper respiratory tract causing irritations but less long-term damage. When entrained in an aerosol, SO_2 can reach far deeper into the respiratory system causing severe respiratory distress.
CO_2	Gas released to the atmosphere when solid waste, fossil fuels (oil, natural gas, and coal), and wood and wood products are burned.	This greenhouse gas leads to climate change. Hot temperatures can cause CVD problems, Heat exhaustion and respiratory problems. There may be an increased risk of infectious diseases due to increased temperature.

2.2.1 Human Respiratory System

The health of lung and entire respiratory system is affected by the quality of the air, we breathe. In addition to oxygen, this air contains other substances such as pollutants, which can be harmful. Exposure to chemicals by inhalation can negatively affect lungs and other organs in the body. The respiratory system is particularly sensitive to air pollutants because much of it is made up of exposed membrane. Lungs are anatomically structured to bring large quantities of air (on average, 400 million litters in a lifetime) into intimate contact with the blood system, to facilitate the delivery of oxygen. Lung tissue cells can be injured directly by air pollutants such as ozone (O_3), metals and free radicals. Ozone can damage the alveoli and the individual air sacs in the lung where oxygen and carbon dioxide are exchanged. More specifically, airway tissues which are rich in bioactivities enzymes can transform organic pollutants into reactive metabolites and cause secondary lung injury. Lung tissue has an abundant blood supply that can carry toxic substances and their metabolites to distant organs. In response to toxic insult, lung cells also release a variety of potent chemical mediators that may critically affect the function of other organs such as those of the cardiovascular system. This response may also cause lung inflammation and impair lung function.

Structure and Function

The human respiratory system is dominated by our lungs, which bring fresh oxygen (O_2) into our bodies while expelling carbon dioxide (CO_2). The oxygen travels from the lungs through the bloodstream to the cells in all parts of the body. The cells use the oxygen as fuel and give off carbon dioxide as a waste gas. The waste gas is carried by the bloodstream back to the lungs to be exhaled. The lungs accomplish this vital process called gas exchange, using an automatic and quickly adjusting control system. This gas exchange process occurs in conjunction with the central nervous system (CNS), the circulatory system, and the musculature of the diaphragm and the chest.

The human respiratory system can be divided into the upper respiratory tract and the lower respiratory tract. The upper respiratory tract includes the following rigid structures:

- Nasal cavities: Filter the air we breathe and provide a sense of smell.
- Pharynx: Acts in the respiratory and the digestive system.
- Larynx: Link between the pharynx and the trachea. Generates the voice with the presence of vocal folds.
- Trachea: The trachea is the bond with the lower respiratory tract. This is a flexible structure allowing the air to go down to the lungs.

In addition to gas exchange, the lungs and the other parts of the respiratory system have important jobs to do relate to breathing. These include: Bringing all air to the proper body temperature. Moisturizing inhaled air for necessary humidity, protecting the body from harmful substances by coughing, sneezing, filtering or swallowing them, or by alerting the body through the sense of smell. Defending the lungs with cilia (tiny hair-like structure), mucus and macrophages, which act to remove harmful substances deposited in the respiratory system. The respiratory system is sensitive to air pollution. The cardiovascular system can be affected as well. (Figure 2.4)
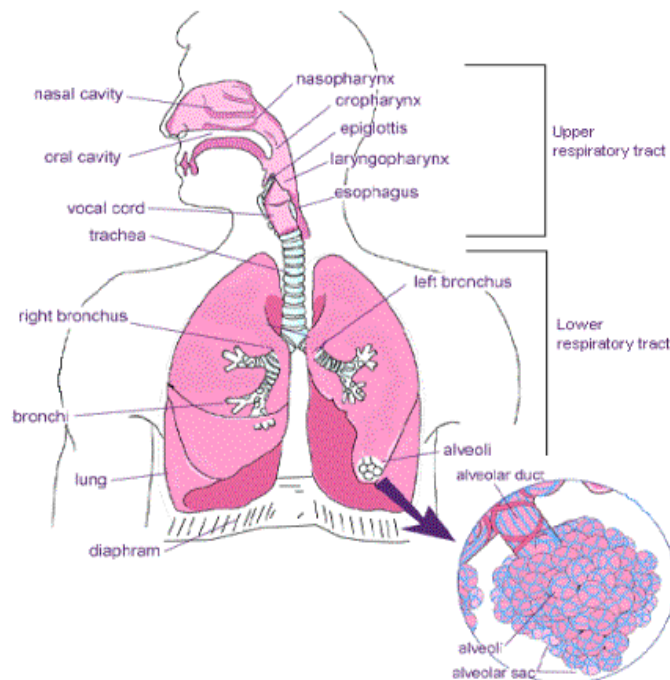
Figure 2.4 Diagram of Human Respiratory System

Environmental & Workplace Health; Health Canada; 2008

http://www.hc-sc.gc.ca/ewh-semt/air/out-ext/effe/health_effects-effets_sante_e.html#1

2.2.2 Human Cardiovascular System

The cardiovascular system has two major components as the heart and a network of blood vessels. The cardiovascular system supplies the tissues and cells of the body with nutrients, respiratory gases, hormones, and metabolites and removes the waste products of cellular metabolism as well as foreign matter. It is also responsible for maintaining the optimal internal homeostasis of the body and the critical regulation of body temperature and pH. The inhalation of air pollutants eventually leads to their absorption into the bloodstream and transport to the heart. A wide spectrum of chemical and biological substances may interact directly with the cardiovascular system to cause structural changes, such as degenerative necrosis and inflammatory reactions. Some pollutants may also directly cause functional alterations that affect the rhythmicity and contractility of the heart. If severe enough, functional changes may lead to lethal arrhythmias without major evidence of structural damage to the myocardium. There also may be indirect actions secondary to changes in other organ systems, especially the central and autonomic nervous systems and selective actions of the endocrine system. Some cytokines released from other inflamed organs may also produce adverse cardiovascular effects, such as reducing the mechanical performance and metabolic efficiency of the heart and blood vessels. Many chemical substances may cause the formation of reactive oxygen. This oxidative metabolism is considered to be critical to the preservation of cardiovascular function. For example, oxygen free radicals oxidize low density lipoproteins, and this reaction is thought to be involved in the formation of the atherosclerotic plaques. Oxidized low density lipoproteins can injure blood vessel cells and increase adherence and the migration of inflammatory cells to the injured area. The production of oxygen free radicals in heart tissues has been associated with arrhythmias, and heart cell death. Epidemiology has clearly demonstrated an association between increases in air Pollution and death and admissions due to heart failure, Myocardial Infarction (MI) and arrhythmia. (Routledge et al., 2005)
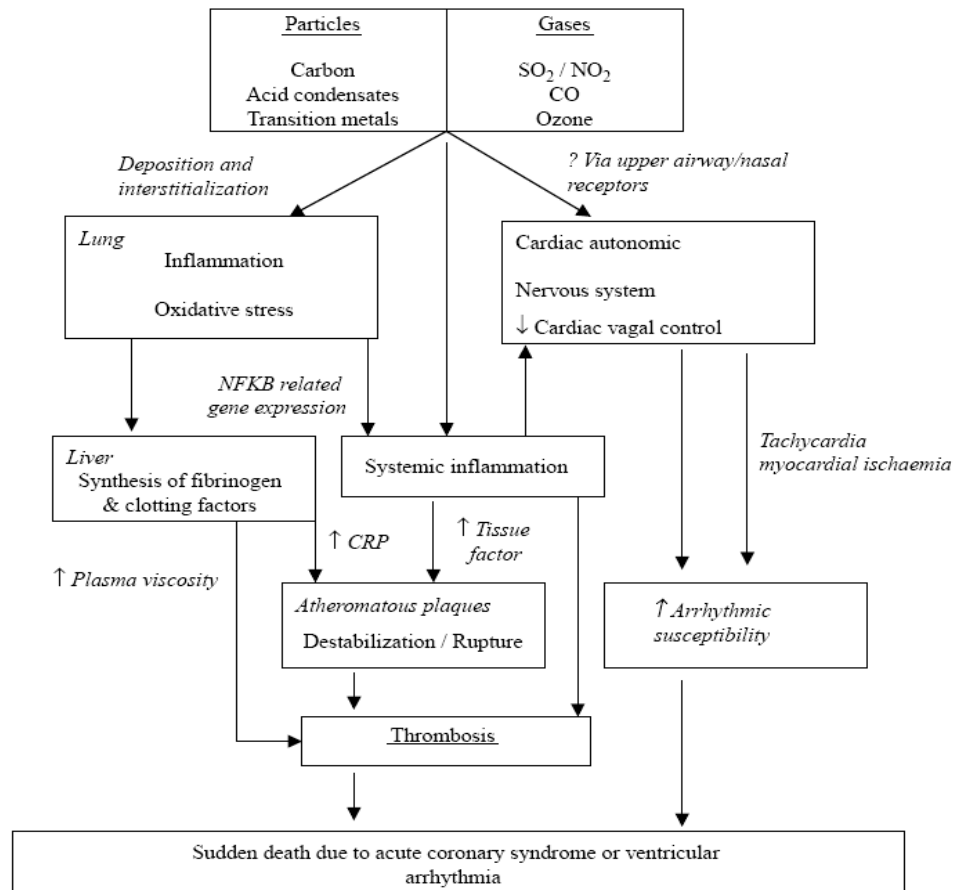
Figure 2.5 Potential patho-physiological mechanisms for the adverse effects of air pollutants on the cardiovascular system.
Source: Routledge et al., 2005.

2.2.3 Heart and Lung Diseases

Heart and lung illnesses diseases are common in the world, and there are many factors that can increase the chances of contracting them such as smoking and genetic predisposition. The role of air pollution as the underlying cause remains unclear but is the subject of considerable research. However, it is clear that air pollution, infections and allergies can exacerbate these conditions. An early diagnosis can lead to appropriate treatment and ensure a normal or close to normal quality of life. In many cases however, there is no cure and those affected may die prematurely. The following are the most prevalent diseases:

- Minor Lung Illnesses the common cold is the most familiar of these, with symptoms including sore throat, stuffy or runny nose, coughing and sometimes irritation of the eyes.

- Lung Infections croup, bronchitis, and pneumonia are caused by viruses or bacteria and are very common. Symptoms may include cough, fever, chills and shortness of breath.

- Asthma is an increasingly common chronic disease among children and adults. It causes shortness of breath, coughing or wheezing or whistling in the chest. Asthma attacks can be triggered by a variety of factors including exercise, infection, pollen, allergies and stress. It can also be triggered by sensitivity to non-allergic types of pollutants present in the air such as smog.

- Chronic Obstructive Pulmonary Disease (COPD) is also known as chronic obstructive lung disease and encompasses two major disorders: emphysema and chronic bronchitis. Emphysema is a chronic disorder in which the walls and elasticity of the alveoli are damaged. Chronic bronchitis is characterized by inflammation of the cells lining the inside of bronchi, which increases the risk of infection and obstructs airflow in and out of the lung. Smoking is responsible for approximately 80% of COPD cases while other forms of air pollution may also influence the development of these diseases. Symptoms include cough, production of mucous and shortness of breath. It is important to note that no cure exists for people suffering from COPD although healthy lifestyle and appropriate medication can help.

- Lung Cancer is the most common cause of death due to cancer in women and men. Cigarette smoke contains various carcinogens and is responsible for most cases of this often fatal disease. The symptoms of lung cancer begin silently and then progress to chronic cough, wheezing and chest pain. Air pollution has been linked somewhat weakly to lung cancer.

- Coronary Artery Disease (COA) refers to the narrowing or blocking of the arteries or blood vessels that supply blood to the heart. This disease includes angina and heart attack which share similar symptoms of pain or pressure in the chest. Unlike angina, the symptoms caused by heart attack do not subside with rest and may cause permanent damage to the heart. Smoking, lack of exercise, excess weight, and high cholesterol levels in the blood, family history and high blood pressure are some of the factors that may contribute to this disease.

- Heart Failure is a condition in which the heart is unable to cope with its work load of pumping blood to the lungs and the rest of the body. The most common cause is severe coronary artery disease. The main symptoms are shortness of breath and swelling of the ankles and feet.

- Heart-Rhythm Problems are irregular or abnormal rhythms of the heart beat. In some cases heart-rhythm problems are caused by coronary artery disease. Symptoms of heart-rhythm problems in fluttering in the chest (palpitation) and feeling light-headed. Some heart-rhythm problems are life-threatening and need emergency treatment.

2.2.4 Pyramid of Health Effects
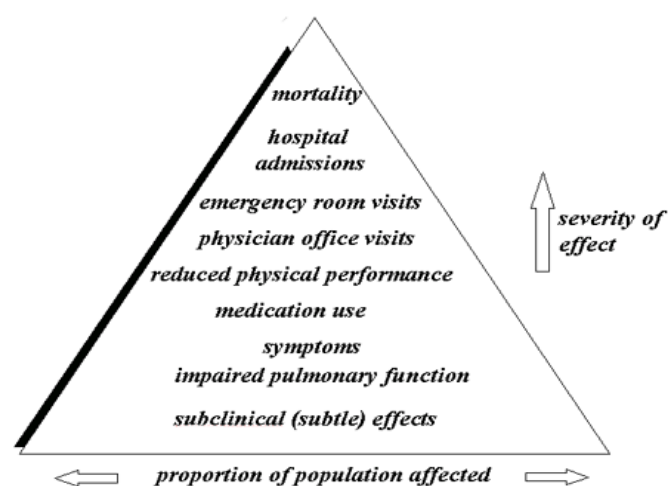
Figure 2.6 Pyramids of Health Effects of Air Pollution.

WHO: European Centre for Environment and Health, 2007.

The health effects of air pollution can be seen as a pyramid, with the mildest but not common effects at the bottom of the pyramid (Figure 2.6) and the least common but more severe at the top of the pyramid. The pyramid demonstrates that as severity decreases the number of people affected increases.

Health endpoints associated with increased air pollutants levels.

- Mortality: All non-accidental mortality causes
- Hospital Admissions: Cardiovascular and respiratory hospital admissions
- Emergency Room Visits: Visit to an emergency department
- Asthma Symptom Days: Exacerbation of asthma symptoms in individuals with diagnosed asthma
- Restricted Activity Days: Days spent in bed, missed from work, and days when activities are partially restricted due to illness
- Acute Respiratory Symptoms: Respiratory-related symptoms such as chest discomfort, coughing and wheezing

2.2.5 Population at Risk

Although everyone is at risk from the health effects of air pollution, certain sub-populations are more susceptible. Individual reactions to air contaminants depend on several factors such as the type of pollutant, the degree of exposure and how much of the pollutant is present. Age and health are also important factors. The elderly and people suffering from cardio-respiratory problems such as asthma appear to be the most susceptible groups. Children and newborns are also sensitive to the health effects of air pollution since they take in more air than adults for their body weight and consequently, a higher level of pollutants. People who exercise outdoors on hot and smoggy days are also at greater risk due to their increased exposure to pollutants in the air.

2.3 Particulate Matter (PM)

Air pollution is composed of many environmental factors. They include carbon monoxide, nitrates, sulfur dioxide, ozone, lead, secondhand tobacco smoke and particulate matter. Particulate matter, also known as particle pollution, is composed of solid and liquid particles within the air. It can be generated from vehicle emission, tire fragmentation and road dust, power construction and demolition activities, residential wood burning, windblown soil, pollens, molds, forest fires, volcanic emissions and sea spray. These particles vary considerably in size, composition and origin. Particulate air pollution is an issue of local, regional, and global importance (Akimoto, 2003), as it is a major component of air pollution in both outdoor and indoor environments (Dockery et al., 1993; Pope et al., 1991; Schwartz, 1993; Stern et al.,1989). Airborne particulate pollution has been associated with increased human morbidity and mortality (Reviewed: UNEP and WHO 1994; USEPA, 1995).Specifically, particulate air pollution has been associated with negative health effects pertaining to respiratory diseases, including asthma (Reviewed: ATS, 1996).Additionally, particulate air pollution has been associated with negative changes in a specific component of cardiac function, heart rate variability (HRV) (Gold et al., 2000; Pope et al., 1999), which have been associated with increased cardiac morbidity and mortality (ESC and NASPE, 1996). As environmental air pollution can be a combination of gases, liquids, and particles, these components could have interactive effects on the respiratory and cardiac systems. Potentially susceptible individuals, including individuals with asthma, have been shown to be at increased risk of negative health effects from exposure to both particulate and gaseous air pollution (Reviewed: Peden, 2002). Currently, the biological mechanisms controlling particle-induced airway inflammation and changes in HRV in asthma are incompletely understood.

Airborne PM consists of a heterogeneous mixture of solid and liquid particles suspended in air, continually varying in size and chemical composition in space and time (Figure 2.7) Primary particles are emitted directly into the atmosphere, such as diesel soot, whereas secondary particles are created through physicochemical transformation of gases, such as nitrate and sulfate formation from gaseous nitric acid and sulfur dioxide (SO_2), respectively. The numerous natural and anthropogenic

sources of PM include motor vehicle emissions, tire fragmentation and re-suspension of road dust, power generation and other industrial combustion, smelting and other metal processing, agriculture, construction and demolition activities, residential wood burning, windblown soil, pollens and molds, forest fires and combustion of agricultural debris, volcanic emission, and sea spray. Although there are thousands of chemicals that have been detected in PM in different locations, some of the more common constituents include nitrates, sulfates, elemental and organic carbon, organic compound (e.g., polycyclic aromatic hydrocarbons), biological compounds (e.g., endotoxin, cell fragments), and a variety of metals (e.g., iron, copper, nickel, zinc and vanadium).Largely because of the complex nature of PM, it has been measured and regulated based primarily on mass within defined size ranges, in 1987, the regulatory focus shifted from total suspended particles to particles that could readily penetrate and deposit in the trachea-bronchial tree, or PM_{10} (PM with a median aerodynamic diameter of <10 µm). In 1997, the US EPA promulgated 24-hour and annual average standards for $PM_{2.5}$ (PM with a median aerodynamic diameter of <2.5 µm), comprising the size fraction that can reach the small airways and alveoli. The existing federal PM_{10} standards were retained, however, to address health effects that could be related to the "coarse fraction" ($PM_{10 \text{ to } 2.5}$).

Currently, a separate $PM_{10 \text{ to } 2.5}$ standards is under consideration. In general, $PM_{2.5}$ originates mostly from combusting sources and includes primary and secondary particles, whereas the coarse fraction derives predominantly from natural sources, especially crustal material (including windblown soil) and grinding processes, important bioaerosols (e.g. endotoxin, pollen grains, and fungal spores) are found mostly in the coarse fraction (and larger particles), although both endotoxin (an essential component of the cell wall of gram-negative bacteria) and the antigenic protein content of pollen grains can also absorb onto the surface of fine PM. Generally, larger particles demonstrate a greater fractional deposition in the extra-thoracic and upper tracheobronchial regions, whereas smaller particles (e.g., $PM_{2.5}$) show greater deposition in the deep lung. Although $PM_{2.5}$ generally behaves as a regional pollutant, there can be considerable small-scale spatial variability due to point source emissions (e.g., a smelter) or features such as street canyons in large cities, in addition, prevailing wind patterns can affect human exposures.

More recently, considerable research attention has been devoted to ultrafine particles (UFPs) <100 nm (0.1µm) in diameter, which result from combustion process. UFPs trend to be short lived, because they agglomerate and coalesce into larger particles. However, they demonstrate very high deposition in human alveoli, account for a major portion of the actual numbers of particles within PM, and have a high surface area to mass ratio, potentially leading to enhanced biological toxicity. UFPs may even be able to pass directly into the circulatory system which could allow them to be disseminated systemically.
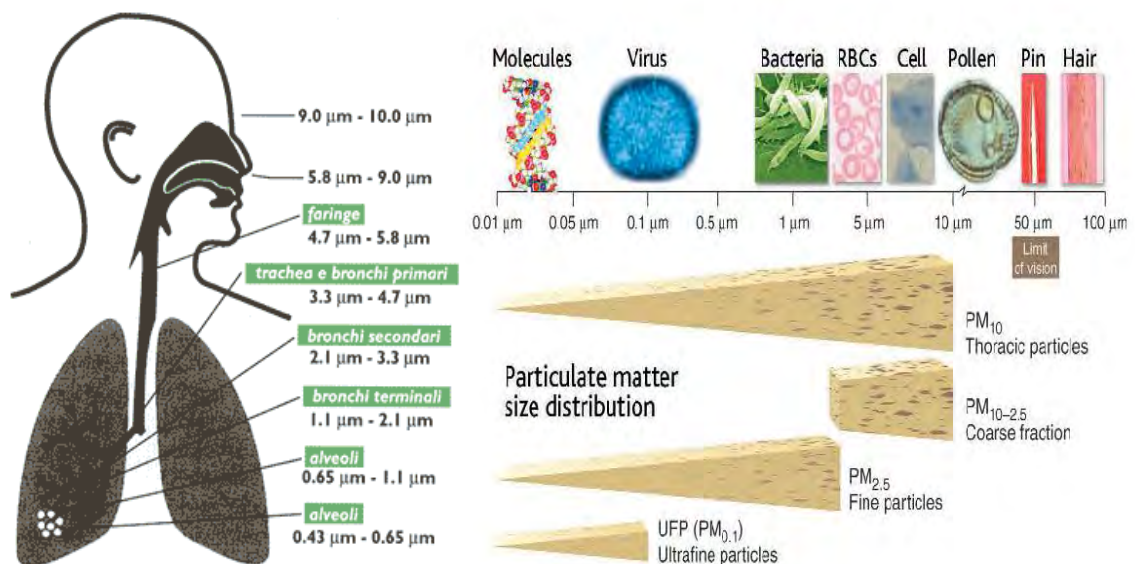
Figure 2.7 Particulate Matters and Size Distribution

Source: Brook et al., 2004.

2.3.1 Physico-chemical Properties of PM_{10}

PM_{10} make up a large proportion of particles that can be drawn deep through the alveoli in lungs. Larger particles tend to be trapped in the nose, mouth or throat. Size is not an absolute criterion as thin flakes or fibers longer than 10 micrometers may be part of a PM_{10} sample because of their aerodynamic properties. Chemical properties of PM_{10} vary depending on sources and chemical adsorbed. It is important to note that PM_{10} is not one particular substance but a classification of dust by size rather than chemical properties (Australian Government, 2006).

2.3.2 Emissions and Composition of PM_{10}

The major sources of particulate matter in Bangkok are motor vehicles, roads and construction dust, industries and power plants (PCD, 2006).

a) Mobile Source

From vehicular registration statistics, it was found that in the year 2007 the number of vehicles registered in Bangkok was 5.67 million (Figure 2.8), increasing trend from year 2004. The increase of vehicles in Bangkok is not proportionate to the increase of roads and has caused traffic congestion and delay in transportation. These large numbers of vehicles and traffic congestion have put severe impact on air quality of Bangkok.
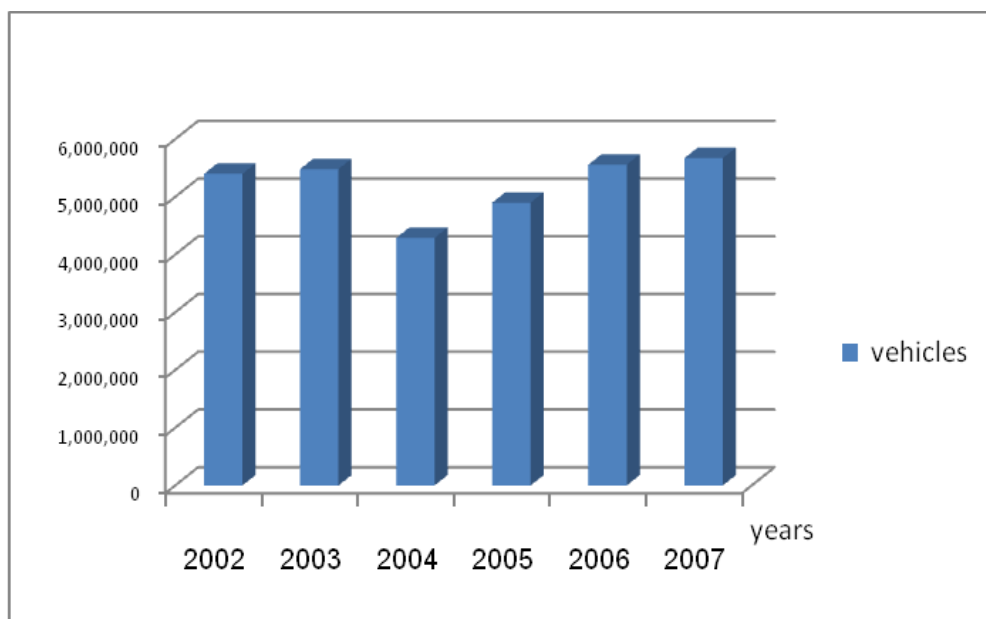
Figure 2.8 Number of vehicles registered in Bangkok, 2002-2007.

Source: Statistics Sub-Division, Technical and Planning Group Land Transport
Management Bureau: Department Land Transport, 2008.

b) Stationary Source

Crematoriums in Bangkok cause both significant nuisance and air quality
problems because of incomplete combustion. The majority (65%) burn wood chips
and charcoal, while the rest primarily burns diesel fuel. Only a few use liquefied
petroleum gas (LPG). The construction of buildings and infrastructures lead to high
level of dust pollution. Lack of proper planning and zoning of housing areas has
aggravated the seriousness of air pollution.

2.3.3   Health Effects of Particulate Matter

2.3.3.1 Health Effects of Particulate Matter to Respiratory System

a) Structure and Function of the Lung

Respiratory system consists of nose, nasal cavity, pharynx, larynx, trachea,
bronchus, bronchioles, and lungs. There may be divided into upper and lower
respiratory tract (CCOHS, 2006). (Figure 2.9)

Lungs lie within thorax, protected by rib cage. Ribs offer support to intercostals muscles and diaphragm. It is the action of these muscles that enlarges the chest during normal breathing. The main function of lungs is rapid gas exchange. This is accomplished by a well-coordinated interaction of lungs with central nervous system, diaphragm and chest wall musculature, and circulatory system (Godwin, 2006).

Gas exchange occurs in alveolus where thin laminar blood flow and inspired air are separated only by a thin tissue layer. Gas exchange takes 0.25 seconds or 1/3 of the total transit time of a red cell. The entire blood volume of the body passes through the lungs each minute in the resting state, which is 5 liters per minute. The total surface area of the lung is about 80 meters square, equivalent to the size of a tennis court.

Only about 10% of the lung is occupied by solid tissue, whereas the remainder is filled with air and blood. Supporting structures of the lung must be delicate to allow gas exchange, yet strong enough to maintain architectural integrity, that is sustain alveolar structure. The functional structure of the lung can be divided into (1) the conducting airways (dead air space), and (2) the gas exchange portions. The two plumbing systems are: airways for ventilation, and the circulatory system for perfusion. Both are under low pressure (Godwin, 2006).

Total lung weight is about 300- 400g. Upper and middle lobes are anterior, while the lower lobes are posterior. Development of each lobe results in division into 19 bronchopulmonary segments which are relatively constant and which often have pathophysiologic correlates, i.e. secondary tuberculosis is seen in the apical segments (Godwin, 2006)
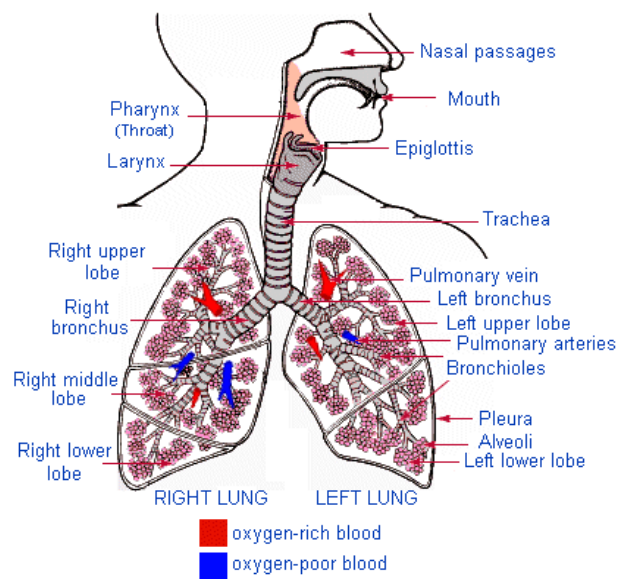
Figure 2.9 Passage of air and the respiratory structures

Source: http://www.sirinet.net/~jgjohnso/respiratory.html

b) Development of the lungs

1. The bronchi grow and branch during the glandular period, which last until approximate the 17 [th] fetal weeks.

2. Bronchi and bronchioles expand and branch during the canalicular period. Respiration becomes possible towards the end of this period around the 25th fetal weeks.

3. The number of terminal sacs increases during the initial part of the alveolar period. Alveolar sacs continue to be formed during early childhood (up to year 8) and mature into alveoli.

c) Defense Mechanisms of the Lung

Protection against particles is at four levels (Godwin, 2006):

1. Upper airway filter

Filtering mechanisms in the nasal cavity trap and eliminate so that larger particles over 15 µm in diameter hit the surface and are carried in the mucus to the

pharynx and swallowed. If the particles are irritated or cause an allergic reaction, two reflexes are sneezing and coughing.

2. Lower airway filter

This level lined by mucociliary epithelium acts as a low resistance filter which removes nearly all of the particles down to about 5 μm in diameter. The particles are carried in the mucus back to the larynx, join the particles from the upper airways and are swallowed or expectorated.

3. Macrophage clearance to the airways

Particles less than 0.5 μm in diameter getting beyond the mucociliary system onto the lining of the alveolar ducts and alveoli and may be retained. Macrophages move out from the wall and engulf the particles, moving back in when fully loaded.

4. Macrophage segregation and clearance via the lymphatics

When the overload of the particles is very heavy then the macrophages damages or cell die. The other macrophages attempt to carry the particles to the hilar lymph nodes either via the lymphatic in the interlobular septa and under the pleura or those along the blood vessels (Figure 2.10)
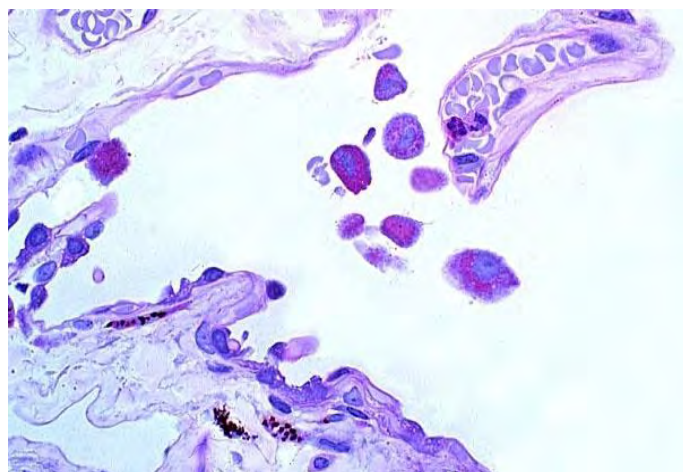
Figure 2.10 Alveolar macrophages of human lung

Source: http://www.bu.edu/histology/ p/13906ooa.htm

Figure 2.11 showed range of the particles size. Particles may be placed into several categories such as dust, ash, fume, smoke, and secondary particles. Dust particles are defined as particles of mechanical or biological origin including soil, sea spray, spores, pollen, and bacteria. Smoke describes carbonaceous residues from incomplete combustion processes. Secondary particles are formed in the atmosphere due to reaction of gases. Mists or fogs are liquid droplets in the atmosphere and fumes result from gaseous materials which nucleate in the atmosphere to form larger aggregates.
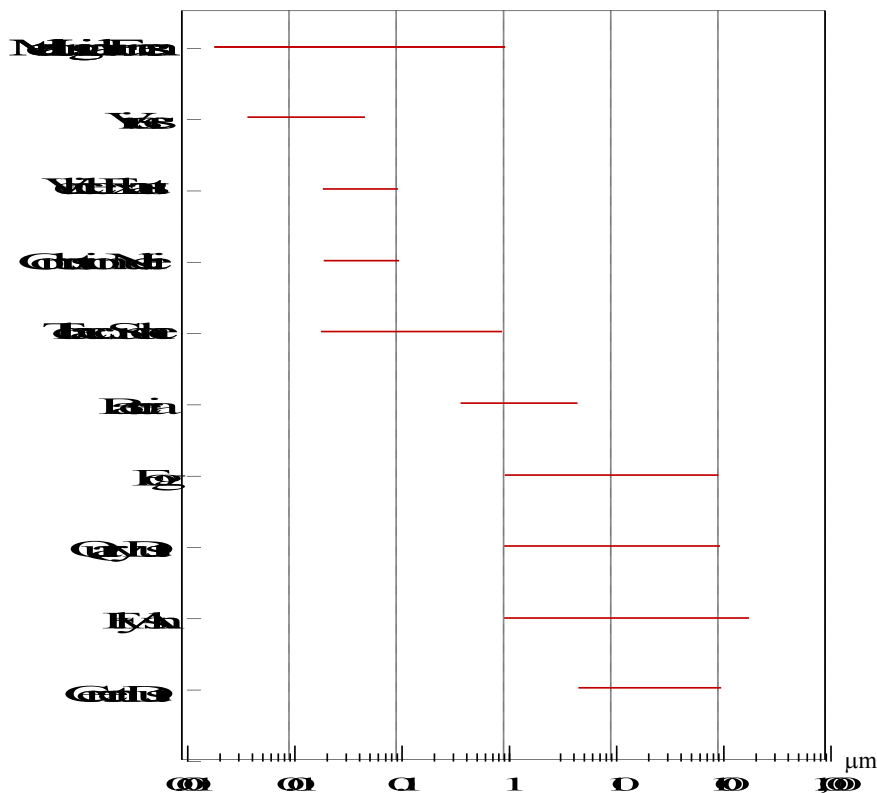
Figure 2.11 Range of particle size (EPA, 1991)

It has been difficult to separate the effects of the particles from cigarette smoking and environment pollutants. However, the severity of the damage depends on the combined effect of the toxicity and the level of exposure.

d)   Lung Dosimetry

Four processes that the particulates deposited in the lungs (CCOHS, 2006):

1. Interception: particle is deposited when it travels so close to a surface of the airway passages that an edge of the particle touches the surface.

2. Impaction: particles having an aerodynamic diameter of 5 to 30 μm are deposited in the nasopharyngeal region.

3. Sedimentation: small particles with an aerodynamic diameter of about 1 to 5 μm are deposited in the tracheobronchial region.

4. Diffusion: small particles with an aerodynamic diameter of about 0.5 μm are deposited in the alveolar region.

2.3.3.2 Health Effects of Particulate Matter to Cardiovascular System

Both coarse and fine particles are of health concern because they can penetrate into the sensitive regions of the respiratory tract. Fine particles are of greatest concern because they are linked to the most serious effects. They can be deeply inhaled into the lungs where they can be absorbed into the bloodstream or remain embedded for long periods of time. They can cause persistent coughs, phlegm, wheezing, and physical discomfort.

a) Mechanisms of Action

Fine particles are easily inhaled deeply into the lung where they can be absorbed into the blood stream and effect to heart. In the same time Particulate Matter can induce pulmonary inflammation then autonomic stress response happening represent the sign of increasing Heart Rate (HR), Blood Pressure (BP) and decreasing of Heart Rate Variability (HRV) and accordingly, it can show acute phrase response such as increasing C-Reactive Fibrinogen and Factor VII (that control coagulation of Blood) all of this mechanism can effect to heart and show symptoms as "Arrhythmia" (Figure 2.12)
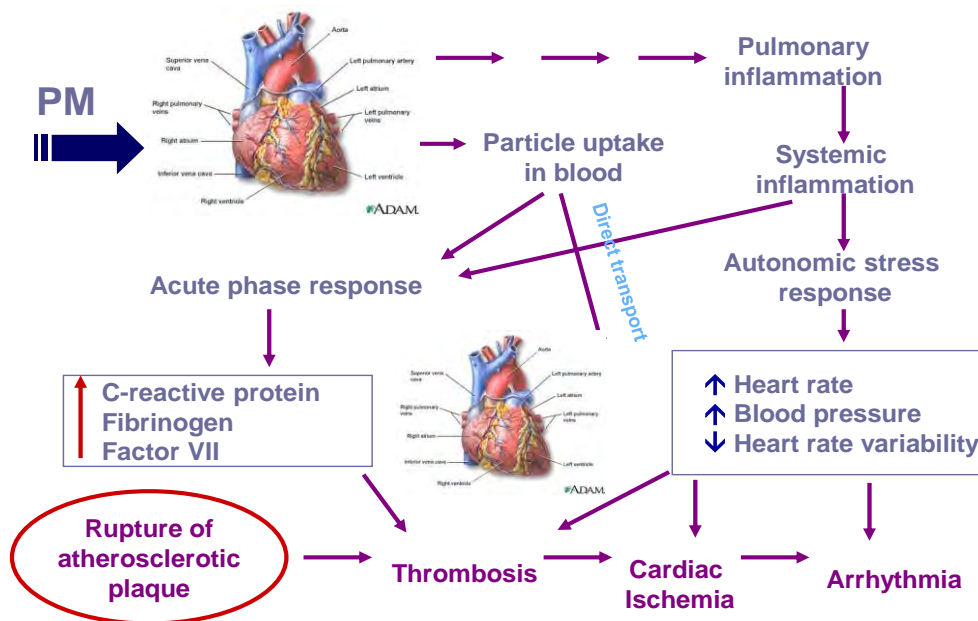
Figure 2.12   Biological mechanisms linking PM with cardiovascular disease (CVD)

Source: Brook et al., 2004
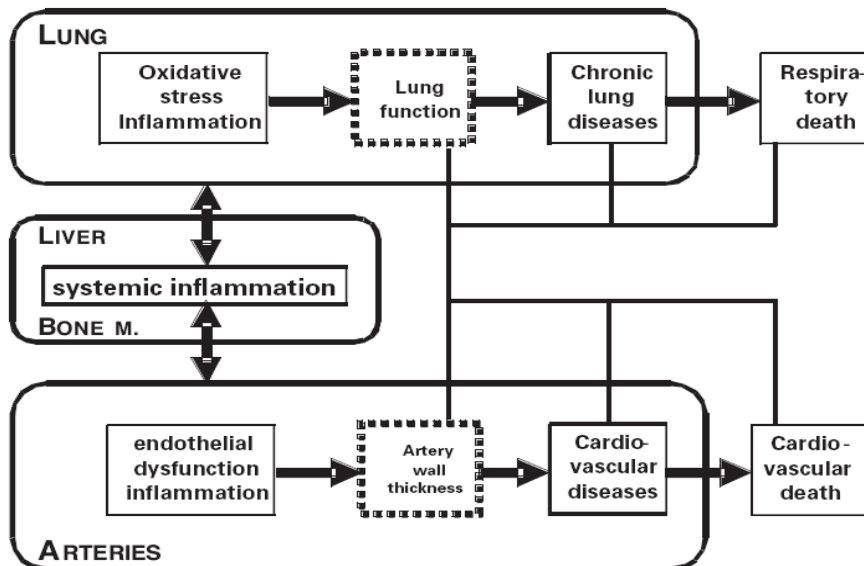
Figure 2.13   Model of the interrelated pulmonary, systemic and vascular chronic inflammatory responses to air pollution. Lung function and artery wall thickness are examples of markers of the continuous chronic process from health to disease.

(Thin lines denote correlations established in epidemiological studies)

Source: Kunzli et al., 2005.

Several recently published community health studies indicate that significant respiratory and cardiovascular-related problems are associated with exposure to particle levels well below the existing particulate matter standards (Aekplakorn et al., 2003b; Duanping et al., 2004; Karita et al., 2001; Karita et al., 2004; Ostro et al., 1999; Tamura et al., 2003 and Kiinzli N et al., 2005). These negative effects include premature death, hospital admissions from respiratory and cardiovascular causes, and increased both symptoms. Short-term exposure to coarse particulate matter can lead to coughing, minor throat irritation and a reduction in lung function. Long-term exposure to particulate matter may increase the rate of respiratory and cardiovascular illness and reduce life span (Figure 2.12 and 2.13)

2.4 Gaseous Co-Pollutants

Air is a mixture of gases that surrounds the earth and makes up our atmosphere. Pure air consists of 21% oxygen and 78% nitrogen by volume, plus traces of other substance and gases both natural and anthropogen (man-made). The air that we breathe may actually contain thousands of chemical and biological substances. Many of these are pollutants such as: ground-level ozone (O_3), total suspended particulate (TSP), fine particulate matter less than 2.5 microns in diameter ($PM_{2.5}$) or particles less than 10 microns in diameter (PM_{10}), sulphur dioxide (SO_2), carbon monoxide (CO), nitrogen oxides (NO_x), volatile organic compounds (VOCs), sulphate (SO_4), and nitrates (NO_3).

Outdoor air contaminants come from both natural and human sources. Natural sources include smoke from forest fires, wind-blown dust from soil and volcanoes, bacteria, fungi and chemicals released by plants and animals. However, air pollution is primarily associated with everyday human activities. Pollutants are released by motor vehicles, industrial processes (pulp and paper mills, ore smelters, petroleum refineries, power generating stations and incinerators), and the burning of fossil fuels such as gas, oil, coal and wood.

Air pollutants can be carried thousands of miles across borders and oceans or from one urban area to another. This phenomenon is common around the world and is referred to as "long-range atmospheric transport" or "transboundary pollution".

2.4.1 Ground-level Ozone (O$_3$)
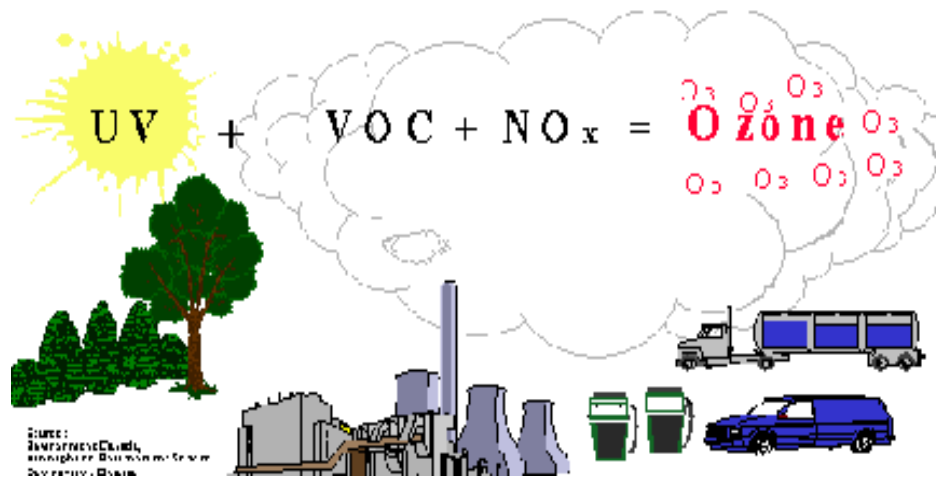
Figure 2.14 Ground-level Ozone Formation.

Source: Environment Canada Atmospheric Environmental Science, 2006.

http://www.hc-sc.gc.ca/ahc-asc/index-eng.php

Ozone is a naturally occurring gas in the lower atmosphere that increases in concentration when volatile organic compounds (VOCs) and nitrogen oxides (NOx) react in the presence of sunlight and stagnant air. High levels of ground-level ozone often occur during hot summer days in or downwind of heavily populated areas, where sources emit the necessary VOCs and NO$_x$ to produce ozone. (Figure 2.14) Ground-level ozone, a primary component of smog, differs markedly from the protective blanket of ozone high above the earth (also known as the 'ozone layer' or 'stratospheric' ozone), which acts to shield the Earth's surface from intense ultraviolet radiation produced by the sun. Ground-level ozone has been linked with a broad spectrum of human health effects. Because of its reactivity, ozone can injure biological tissues and cells. Exposure to ground-level ozone for even short periods at relatively low concentrations has been found to significantly reduce lung function in healthy people during periods of exercise. This decrease in lung function is generally accompanied by other symptoms including tightness of the chest, pain and difficulty breathing, coughing and wheezing. The data on health effects of ozone have been examined in human epidemiological studies and exposure to ozone has been associated with mortality, hospital admissions, emergency department visits, and other adverse health effects.

2.4.2 Nitrogen Oxides (NO_x)

Nitrogen oxides are reactive substances commonly understood to encompass nitric oxide (NO), nitrogen dioxide (NO_2), nitrogen trioxide, nitrogen tetroxide (N_2O_4), and dinitrogen pentoxide (N_2O_5). These compounds are referred to collectively as "NO_X" Gaseous nitric acid (HNO_3), a major source of particulate nitrate, is formed when NO_2 reacts with hydroxyl radicals during the day and when N_2O_5 reacts with water vapor at night. Other members of the larger family of nitrogen oxides include nitrous acid, nitrous oxide, peroxyacetyl nitrate (responsible for some of the irritant effects of photochemical smog), nitrites, nitroso-compounds, and other nitrogen-containing acids. Most toxicological and epidemiological research has focused on NO_2, because of the fact that (1) NO_2 is one of the regulated air pollutants for which standards are available worldwide; (2) NO from vehicular exhaust and power plants is largely converted to NO_2; and (3) NO_2 plays a primary role in the formation of tropospheric ozone (O_3).

The main anthropogenic source of NO_X in ambient air is fossil fuel combustion in motor vehicles and industrial processes, particularly in power generation. High temperature combustion results in the oxidation of atmospheric N_2 first, to NO and then to NO_2. Motor vehicle emissions near busy streets can result in high local NO_X concentrations. The typical diurnal NO_X pattern consists of a low background concentration, with morning and late afternoon peaks resulting from rush-hour traffic. Nitrogen in fossil fuels such as coal can be oxidized to NO_2 under oxygen-rich combustion conditions. NO_2 and NO are both formed naturally as a result of bacterial metabolism of nitrogenous compounds and, to a lesser extent, from fires, volcanoes, and fixation by lightning. The generation of tropospheric ozone and other photochemical oxidants is initiated with photolysis of NO_2, whereas NO acts as an ozone scavenger. (Lipsett et al., 2001) Significant human exposure can occur in non occupational indoor settings. Gas-burning appliances, such as unvented furnaces and stoves, are the principal sources of indoor NO_X, although kerosene space heaters and tobacco smoke may also play a role. In urban areas, infiltration of ambient NO_2 from vehicular emissions may also influence indoor exposures.

At elevated levels, NO_x can impair lung function, irritate the respiratory system and, at very high levels, make breathing difficult, especially for people who already suffer from asthma or bronchitis.

2.4.3 Volatile Organic Compounds (VOCs)

Volatile organic compounds are a group of carbon-containing compounds that tend to evaporate quickly at ordinary temperatures. VOCs are present in our atmosphere at very low levels. Generally, VOCs are found in higher concentrations indoors than outdoors. VOCs can react with nitrogen oxides to form ground-level ozone. Thousands of natural and synthetic chemicals are VOCs, including benzene which is a natural component of crude oil and petroleum products. Some VOCs are carcinogenic, such as formaldehyde and benzene, and some are irritants as a group of precursors to ozone.

2.4.4 Sulphur dioxide (SO_2)

SO_2 is a naturally occurring substance that becomes problematic at higher concentrations. Like nitrogen oxides, sulphur dioxide is produced primarily by industrial processes and fuel combustion. SO_2 can be chemically transformed in the atmosphere in the presence of other chemicals and sunlight to form acidic pollutants such as sulfuric acid and sulphates. SO_2 is a common air pollutant found in outdoor environments. SO_2 can cause breathing problems in people with asthma, but at relatively high levels of exposure. There is some evidence that exposure to elevated SO_2 levels may increase hospital admissions and premature deaths.

2.4.5 Carbon Monoxide (CO)

The principal human source of CO is from fuel combustion, primarily vehicles. CO concentrations are much higher in urban areas due to the number of human sources, although this gas is also released by natural sources such as volcanoes and forest fires. CO is an odorless, colorless, and tasteless gas that binds to hemoglobin with an affinity 250 times that of oxygen, thereby interfering with the systemic delivery of oxygen to tissues. In addition, binding of CO to hemoglobin causes an allosteric change in the conformation of the oxy-hemoglobin complex that

increases the oxygen affinity of the remaining binding sites and interferes with the release of O_2 at the tissue level. In addition, CO binds to cytochrome oxidase, exacerbates cellular hypoxia, and binds to other extravascular proteins that include myoglobin, cytochrome P-450, catalase, and peroxidases. (Seger et al., 2001) Health effects associated with relatively low-level, short-term exposure to CO include decreased athletic performance and aggravated cardiac symptoms. At the levels typically found in large cities, CO could attain concentrations sufficient to lead to physiologically meaningful increases in carboxyhemoglobin in persons with significant atherosclerotic disease or other cardiac conditions and may increase hospital admissions for cardiac diseases, and there is also evidence of an association with premature deaths.

2.4.6 Smog

The term smog was first used to describe the combination of smoke and fog in the atmosphere. In recent years it has become the term given to the chemical soup that is often visible as a yellow-brown haze that hangs over many cities on calm summer days. Smog is a mixture of airborne chemicals which originate from or are produced by motor vehicle and industrial pollution.
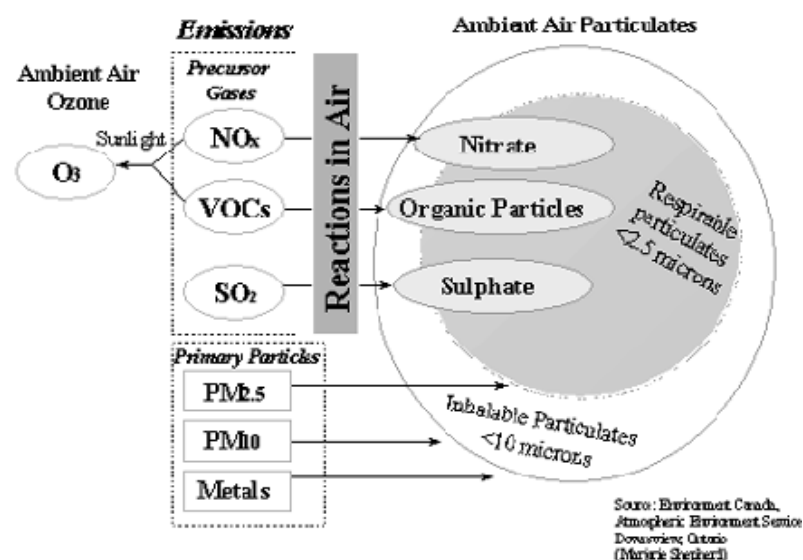
Figure 2.15 Origins of Particulate Matter and Ozone.

Source: Environment Canada Atmospheric Environmental Science, 2006.

http://www.hc-sc.gc.ca/ahc-asc/index-eng.php

A major component of smog is ground-level ozone (O_3), which is formed when two main pollutants, nitrogen oxides (NO_x) and volatile organic compounds (VOCs) react in sunlight and stagnant air. Airborne particles such as fine particles or sulphates are also an important component of smog. Because smog formation depends on heat and sunlight, smog generally peaks in late afternoon and early evening. Smog is most obvious in large cities, although suburban and rural communities are not spared. Breathing in smog has adverse and varied consequences for human health with the cardio-respiratory system being the main target of concern. Wherever its location and whether visible or not, smog is hazardous to human health.

2.5 Epidemiology Study

Epidemiology is the study of the determinants, occurrence, and distribution of health and disease in a defined population. Infection is the replication of organisms in host tissue, which may cause disease. A carrier is an individual with no overt disease who harbors infectious organisms. Dissemination is the spread of the organism in the environment (Brachman, 2006). Assessing the health effects of air pollution most evidence linking the various human health effects to ambient levels of air pollution comes from the fields of epidemiology and toxicology. This section consists of a description of the main features of these fields as it applies to the assessment of effects from air pollution.

2.5.1 Assessing the health effects of air pollution

The relationship between changes in air pollution levels over the short term and changes in various indicators of population health or health of individuals is studied in time series, panel, meta-analysis and case-crossover studies.

a) Time series studies

Time series studies estimate the influence of temporal (usually daily) variations in air pollutant concentrations on mortality or morbidity, using statistical models linking the daily counts of health events in a geographically defined population with daily measures of air pollution and other time-dependent variables. It is by conducting studies using this type of design that most of the evidence of the role of air pollution in producing acute health effects has been generated. These include primarily studies of daily mortality, hospital admissions, and visits to emergency departments and primary care facilities (Ballester et al., 2001)

Increased access to health and air pollution data is one factor that has facilitated the implementation of time series methods in air pollution epidemiology. Mortality data are obtained from death registration agencies, while data on hospital admissions and visits to emergency departments and primary care facilities are usually obtained from computerized medical records. Access to air pollution data has been increased by the enhancement of air monitoring capacities in many urban areas of the world. This has made possible the assessment of effects of air pollution on relatively large populations, whose analysis would not be feasible if it required personal interviews to be conducted to obtain both health and exposure data. A large population size is necessary to ensure statistical power in situations where the magnitude of the individual effect is relatively small, as is observed when quantifying air pollution effects.

Another aspect determining the quantity and quality of time series studies is the substantial developments in statistical methods for time series analyses, particularly on the issue of controlling for potential temporal confounding by time varying factors such as weather and seasonality. Inadequate controlling for these factors can lead to spurious associations, and this methodological drawback was the main argument used by those questioning its validity in the past. Flexible smoothing techniques such as the Generalized Additive Models (GAM) (Hastie et al., 1990), which allows non-parametric smooth functions to control for the non-linear effects of season and temperature, have been introduced to provide a better fit to the data and thereby tighten confounding control. (Schwartz et al., 1996) This method first

appeared in the air pollution literature around 1993 and has since become the standard approach in time series analyses (Schwartz et al., 1993). Problems were identified in the application of GAM routines generated with a widely used statistical software product. This was responsible for an overestimation of the effects of air pollution on mortality in studies conducted with this software (Dominici et al., 2002). Problems in the generation of standard errors, leading to an incorrect estimation of confidence intervals, were also identified. Both these problems generated a series of re-analyses of key studies, using alternative approaches, and have since been resolved (Dominici et al., 2003). Methods have also been developed to obtain estimates resistant to short-term mortality displacement, reducing the possibility that the increased mortality associated with higher pollution levels is restricted to very frail persons for whom death would be brought forward only a few days or weeks. Time series studies consider short-term exposures and, for this reason, are especially suited to examining the acute effects of air pollution. In fact, if there are short-term relationships (for example, air pollution has an effect on hospital admissions or mortality observed one or two days from the time of exposure) these can only be detected through daily analysis. In contrast, chronic effects of air pollution cannot be completely quantified with time series methods. Long-term exposure may increase individual frailty, but those who are frail might die at a time unrelated to an acute exposure and they are therefore not captured by a time series study.

One of the great advantages of the time series approach is that factors such as socioeconomic conditions, occupation or tobacco use cannot confound the relationship between air pollution and health effects, since these factors do not present daily variations. Moreover, the use of already collected health and exposure data reduces the costs associated with data collection, making this type of study less expensive to conduct than other epidemiological designs. Its lower costs make it easy to replicate in different locations. Nevertheless, the use of data that have been generated for purposes other than research has some limitations. Issues with quality of health data include differences in diagnosis, recording and reporting, which introduce variability and may explain differences in individual risk estimates when comparing results from different studies.

Pollutant concentrations used in studies usually come from established monitoring networks. Measurement methods, especially for ambient particles, differ among cities but specific practices are not always reported. This difference in methodology can influence the estimates obtained in time series studies. In addition, the sources, levels and composition of the air pollution mix, as well as other individual exposure factors such as population mobility and daily activity patterns, may vary greatly from city to city and thus influence these estimates. Overall, this design has advanced our understanding of the relationship between air pollution and health effects. It has allowed the exploration of effects associated with acute (and to some extent sub-acute) exposure durations in different population subgroups for different outcomes, facilitating the gathering of evidence and suggesting determinants of susceptibility. Finally, the consistent replication of results in many locations under different exposure conditions provides evidence in support of a causal relationship.

b) Panel studies

In such studies a group of individuals, ideally homogeneous, is followed up prospectively for a short period of time. Multiple measurements are obtained from each subject at different times and analyzed using time series methods. This design has been employed to assess the association of short-term exposure to air pollutants with respiratory symptoms such as sore throat, common cold, cough, wheeze and shortness of breath, related medication use, and changes in pulmonary function (Anderson et al., 2004). The design allows the exploration of these outcomes on more susceptible individuals, such as those with underlying respiratory disease, children and the elderly. Individuals are followed for a predetermined period, during which they record the daily occurrence of the outcome under investigation. One benefit of this design is the ability to obtain health- and exposure-related information from each individual, including a detailed health history, smoking history, socioeconomic status, and behavioral and time-activity patterns. Exposure information can also be obtained by means of personal monitoring, as the number of participants in panel studies is usually not large. Because exposure is common to all members of the panel, each individual serves as his or her own control, thereby eliminating the need for a control group. Only covariates, that varies across time for a particular individual need to be controlled during the analysis.

c) Meta-analysis

A meta-analysis consists of a statistical synthesis of data from a number of independent but comparable studies of a problem, leading to a quantitative summary of the pooled results. Many efforts have been made to integrate the findings of time series studies, pooling results to identify overall trends in the influence of temporal variations in ambient particle concentrations on mortality or morbidity over a geographical area. Meta-analyses of panel studies have also been conducted. Some of these initiatives have been conducted through a multicentre approach, whereby protocols are developed to standardize all aspects of data collection and analysis. This approach ensures that data are highly comparable and that differences in results between individual centres are not explained by variability in study methods. In Europe, the APHEA-2 project used this methodology to estimate the influence of daily variations in various pollutants on mortality and morbidity for 29 cities whose data were later pooled (Katsouyanni et al., 2001). A similar approach was undertaken in 90 American cities by the NMMAPS (Dominici et al., 2003).

Because time series studies have been conducted in many parts of the world, there is quite a large body of literature published by independent investigators. These results have also been pooled in order to identify overall trends. While the generation of quantitative summary estimates arising from these analyses did not benefit from a multicentre approach, steps were taken to make the results as comparable as possible. This was achieved by conducting a systematic critical appraisal of the studies, applying a predetermined set of criteria to ascertain study methods and data quality. W.H.O has formulated guidelines for the systematic evaluation of epidemiological evidence. Such quantitative summary estimates have been generated for Asia, Europe and Latin America. Another such effort combined data from 109 studies conducted in different parts of the world. Quantitative summary estimates provide more robust information than data from individual studies, and therefore facilitate regional comparisons and the calculation of health impacts. One important problem in meta-analysis is the potential for publication bias, which refers to the tendency of editors to publish articles containing positive findings rather than those that do not yield "significant" results. Statistical techniques are available to assess this bias and should be used when conducting meta-analysis.

Quantitative summary estimates are often used for estimating the costs and benefits of air pollution. A limitation related to the usefulness of quantitative summary estimates for decision-making has to do with the heterogeneity of effect estimates from individual studies. Often in meta-analysis, effect estimates are pooled without consideration of the location of the individual studies. This may lead to the generation of quantitative summary estimates based on results that are not comparable. As observed with the development of exposure–response curves, more thought needs to go into how to address subgroup variations to enhance generalizability without losing power. Similarly, sources of heterogeneity include the air pollution mix, climate, and individual population sensitivities and demographics.

d) Case-crossover analysis

The case-crossover study design was proposed by Maclure, 1991 to study the effects of momentary and intermittent exposures on the risk of developing an acute and rare health event supposed to occur soon after the exposure. Since this design focuses on individual deaths rather than death counts, it is possible to control for factors that may modify or influence the effects of air pollution on mortality at the individual level. Therefore, this approach has been applied in studies of the effects of air pollution on health as an alternative to time series analysis, since it may improve causal inferences about air pollution effects (Drew et al., 2001). The design can be seen as a variation on the case-control study, in which each individual bearing the event of interest (the case) acts as his or her, own control. For each case, the distribution of exposures in the period just before the event is compared with the distribution of exposures estimated from some separate referent time period. Thus, by making within-subject comparisons, time-independent confounders are controlled by design. When this design is applied to exposures that exhibit a time trend, however, there is great potential for confounding in the risk estimate owing to this trend in the exposure series. Therefore, an important methodological feature of this strategy is adequate selection of control or referent periods. Several simulation analyses have explored the potentials and problems of different strategies for sampling control periods but, in general terms, they agree that they should be sampled bi-directionally, i.e. before and after the event.

2.5.2 Burden of diseases in Thailand

Currently, non communicable diseases and cancer have become the leading causes of morbidity and mortality among Thai people, such as increasing trend results from unhealthy consumption behaviors and physical inactivity, as evidently demonstrated by the following hospital admission rates and the number of patients with coronary atherosclerosis treated. (Figure 2.16 and 2.17)

- Heart Diseases. The admission rate per 100,000 populations has risen from 56.5 in 1985 to 109.4 and 618.5 in 2006
- Cancer. The admission rate per 100,000 populations has risen from 34.7 in 1994 to 124.4 in 2006
- Diabetes. The admission rate has also risen from 33.3 per 100,000 populations in 1985 to 91.0 in 1994 and 586.8 in 2006
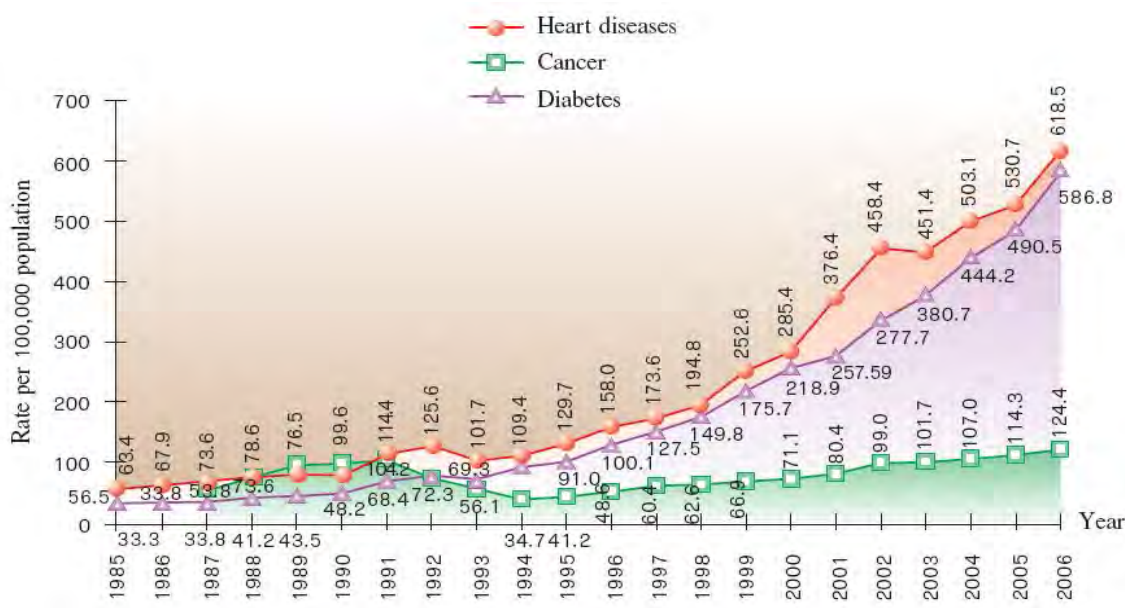
Figure 2.16 Rate of Hospitalizations of patient with heart disease, cancer and diabetic, 1985-2006.

Source: Inpatient Report, Bureau of Policy and Strategy, Ministry of Public Health; 2007. (Thailand Health Profiles; 2005-2007)

Note: the rate for cancer, since 1994, covers only liver, lung, cervical and breast cancers.
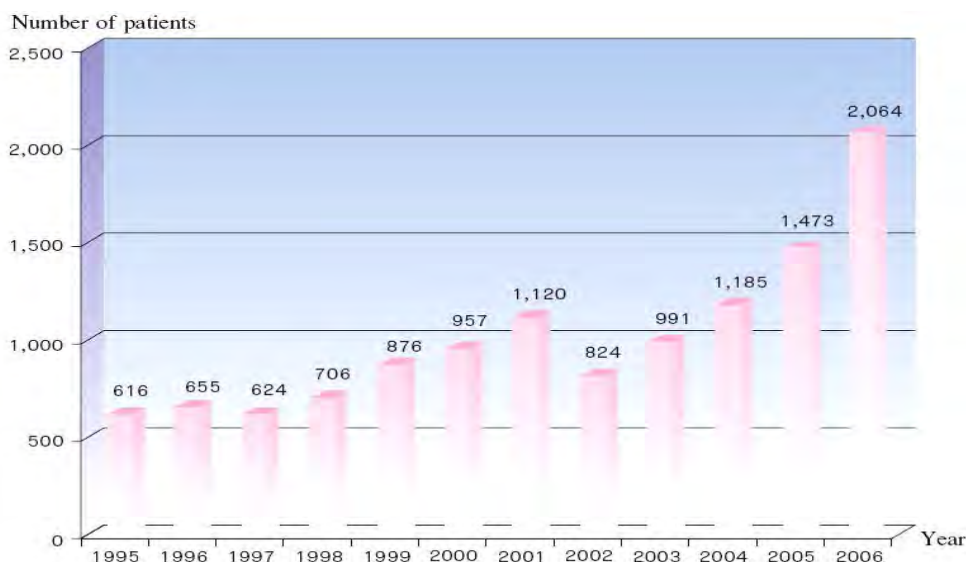
Figure 2.17 Number of patients with coronary atherosclerosis treated at the Cardiology Institute, 1995-2006.

Source: Institute of Cardiology, Department of Medical Services, MOPH; 2007.

2.6   Literature Reviews

Jinsart et al., 2002 reported $PM_{2.5}$ and PM_{10} in Bangkok, Nonthaburi and Ayuttaya were measured from December 1998 to March 1999 and from November to December 1999. The personal exposure results showed a significantly higher proportion of $PM_{2.5}$ to PM_{10} in the High-polluted area (H) than in the Low-polluted area (L) (H= 0.80±0.08 and L= 0.65±0.04). Thailand Pollution Control Department (PCD) showed air quality data for 1997-2000, including 24-hour average PM_{10}, No_2, SO_2 and O_3. In Bangkok, vehicle emission is the main source of the particulate air pollution. $PM_{2.5}$ and PM_{10} indicate the potential environmental health hazard of fine particles. Bangkok traffic policemen were exposed to high levels of automobile-derived particulate air pollution.

Pope et al., 2002 reported that each 10 µg m^{-3} increase in fine particulate air pollution was accompanied by an 18 percent increase in risk of death from ischemic heart disease and a 13 percent increase in risk of death from altered heart rhythm, heart failure or cardiac arrest. Further analysis also showed higher risk associated with air pollution for former and current smoker 26% and 94% respectively. Pope

noted that "smoking is clearly a much larger risk factor, but air pollution increases the risk of cardiovascular death in non-smokers and seems to additional risk to smokers."

Karita et al., 2001 examined the relationship between traffic-based air pollution and chronic, nonspecific respiratory symptoms among traffic policemen in Bangkok, Thailand. A total of 1,603 policemen who lived and worked in areas that had 3 different levels of airborne particulate were evaluated. The authors used a modified standardized questionnaire to identify Non Specific Respiratory Disease (NSRD) in participants. The prevalence of NSRD in heavily polluted, moderately polluted, and suburban areas was 13.0%, 10.9%, and 9.4%, respectively. Among nonsmoker, the age-adjusted prevalence of NSRD in the heavily polluted areas was significantly higher than in the suburban control area. Also among nonsmokers, the odd ratio for NSRD for each 10 μg m^{-3} increase in ambient particulate matter was 1.11. The authors concluded that the increased prevalence of respiratory symptoms among traffic policemen in Bangkok was associated with urban traffic air pollution.

Liao et al., 2003 reported an association between air pollution and increased cardiovascular disease (CVD) mortality but underlying mechanisms are unknown. The authors examined short-term associations between ambient pollutants (PM$_{10}$, O$_3$, CO, NO$_2$ and SO$_2$) and cardiac autonomic control using data from the fourth cohort examination (1996-1998) of the population-based Altherosclerosis Risk in Communities Study. For each participant, the authors calculated PM$_{10}$ and gaseous pollutant exposures as 24-hour averages and ozone exposure as an 8-hour average 1 day prior to the randomly allocated examination date. They calculated 5-minute heart rate variability indices and used logarithmically transformed data on high-frequency (0.15-0.40 Hz) and low-frequency (0.04-0.15Hz) power, standard deviation of normal R-R intervals, and mean heart rate. Linear regression was used to adjust for CVD risk factors and demographic, socioeconomic, and meteorological variables. Regression coefficients for a one-standard-deviation increase in PM$_{10}$ (11.5 μg m^{-3}) were –0.06 ms (standard error, 0.018), -1.03 ms (SE, 0.31), and 0.32 beats/minute (SE, 0.158) for log-transformed high-frequency power, standard deviation of normal R-R interval, and heart rate, respectively. Similar results were found for gaseous pollutants. These cross-sectional findings suggest that higher ambient pollutant concentrations are associated with lower cardiac autonomic control, especially among persons with

existing CVD, and highlight a putative mechanism through which air pollution is associated with CVD.

Anderson et al., 2003 studied a systematic literature review and suggests that particulate air pollution is associated with daily admissions for both respiratory and cardiac diseases in people aged ≥65 yrs. A model of acute effects is proposed which shows how admissions can be brought forward by a relatively short period of time as well as events being added that would not have happened at all except for air pollution. A model of the effects of air pollution on chronic disease is proposed that provides the background of long-term vulnerability upon which the increased short-term vulnerability is superimposed. A study of daily hospital admissions in London shows that for respiratory disease the relative risks of admission associated with particles reduce with increasing age, while for cardiac disease, there is no trend, when the attributable risk is estimated using baseline admission rates for respiratory diseases; it is children who have the highest attributable risk, followed by the elderly. In cause of heart diseases, there is a steep increase in attributable risk with age, reflecting the dominant influence of baseline risks. The attributable risk for cardiovascular disease in the elderly is considerably greater than for respiratory disease, due to higher baseline admission rates.
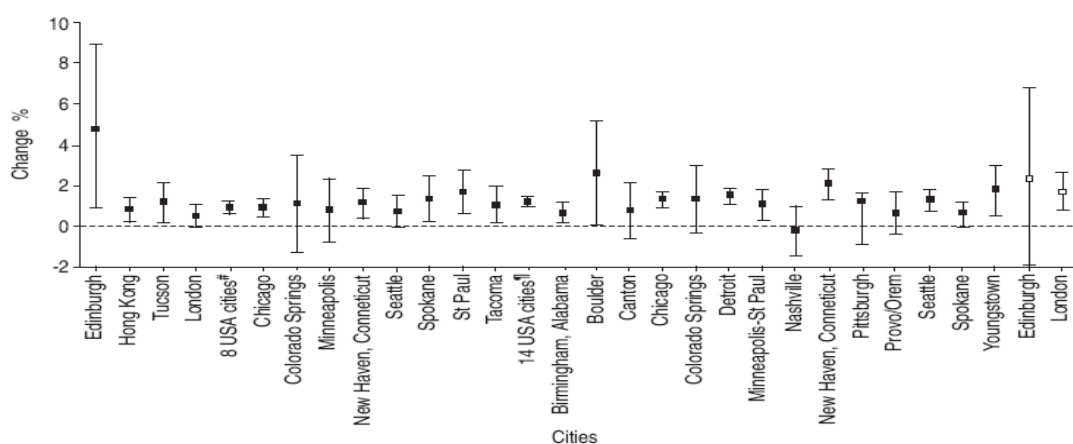
Figure 2.18 Published studies of particles and daily emergency admissions for cardiovascular diseases. The percentage change for a 10 unit increase in particles is shown, with 95% confidence intervals. &: particles with a 50% cut-off aerodynamic diameter of 10 mm (PM_{10}); black smoke. Summary estimate for the eight USA cities listed to the right; summary estimate for the 14 USA cities listed to the right.
Source: Anderson et al., 2003.

Schwartz et al., 2004 reported the association between deaths and particulate matter PM_{10} using a case-crossover design. In this approach, the pollution on the day of each death is contrasted with the pollution level on control days when the subject did not die. Season and gaseous air pollutants were controlled by matching. Control days were chosen within the same month of the same year to control for season, and match on either sulfur dioxide (SO_2: within 1 ppb), nitrogen dioxide (within 1 ppb), maximum ozone (within 2 ppb), or carbon monoxide (within 0.03 ppb). The analysis was conducted in 14 U.S. cities that have daily PM_{10} monitoring. After matching, there were about 400,000 deaths in each analysis. Results were combined across cities using a maximum likelihood method. PM_{10} was a significant predictor of mortality when controlling for gaseous air pollution, with effect sizes ranging from a 0.45% increase per 10 $\mu g \ m^{-3}$ increment of PM_{10} (95% confidence interval (CI): 0.12-0.79%) when matched on maximum hourly ozone levels, to a 0.81% increase per 10 $\mu g \ m^{-3}$ increase of PM_{10} (95% CI: 0.47-1.16%) when matched on 24-hour average SO_2.

Karita et al., 2004 reported that effect of working and residential location areas on air pollution related respiratory symptoms in policemen and their wives in Bangkok. Factors, including air pollution, influencing the prevalence of respiratory symptoms were investigated in a cross-sectional study in policemen and their wives (530 couples) in Bangkok. Information on respiratory symptoms was obtained using the American Thoracic Society Division of Lung Diseases (ATS-DLD) questionnaire. Effects of working and residential locations were evaluated using a multiple logistic model adjusted for several potential confounding factors. In the policemen the increased risk of frequent cough or phlegm was related to smoking (OR=2.19, 95% CI: 1.47 - 3.26) and working in heavy traffic location (OR=1.27, 95%CI: 1.01 - 1.61), whereas in their wives it was related to their residential location (OR=1.53, 95%CI: 1.10 - 2.13).

Wheeler et al., 2006 studied about the association between concentration of ambient $PM_{2.5}$ and Heart Rate Variability (HRV) has differed by study population . The author examined the effects of ambient pollution on HRV for 18 individuals with chronic obstructive pulmonary disease (COPD) and 12 individuals with recent Myocardial Infarction (MI) living in Atlanta , Georgia. HRV, baseline pulmonary

function, and medication data were collected for each participant on 7 days in fall 1999 and/or spring 2000. Hourly ambient pollution concentrations were obtained from monitoring sites in Atlanta. The association between ambient pollution and HRV was examined using linear mixed- effect models . Ambient pollution had opposing effects on HRV in COPD and MI participants , resulting in no significant effect of ambient pollution on HRV in the entire population for 1-hr., 4-hr., or 24-hr. moving average. For individuals with COPD , interquartile range (IQR) increases in 4-hr ambient $PM_{2.5}$ (11.65 µg m^{-3}) and NO_2 (11.97 ppb.) were associated with 8.3% (95% CI: 1.7 to 15.3) and 7.7% (95% CI: 0.1 to 15.9) increase in the SD of normal R- R intervals (SDNN), respectively. Individuals with MI , IQR increases in 4 hr $PM_{2.5}$ (8.54 µg m^{-3}) and NO_2 (9.25 ppb) were associated with a non significant -2.9% (95% CI: -7.8 to 2.3) and significant -12.1 (95% CI; -19.5 to -4.0) decreases in SDNN . Beta-blocker and bronchodilator intake and baseline forced expiratory volume in 1 sec modified the PM– SDNN association si gnificantly, with effects consistent with those by disease s group. The result indicate heterogeneity in the autonomic response to air pollution due to difference in baseline healt h with significant association s for ambient NO_2 suggesting an important role for traffic-related pollution.

Lipsett et al., 2006 studied alterations in cardiac autonomic control, assessed by changes in heart rate variability (HRV), provide one plausible mechanistic explanation for consistent associations between exposure to airborne particulate matter (PM) and increased risks of cardiovascular mortality. Decreased HRV has been linked with exposures to PM_{10} (PM with aerodynamic diameter ≤ 10 µm) and with fine particles (PM with aerodynamic diameter ≤ 2.5 µm) originating primarily from combustion sources. However, little is known about the relationship between HRV and coarse particles, PM with aerodynamic diameter 10-2.5 µm ($PM_{10-2.5}$), which typically result from entrainment of dust and soil or from mechanical abrasive processes in industry and transportation. The study measured several HRV variables in 19 nonsmoking older adults with coronary artery disease residing in the Coachella Valley, California, a desert resort and retirement area in which ambient PM_{10} consists predominantly of $PM_{10-2.5}$. Study subjects wore Holter monitors for 24 hr once per week for up to 12 weeks during spring 2000. Pollutant concentrations were assessed at nearby fixed-site monitors and used mixed models that controlled for individual-

specific effects to examine relationships between air pollutants and several HRV metrics. Decrements in several measures of HRV were consistently associated with both PM_{10} and $PM_{10-2.5}$; however, there was little relationship of HRV variables with $PM_{2.5}$ concentrations. The magnitude of the associations (~ 1-4% decrease in HRV per 10 $\mu g\ m^{-3}$ increase in PM_{10} or $PM_{10-2.5}$) was comparable with those observed in several other studies of PM. Elevated levels of ambient $PM_{10-2.5}$ may adversely affect HRV in older subjects with coronary artery disease.

Langkulsen et al., 2006 studies have shown acute effects of ambient air pollutants in children with respiratory disorders. The chronic effects of air pollution in Bangkok children were investigated. Children aged 10-15 years were examined for lung functions using Spirometry tests and for respiratory symptoms by the American Thoracic Society's Division of Lung Diseases (ATS-DLD-78-C) questionnaire during May to August 2004. Effects of residential area were estimated by multiple logistic regression analysis. Of the 878 children, 722 (82%) had completed lung function test and ATS-DLD questionnaire. In children, who live in roadside (R) and general (G) areas with high (H) pollution, the prevalence of respiratory symptoms increased significantly [odds ratios (95% Confidence Interval) in HR and HG are 2.44 (1.21–4.93) and 2.60 (1.38–4.91), respectively]. Children with normal lung function were less observed in H- and M-polluted roadside and general area [HR, OR, 1.41 (95% CI: 0.89–2.22); HG, 1.08 (0.71–1.64); and MR, 0.99 (0.63–1.57)]. Residential locations and family members were associated with the prevalence of respiratory symptoms, whereas factors such as the responder of ATS-DLD, gender, age, residential years, home size, parental smoking habits, use of air conditioners, and domestic pets were not associated. Age was associated with the impaired lung function, whereas others factors were not associated. Conclusion: The prevalence of respiratory symptoms and impaired lung function were higher among children living in areas with high pollution than those in areas with low pollution.

Table 2.5 Summary of the studies that assessed the association between ambient particulate matters (PM) and HRV

reference	design	Population (no./mean or age range/ study area)	Ambient PM level (µg m^{-3})	Covariates adjusted	Main Results[*]
Liao et al, 1999	longitudinal	N=26 Mean, 81yrs; Baltimore	24-hr PM$_{2.5}$ 16.1±6.9	Age, sex cardiovascular health status	SDNN,-8.8(-1.4to0.0) HF,-24.1(-42.5to0.0) LF,-22.4(-39.7 to 0.0)
Pope et al, 1999	longitudinal	N=7 Mean,70 yrs; Utah Valley	PM$_{10}$, no concentration reported	Barometric pressure, HR	SDNN,-1.4(-2.1to-0.6) SDANN,-1.4(-2.4to-0.5) r-MSSD,1.9(-0.2to3.9)
Creason et al, 2001	longitudinal	N=56 nonsmoker (4 weeks) Mean=82 yrs. Baltimore	24-hr. PM$_{2.5}$ Mean, 20.5 (Range 7.8-45.3)	Age, sex, CV status, temp, mean dew point.	HF,-14.9(-25.9 to-4.5) LF,-12.9(-20.6to-2.3)
Liao et al, 2004	Cross sectional	4,899 Mean 62 yrs. ARIC Study	24-hr, PM$_{10}$ 24.3±11.5	Age, sex, ethic, BMI, education, smoking, medication, CHD,DM,HT,HR season, temp, RH, sky cover	SDNN,-2.4(-3.8to-1.0) HF,-5.1(-8.0to-2.1) LF,-1.7to(-4.7to1.3)
Park et al, 2005	Cross sectional	497 males Mean, 73 yrs. Normative aging study in Boston	24-hr PM$_{2.5}$ 11.4±8.0	Age, smoking, MAP,FBG, temp, season	SDNN,-2.7(-9.5to4.6) HF,-16.2(-30.7to1.3) LF,-0.7(-14.6to15.4) LF:HF,18.5(3.7to35.4)

Abbreviations: SDANN, standard deviation of all 5-min NN interval means;

CHD, coronary heart disease; CV, cardiovascular disease; HR, heart rate;

DPT, dew-point; temperature; RH, relative humidity

[*] Percentage change (95% Confidence Interval) for an increase of 10 µg m^{-3} in PM$_{2.5}$

Source: Park et al., 2005.

CHAPTER III

RESEARCH METHODOLOGY

3.1 PM$_{10}$ and Hospital Visit

3.1.1 Study Design

This part of the study was studied about the association between daily particulate matter those diameter less than 10 micron (PM$_{10}$) and daily number of hospital visit for categories of cardiovascular diseases (ICD-10th; I00-I99) as time series analysis in inner Bangkok, high pollutant area.

3.1.2 Study Area and Population

Bangkok areas are divided into 50 districts with a total registered population in 2007 of 6.6 million. (Bangkok Metropolitan Administration Thailand, 2007) In these 50 districts, the residential zip codes were classified from nos. 10002 to 10800 with excluded 10130, 10270, 10540 and 10550 (the outer sub-districts in Bangkok namely; Phrapradaeng, Samutprakarn, Bangplee and Bangbua). The studied subjects were selection only the 25 inner districts of Bangkok where 2,693,292 residents were resided (Figure 3.1). The total number of hospital visits for CVD between 1 April 2002 and 31 December 2006 was 33,458. The study protocol was approved by the institutional review board of the Faculty of Medicine; Chulalongkorn University who reviewed the protocol based on the International Guidelines for Human Research Protection and ICH/GCP.

Figure 3.1 Map of Bangkok areas divided by the districts.

Source: BMA, 2007

3.1.3 Data Collective

a) Daily Hospital Data

The hospital visit data between the years of 2000 and 2006 were collected using the first acute cardiovascular diseases (CVD) records from 3 major government hospitals in Bangkok namely, Ramathibodi, Siriraj and Chulalongkorn hospitals as representative of the population in inner districts of Bangkok (25 districts).

The Primary Care Unit System (PCUS) of 30 Baht (US$ 0.80) per head for a low income population was launched in 2001 (Pongsupap et al., 2005). During a transition stage after the introduction of this charge at the beginning of 2002, there was an unusual fluctuation in hospital visit numbers; therefore, in this study were excluded data from April 2002. Daily counts of total hospital visit were aggregated for age, sex, patient's address (Zip code), date of hospital visit and first diagnosis. The primary cause of hospital visit was coded from the disease certificate according to the two-digit ICD 10th (International Classification of Diseases) system, Tenth Revision;

World Health Organization; WHO. 2002. This is a standardized system for recording diagnoses used throughout the world. Hospital data in this study were based on the first diagnosis of CVD (ICD10[th] code I00-I99) in emergency hospital visit. (Figure 3.2) The descriptive data of hospital visit with CVD patients were summarized, classified variables into three age groups as children (0-14 years), adult (15-64 years) and the elderly ($\geq$ 65 years) and they were classified according to primary cause as Arrhythmia (I46-I49), Myocardial Infarction (MI; I21) and Ischemic Heart Disease (IHD; I20-I25).
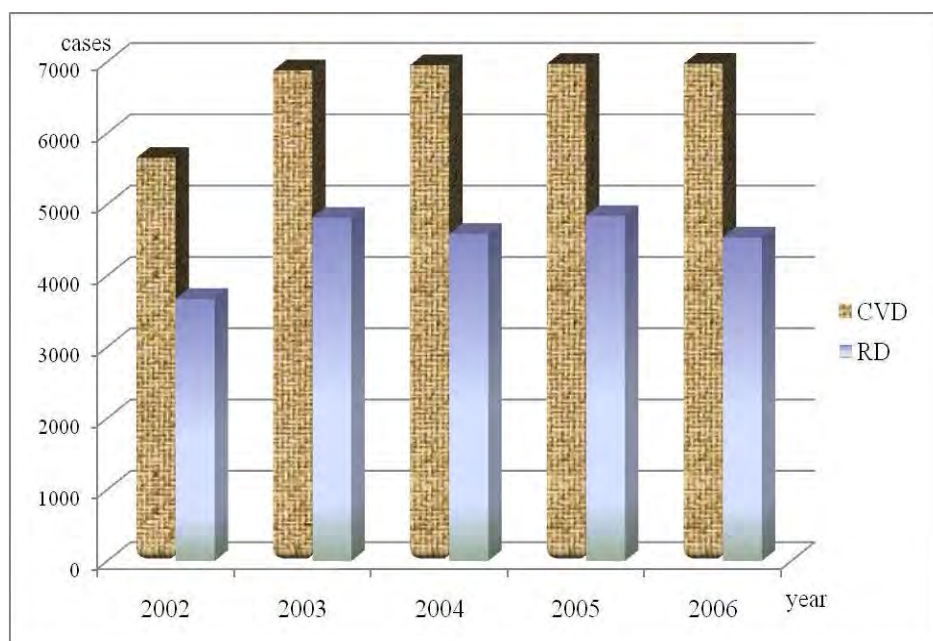
Figure 3.2 Total number of hospital visit with cardiovascular diseases (CVD) and respiratory diseases (RD) in inner Bangkok, from 3 hospitals in 2002 to 2006.

b) Air Quality Data

Air quality data in Bangkok were obtained from Pollution Control Department (PCD) network monitoring stations. From 2002-2006 data, daily air pollutants (PM$_{10}$) concentrations in site 4 (Figure 3.3) were measured by Taper Element Oscillating Microbalance (TEOM) and data from other sites were measured by Beta Attenuation Mass Monitor. (www.aqnis.pcd.go.th/station/allstation.htm)

This study used the daily (24-hr) data of PM_{10} in 7 sites among 13 fixed ambient monitoring PCD stations in inner area of Bangkok (Figure 3.3), where accurate data covered data for more than 75% of the whole study period. Daily weather data were obtained from Bangkok Meteorology Department between 1 April 2002 and 31 December 2006 (1,736 days). These data included daily average temperature, dew point, wind, and daily rainfall.
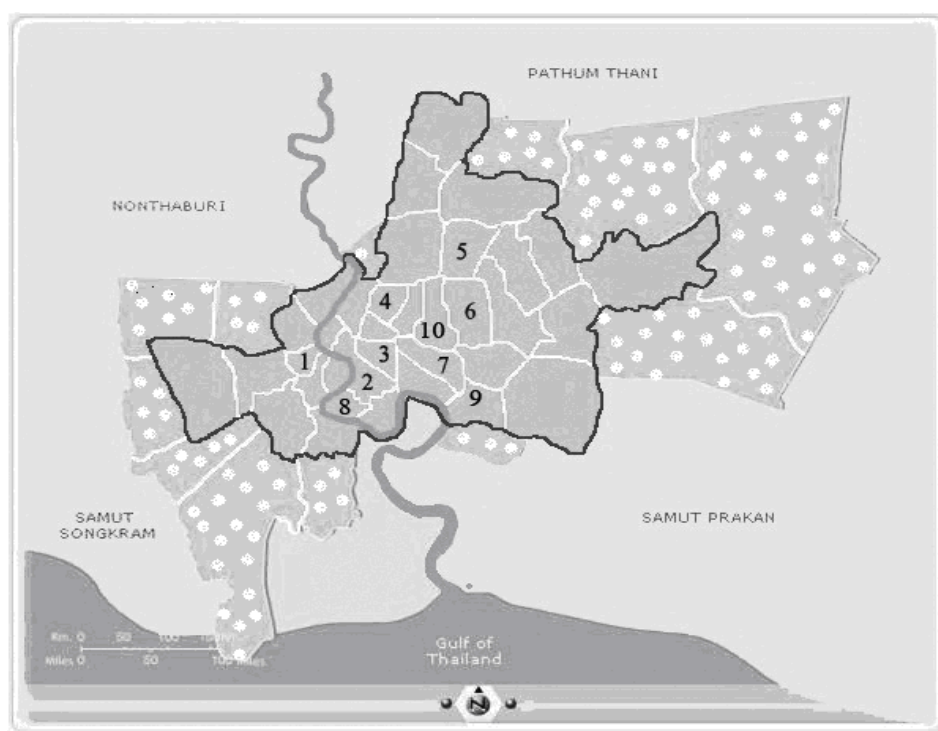
Figure 3.3 Map of Bangkok: Non studied area studied area.
Nos. 1–10 indicates the locations of the Pollution Control Department (PCD) ambient monitoring stations: (1) Thonburi Power Substation, Intrapitak Road; (2) 22 Odien Circle, Sampantawong; (3) Ministry of Science and Technology; (4) Dindaeng-National Housing Authority; (5) Chokchai4 Police Box; (6) Land and Transport Department; (7) Chulalongkorn Hospital. (8) Rat- Burana Post Office; (9) Thai Meteorological Department, Bangna; (10) Chandrakasem Rajabhat University; Jatujak (Number of station 1-7 for PM_{10} and 1-10 for Ozone)
Source: PCD; 2007.
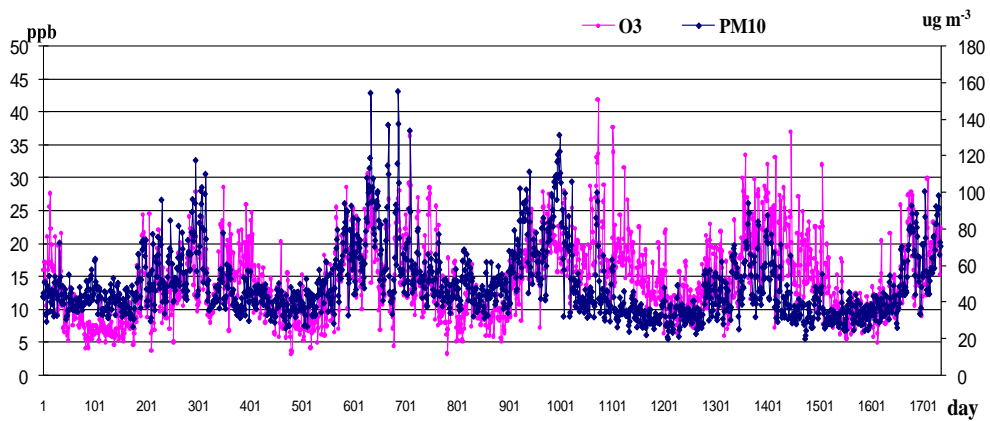
(3.4 a)
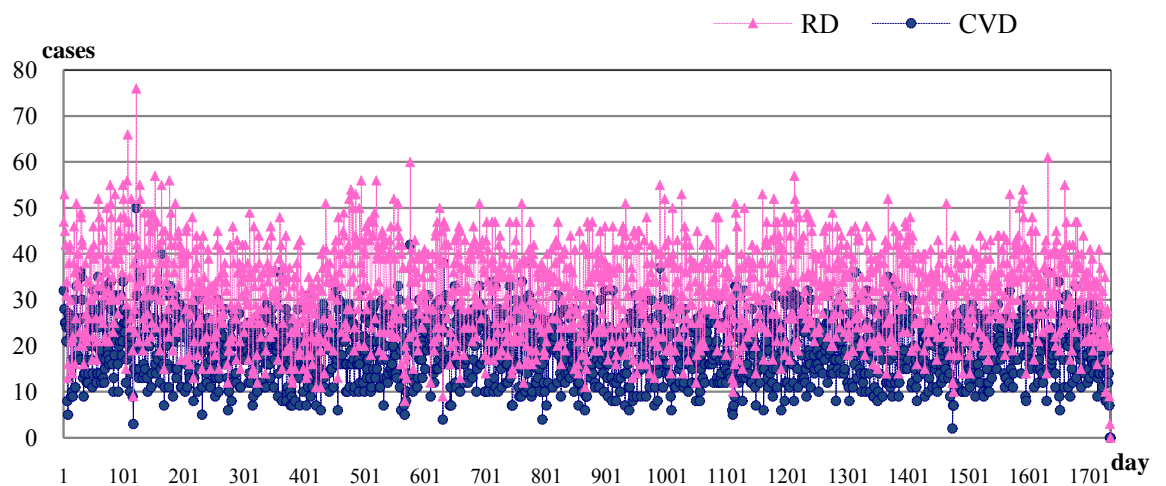
(3.4 b)

Figure 3.4   The comparison between daily hospital visit counts and air pollutants emissions in inner Bangkok, 2002-2006.

(3.4 a) Daily averages of ambient air pollutants (O_3 and PM_{10} levels) in inner Bangkok from 1 April 2002 to 31 December 2006

(3.4 b) Daily number of hospital visit count of patients with CVD and RD in inner Bangkok from 1 April 2002 to 31 December 2006.

c) Daily Weather Data

Daily weather data were obtained from the Bangkok Meteorology Department for 1 April 2002 to 31 December 2006. The data obtained include:

- average daily temperature
- average daily dew point
- daily rainfall totals
- daily average wind

Daily weather data are potentially important control variables for the health effects analysis. Bangkok's climate is classified as tropical savannas. A seasonal pattern is noticeable in the temperature data, with relative low daily average temperature spikes occurring occasionally during November, December, and January and the highest temperatures occurring during March, April, May and June. Consistent with these temperature patterns and the Meteorology Department's definition, the study used the following definitions of seasons in the retrospective analysis.

- Winter: October 16 to February 15
- Summer: February 16 to May 15
- Rainy: May 16 to October 15.

3.1.4 Statistical Analysis

Time series data of health outcome and air pollutants were analyzed from 1 April 2002 to 31 December 2006 (1,736 days). The daily counts of hospital visit was used as the dependent variables in the statistical analysis, Poisson regression model was applied, the relative risk of hospital visit was estimated with regression, controlling for seasonal pattern, effect of day of week, temperature and dew point. This was done to control for factors beside air pollutants that vary on a daily basis and that might explain variation in daily hospital visit.

1) Loess smoothing technique was utilized to adjust for the confounding effects of temperature and dew point. This technique can accommodate nonlinear and non-monotonic patterns between time and health outcome, offering a flexible nonparametric modelling tool.

2) The study accounted for possible serial correlation in daily hospital visit by using a locally weighted smooth function of daily visit count overtime (Hastie et al., 1990). The smoothing parameters are selected by optimizing the Generalized Cross Validation (GCV) criterion.

Generalized Additive Models (GAM) was chosen for determining predictor-response relationships in many kinds of data without using a specific model. They combine the ability to explore many nonparametric relationships simultaneously with the distributional flexibility of Generalized Linear Models. (Dominici et al., 2002)

GAM has become a standard method in time-series studies on the association between air pollution and health effects, because it allows for non parametric adjustment (LOESS smoothers) for non linear confounding effects of seasonality and weather variables. Time-series analysis reduces the potential problems of confounding factors and other risk factors that do not vary significantly day to day. This model is suitable for exploring the short-term health effect of daily average air pollutions. (Wood et al., 2002 and Aschengrau et al., 2008) The dependent variable was the natural logarithm of the expected hospital visit count, while the regression coefficients were the natural logarithms of the rate ratio. The association between air pollutants and hospital visit were examined by the following.

$$\log (Y) = \sigma + \beta_i X_i, \qquad \qquad \text{--------- (1)}$$

where;

Y = Dependent variable, Daily number of hospital admission

X_i = Explanatory variables, including PM_{10} and O_3

$\sigma + \beta_i$ = Estimated parameter

Poisson regression with GAM was functioned as semi-parametric model in equation (2) and (3).

$$\log \{E(Y)\} = \text{Parametric (linear effect, } \beta) + \text{Nonparametric (LOESS)} \quad \text{-------- (2)}$$

$$\log \{E(Y)\} = \beta \text{ intercept} + \beta \text{ PM} + \beta \text{ DOW} + \beta \text{ Holiday} + \beta \text{ Season}$$
$$+ f \text{ Temperature} + f \text{ Dew point} + f \text{ Day} \quad \text{-------- (3)}$$

where;

Y	= daily number of hospital visit
β	= regression coefficients
PM	= primary parameter Air Pollutants (PM_{10} and O_3)
DOW	= day of week 7 categories (Monday to Sunday)
E	= expectation
f	= loess, smoothing function

The association between daily air pollutants (PM_{10}) and daily number of hospital visit variables (CVD) were analyzed. Individual lag pollutant exposures in same day (lag 0), the day before or the previous day (lag 1), and two days average (lag 0+ lag 1), three days average (lag 0+ lag 1+ lag 2) were examined. Lag time is the likelihood of an acute exposure exerting an effect 1, 2, 3 or more days later; lag 0 was defined as the 24-hr period from noon of the day of the hospital visit to noon of the previous day. The previous day (lag1) was the previous 24-hr period and so on. (Koken et al., 2003) PM_{10} were fitted as linear terms. This statistical analysis provided a relative risk estimate for air pollutants PM_{10} with a 95% Confidence Interval (CI). The relative risk of CVD subsets associated with the 10 µg m^{-3} increase of PM_{10} were presented as a percentage change in daily hospital visit with CVD. All analyses were conducted using GAM procedure by SAS 9.1.2 (SAS institute. Inc, 2004)

3.2 PM$_{10}$ and HRV Function Test

3.2.1 Study Design

This part of the study aims to examine the association between ambient particulate matter exposure (PM$_{10}$) and alterations in cardiac autonomic control which were examined by Heart Rate Variability (HRV) in the elderly people with pre-existing cardiovascular diseases (CVD) who lived in inner part of Bangkok, Thailand.

3.2.2. Study Site

Bangkok has about 6 million inhabitants with a very high population density, which was 10% of the total population of Thailand. The population density is 4,051 per km^2 with an increase of 0.98% per year. The city is divided in to 50 districts and 154 sub districts. The total area of Bangkok is 1,568,737 km^2. (BMA, 2007) Bangkok Metropolitan Administration (BMA) is classified Bangkok in to two areas as inner and outer Bangkok. Inner Bangkok is 25 districts; locating in center of Bangkok with heavy traffic jams and crowded building. (Figure 3.1) Climate in Bangkok is classified as tropical savannas. Temperature is warm all year round and very hot in April. There are three seasons: winter (November- mid February), summer (mid February to mid May) and rainy season (mid May to October) Southwest wind predominates during the rainy season and wind is generally northeast during the winter. During the summer, average temperature is around 30°C and reduces to 25°C during the winter. Annual rainfall is approximately 1,400 mm and 80-90% of this occurs during rainy season. (Bangkok Meteorology Department, 2007) Flat plains around Bangkok allow free air movement, so pollutants are generally efficiently dispersed, except when the air is still.

3.2.3 Data Collective

a) Study Population

The sample selection for HRV measurement, the standard American Thoracic Society's Division of Lung Diseases (ATS-DLD-78C) and cardiovascular diseases questionnaires (CDQ) were purposively distributed to all elderly hospital visit of Out Patients Department (OPD-Medicine), based on first diagnosis of CVD (I00-I99). Total subjects from June to October 2007 were 330 visiting patients at Ramathibodi Hospital. Only 200 questionnaires were completed. From these 200 subjects, screened and adjust confounding from these following criteria: confounding factors by this protocol:

- Existing CVD patients who got the first diagnosis based on cardiovascular disease (ICD-10th; coding I00-I99).
- Both male and female; Age ≥ 65 years old
- The residents in inner Bangkok (25 districts), who lived in the study areas (High Pollutants area) more than 6 months
- The subject's addresses were closed to, or within 6 km. or 5 miles of either of the PCD roadside and general ambient air quality monitoring stations.
- No smoking, No alcohol consumption
- No respiratory diseases (RD) symptoms
- Housing characteristic: no air condition. , no pets, non smoke residents
- retirements, no occupational exposure to dusts and fumes
- medications history, screen medication use
- No genetic illness
- Blood pressure (BP) stable
- Body Mass Index (BMI) calculated as the ratio of weight (Kg.) to standing height (m.) squared was normal
- Co-operated; signed a written consent form.
- Exclusion criteria included the condition associated with autonomic dysfunction Ex: DM, chronic renal failure, Parkinson and chronic alcohol abused, cardiac transplant, cardiac pacemaker, implantable defibrillator, fibrillation or significant cognitive impairment.

To reduce confounding effects in this study, excluded the following subjects from the recruitments. After the above criteria screening followed the study of Lipsett et al., 2006 and Gold et al., 2000, there were only 20 that passed these confounding adjusting. Finally, this study has only 8 patients from 20 who agreed to participate in daily personal HRV measurement. Eight panels of elderly (≥65 years) pre-existing CVD patients of inner Bangkok communities were recruited to participate in 24 hour ambulatory electro-cardiographic (ECG) monitoring. (Figure 3.5) Potential participants were initially recruited by directly contacting persons living in the neighborhoods adjacent to the PCD monitoring sites and asking for willingness to participate, all subject signed a written consent, an eligibility Thai standard about the Cardio-respiratory questionnaires (Appendix A) were completed.
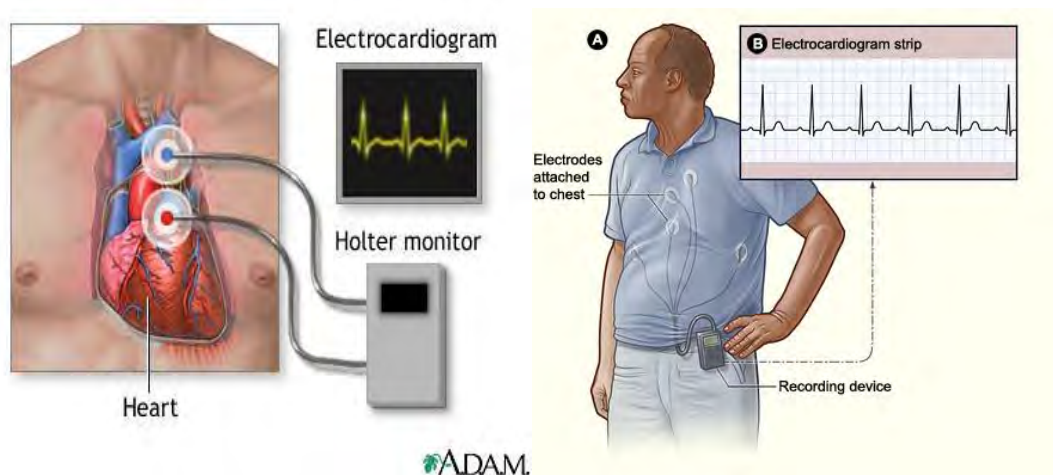
Figure 3.5 Twenty-four hour ambulatory electro-cartographic (ECG) monitoring
Source: http://www.nhlbi.nih.gov/health/dci/images/holter_monitor.jpg

Twenty-four hour ambulatory ECG monitoring (HRV measurement) was conducted on the subjects during periods of both high and low air pollution, during the monitoring, subject performed their normal daily activities, except those that would be interfere with the recording such as showering. Staff gave the subject a simples 24 hour time activity daily to record time spent indoor or outdoor, air condition use. Research protocols and consent forms were approved by the institutional review board of the Faculty of Medicine Chulalongkorn University, Bangkok, Thailand, has approved the following study which is to be carried out in compliance with the ICH/GCP according to the protocol of the principal investigator. (The institutional Review Board of the Faculty of Medicine, Chulalongkorn

University reviewed the protocol based on the international guidelines for human research protection and International Conference on Harmonization/ WHO Good Clinical Practice Standards; ICH/GCP). (Appendix D)

b) Air Pollution Data

This study used the annual average air pollution concentration in each area as an indicator of high air pollution in inner part of Bangkok and collected hourly ambient air pollution data from PCD monitoring stations nearby the subjects' address.

c) Cardio-Respiratory Questionnaires

Cardio-respiratory questionnaire (Appendix A) is an eligibility Thai standard comprised of American Thoracic Society Division of Lung Disease (ATS-DLD-78-C) and Cardiovascular Disease Questionnaires (CDQ). The prevalence of cardiovascular disease symptoms (CVD) and chronic respiratory symptoms (Non-specific respiratory disease: NSRD, and Persistent Cough and Phlegm: PCP) was assessed by using Thai version of ATS-DLD-78-C (Ferris, 1978) and cardiovascular disease questionnaire: CDQ. (Rose et al., 1986) The questionnaire consists of general information, respiratory symptoms (cough, phlegm, wheeze, and chest tightness), cardiovascular disease symptoms, smoking history and family history.

Criteria of NSRD are (1) Chronic Bronchitis: phlegm production from the chest $\geq$ two times/day for $\geq$ 4 day/week for $\geq$ 3 month/year for at least 3 year; (2) Bronchial Asthma: doctor-diagnosed asthma and still have asthma; (3) Dyspnea and wheezing: wheezing or whistling in the chest apart from colds on most days or nights.

Criteria of PCP are (1) Persistent Cough: cough apart from colds on most days more than 4 day/week for 3 month/year at least 1 year; (2) Persistent Phlegm: congested in the chest or bring up phlegm, sputum, or mucus apart from colds on most days more than 4 day/week for 3 month/year at least 1 year.

Criteria of CVD symptoms are (1) defined shortness of breath either when hurrying on the level or walking up a slight (2) stop for breath when walking, have to stop for breath after walking about 100 yards or after a few minutes on the level, (3) ever been awakened by trouble breathing or shortness of breath, other than when you had a cold and (4) ever had to sleep on 2 or more pillows to help breathing.

d) Heart Rate Variability (HRV) Function Test

Heart rate variability (HRV) is an indicator of cardiac autonomic function, reflecting the balance between sympathetic and parasympathetic nervous system input to the heart (Akselrod et al., 1981; ESC and NASPE, 1996). Decreased HRV is correlated with increased risk of cardiovascular morbidity and mortality (Bigger et al., 1992; ESC and NASPE, 1996, Kleiger et al., 1987; Truji et al., 1994; Truji et al., 1996). This correlation may be explained by that loss of autonomic nervous system balance being the leading event in cardiovascular death. (Appendix B)

Heart Rate Variability (HRV) is a very sophisticated measure of physiological health. It can predict risks of major disease and underpins vitality and performance. In learning to master the physiology the most important physiological signal of which to gain control is the one generated by the heart. This is because the heart is the most powerful signal generator in the human body and the stream of information entering the brain from the heart is constantly changing. This beat-to-beat change in the heart rate is called Heart Rate Variability (HRV) and it can be measured continuously throughout an individual's day. (Figure 3.5)
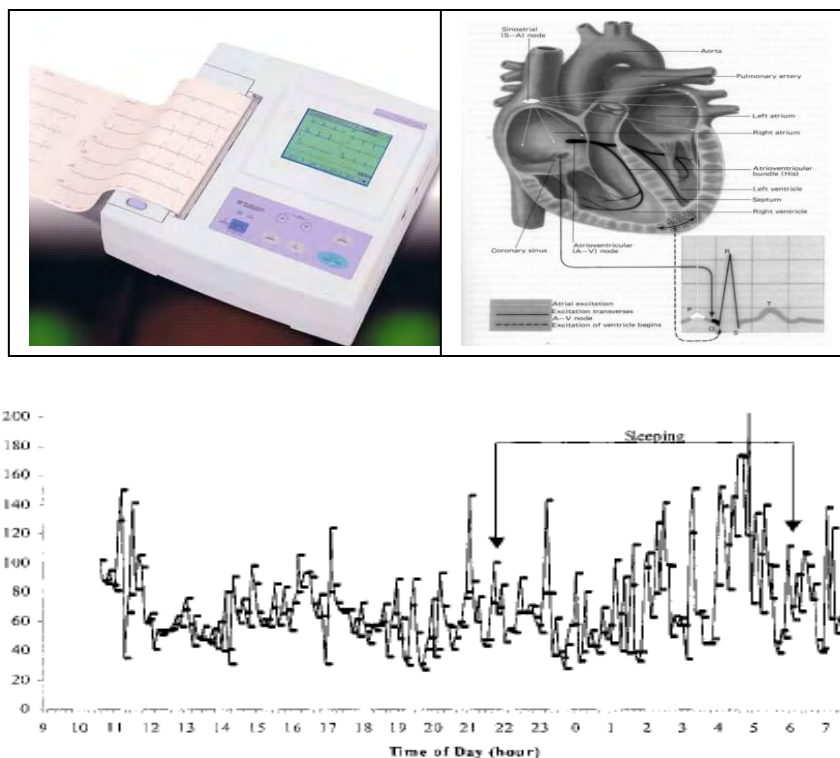
Figure 3.6 Heart Rate Variability (HRV) measurements

Source: www.Circulationaha.org; 2004
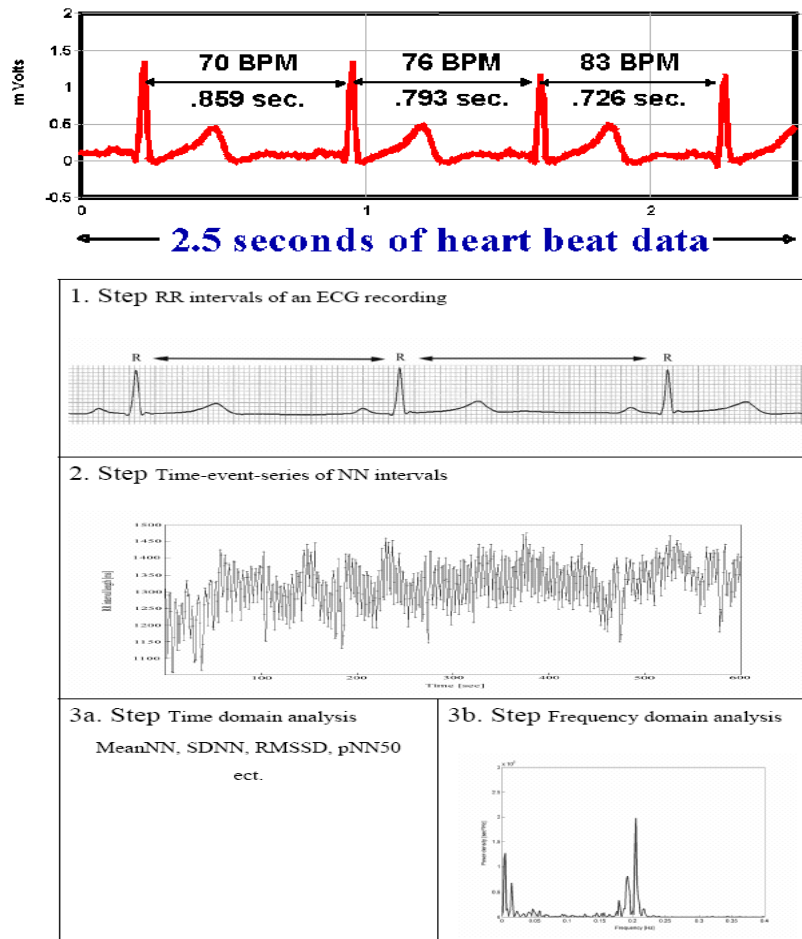
Figure 3.7 Heart Rate Variability (HRV) measurement data.

Source: www.Circulationaha.org; 2004.

Heart Rate Variability (HRV) can be used to detect early warning signs of any dysfunction long before routine medical investigation detects a problem or before any symptoms arise. HRV can also be used to track the progress of any training intervention and monitor the degree of improvement.

- HRV is an indicator of cardiac autonomic function, reflecting the balance between sympathetic and parasympathetic nervous system input to the heart.
- HRV is the beat-to-beat variability in the interval between two consecutive R-waves, as measured on ambulatory electrocardiography. (Figure 3.7)
- Decreased HRV has been shown to correlate well with increased risk of cardiovascular morbidity and mortality.
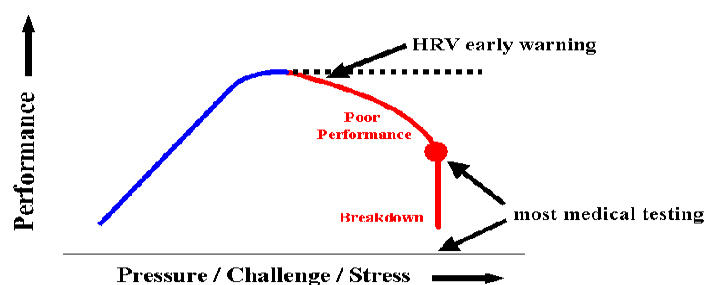
Figure 3.8 HRV indicators**. (**Hunter Kane, with Heart Math; LLC; 2004)

Monitoring Process**,** the Heart Rate Variability (HRV) monitor is a small piece of digital recording technology about the size of a mobile phone which clips onto a waistband. In order to comply with the Medical Records Act, a consent form must be signed by anyone being monitored. Three self adhesive electrodes are attached to the body, one on the upper chest and one either side of the lower ribcage. Whilst wearing the monitor, the individual cannot bath or shower (strip wash only) and is advised to keep away from microwaves and electric blankets (since this affects the signal and is safe to the person being monitored). This study chose specific time intervals for which the HRV variables would be calculated and then extracted them manually into the database. In summary, for each individual personal monitoring day obtained HR, HRV parameters as: SDNN and r-MSSD (Figure 3.7) for the full 24-hr of period and for two 2-hr periods in the morning and evening, as well as frequency-domain HRV variables for two 5-min intervals.

3.2.4 Statistical Analysis

This study screened the confounding factors and selected the study with each total of 330 questionnaires in the population. Questionnaires: use a modified Thai version about cardiovascular-respiratory diseases. (ATS-DLD and CDQ)

Confounding factors as: (Utell MJ et al., 2002)

a) Inborn factors (including e.g. genetic predisposition, gender and age)

b) The underlying disease process e.g. Ischemic Heart Diseases (IHD), cardiomyopathy, COPD or smoldering pathology (ongoing inflammatory process, endothelial dysfunction, increased thrombosis)

c) Environmental factors (e.g. diet, smoking, pollution and weather data)

Participants completed the confidential Thai cardiovascular and respiratory questionnaires (Appendix A), which included questions about age, sex, weight, height, BMI, smoking history, alcohol use, occupational exposure, diet, educational, marital status, and other characteristics. (Pope et al., 2004) Personal Heart Rate Variability (HRV) sampling among studied eight elderly subjects with pre-existing cardiovascular diseases who living in inner Bangkok, the heavy pollutant area. Data from baseline questionnaires, medical records abstraction, daily diaries, and extracted HRV variables were entered into the database, and then merged with air quality and meteorological data for analysis. Data analysis, only normal sinus R-R intervals were used in the HRV analysis. (The normal-to-normal (NN) intervals between 150 and 5000 ms with NN ratios between 0.8 and 1.2 were included for the analysis). The artifacts, ectopy (both supraventricular and ventricular), and uninterpretable complexes were excluded. The study examined time-domain and HRV variables. Time-domain variables included (a) the standard deviation of normal sinus rhythm (normal-to-normal; or N-N) beats (SDNN), representing the average of the standard deviations of normal beats of successive 5-min blocks over the duration of the monitoring period (SDNN estimates overall HRV), (b) the standard deviation of the average N-N intervals (SDANN) within successive 5-min blocks (an estimate of long-term components of HRV); and (c) the root mean square of successive differences (r-MSSD), which is the square root of the mean of the sum of the squares of differences between adjacent normal R-R intervals, which estimates short-term components of HRV and is a sensitive indicator of vagal tone (Task Force, 1996).

Statistical analysis: Association of average hourly PM_{10} data with personal HRV sampling. Analyze by multivariable linear regression and regression coefficient. Average hourly PM_{10} data from PCD stations and meteorology data near the subject's address were analyzed. Data of personal HRV sampling in studied participants. Mean of population, confounding factors. Use program "SPSS for Windows version.14" as: mean, SD, SE, analysis of variance, correlation, the multiple logistic regression analysis.

CHAPTER IV

RESULTS AND DISCUSSION

4.1 PM$_{10}$ and Hospital Visit

4.1.1 Air quality and Meteorology data

The monitoring data for daily average air pollutants (PM$_{10}$ and O$_3$) concentrations for more than 75% of the whole study period were obtained from average 7 out of 13 stations (PM$_{10}$) and 10 out of 11 stations (O$_3$). The mean level (and range) of daily PM$_{10}$ and daily O$_3$ (1-hr.) was 48.9 µg m^{-3} (19.3–154.9 µg m^{-3}) and 14.4 ppb (3.3–41.9 ppb), respectively. The daily weather data showed a seasonal pattern in temperature, with relatively low daily average temperatures in November, December, and January. The mean (and range) of daily temperature, dew point, and wind speed during the studied period; 1 April 2002 to 31 December 2006 (1,736 days) was 29.1°C (21.6–39.9°C), 23.7°C (11.4–28.1°C), and 4 km hr^{-1} (0–12 km hr^{-1}), respectively. (Table 4.1) Normally, high summer temperatures occur from February through May, and the rainy season is between May and October. These patterns and the seasonal definitions are consistent with the standard of the Meteorology Department, Thailand. (Bangkok Meteorology, 2007)

Table 4.1 Daily average air pollution (PM_{10} and O_3), and related meteorology data in Bangkok, from 1April 2002 to 31 December 2006.

Daily Variables	Mean	Minimum	Maximum
24-hour PM_{10} ($\mu g\ m^{-3}$)	48.8	19.3	154.9
hourly O_3 (ppb)	14.4	3.2	41.9
Dew point (^{o}C)	23.7	11.4	28.1
Wind (km/hr.)	4.1	0.0	12.1
Temperature (^{o}C)	29.1	21.6	39.9

National Ambient Air Quality Standards (NAAQS) of 0.10 ppm averaged over 1 hour and 0.07 ppm averaged over 8 hour.

Ozone (O_3) is a photochemical reaction product, occurred in the heavy traffic areas. This co-pollutant is formed from many precursors such as hydrocarbon, CO and NO_x. An urban environment containing high levels air pollutants can result in high O_3 formation (Colls, 2002). Ambient daily O_3 and PM_{10} profiles from year 2002 to 2006 in inner Bangkok, PCD data were illustrated in Figure 4.1 and 4.2. The co-linearity between PM_{10} and O_3 were significant in pair wise correlation tests ($r^2 = 0.25$, $p < 0.001$). The ambient air quality data for 2005 (Figure 4.2) showed that PM_{10} decreased but O_3 continued to increase, suggesting that other sources apart from PM_{10} influence O_3 formation. However, there was a positive association between daily number of hospital visits and air pollution levels.
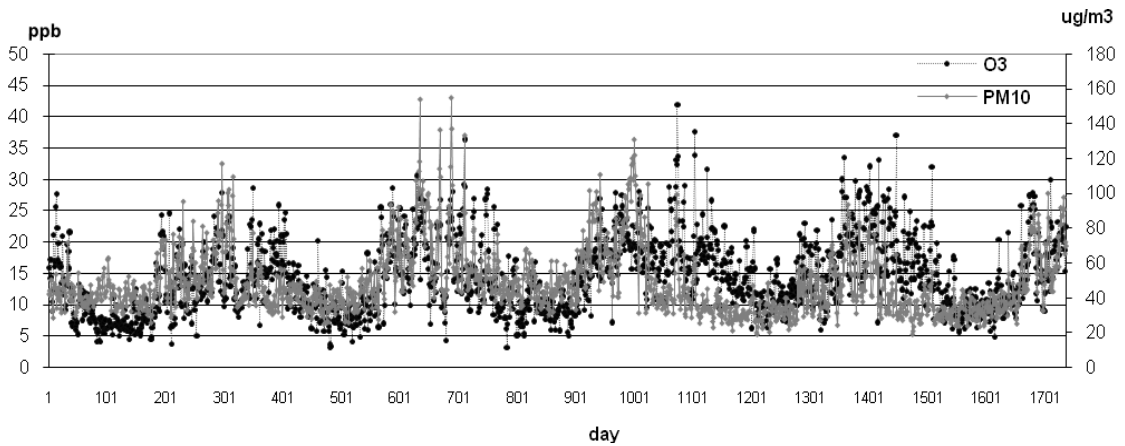
Figure 4.1 Daily averages of ambient air pollutants (O_3 and PM_{10} levels) in inner Bangkok, from 1 April 2002 to 31 December 2006. (Total number of days= 1,736 days)
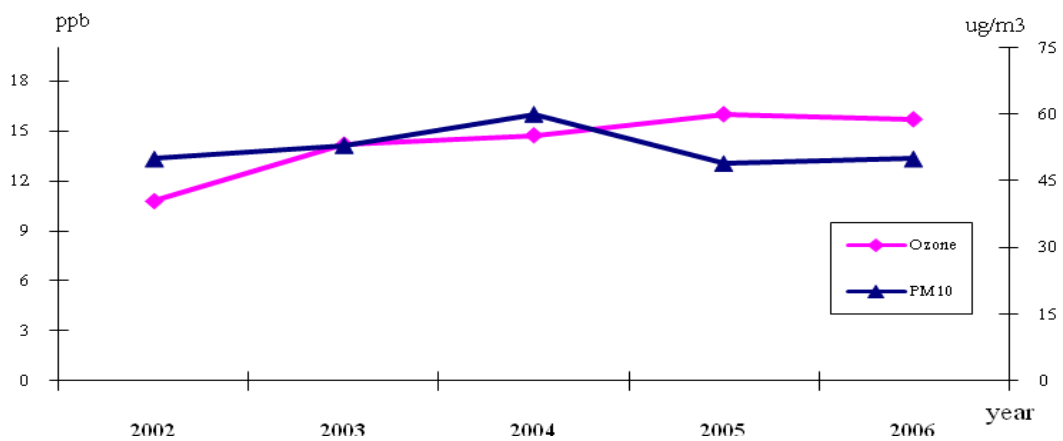
Figure 4.2 Annual ambient O_3 and PM_{10} level profiles from year 2002 to 2006

4.1.2 Hospital visit

Daily counts of total hospital visit were aggregated for all age, sex, patient's address (Zip code), date of hospital visit and first diagnosis. The primary cause of hospital visit was coded from the disease certificate according to the two-digit ICD 10th system (International Classification of Diseases, Tenth Revision; World Health Organization; WHO, 2002). This is a standardized system for recording diagnoses used throughout the world. Hospital data in this study were based on the first diagnosis of CVD (ICD10[th] code I00-I99) in emergency hospital visit. The descriptive data of hospital visit with CVD patients were summarized (Table 4.2), divided variables by three age groups as children (0-14 years), adult (15-64 years) and the elderly (≥ 65 years) and primary reason of sub categories coding as: Arrhythmia (I46-I49), Myocardial Infarction (MI; I21) and Ischemic Heart Disease (IHD; I20-I25)

Table 4.2   Descriptive data of hospital visit with cardiovascular diseases (I00-I99)

Variables	Number of visit (cases)	Mean number of visit (cases / day)	Range of cases/day (min-max)
1) All I ,code (I00-I99)	33,458	19	0-50
1.1) Age < 15 years	681	1	0-4
1.2) Age15-64 years	16,710	10	0-25
1.3) Age≥ 65 years	16,067	10	0-23
2) Arrhythmia (I46-I49)	1,876	1	0-8
3) MI* (I21)	2,566	2	0-8
4) IHD** (I20-I25)	10,158	6	0-19

*MI= Myocardial Infarction, ** IHD= Ischemic Heart Disease

4.1.3   Correlation between daily air pollution (PM$_{10}$ and O$_3$) with hospital visit for cardiovascular diseases

a) Hospital visits with cardiovascular diseases (CVD) in relation with Particulate Matters (PM$_{10}$) concentration.

The descriptive data on hospital visits for CVD are summarized in Table 4.2. No significant association was found between PM$_{10}$ exposure with total CVD and sub-coding of arrhythmia, MI and IHD on the concurrent day (lag 0) or the previous day (lag 1). However, after controlling for covariate factors, the daily PM$_{10}$ concentrations were positively associated with hospital visits for CVD in the elderly ($\geq$ 65 years). A 0.10% (95% CI: 0.03 to 0.19) increase in CVD visits in this group was associated with a 10 µg m^{-3} increase in PM$_{10}$. The two cumulative days average of PM$_{10}$ concentration was associated with increased hospital visits for CVD visit in the elderly group of 0.09% (95% CI: 0.00 to 0.20) for each 10 µg m^{-3} increase in PM$_{10}$ (Table 4.3)

Figure 4.3 Daily average PM$_{10}$ and daily number of hospital visit with cardiovascular diseases (CVD) patients

b) Hospital visits with cardiovascular diseases (CVD) in relation with Ozone (O_3) concentration.

No association was found between Ozone exposure with total CVD and sub coding of arrhythmia, MI and IHD on the concurrent day (lag 0). However, after controlling for covariate factors, the total number of CVD visits also increased by 0.23% (95% CI: 0.02 to 0.44) with increase in O_3 on the previous day (lag 1). In addition; the daily O_3 concentration was positively associated with hospital visits for CVD in the elderly ($\geq$ 65 years). A 0.50% (95% CI: 0.19 to 0.81) increase was associated with a 10 ppb increase in O_3 and the cumulative two day average O_3 concentration were associated with increased hospital visits for CVD visit in the elderly 0.48% (95% CI: 0.13 to 0.83) for increase in O_3. (Table 4.3) This study found no evidence of modifying effects of weather conditions on the results.
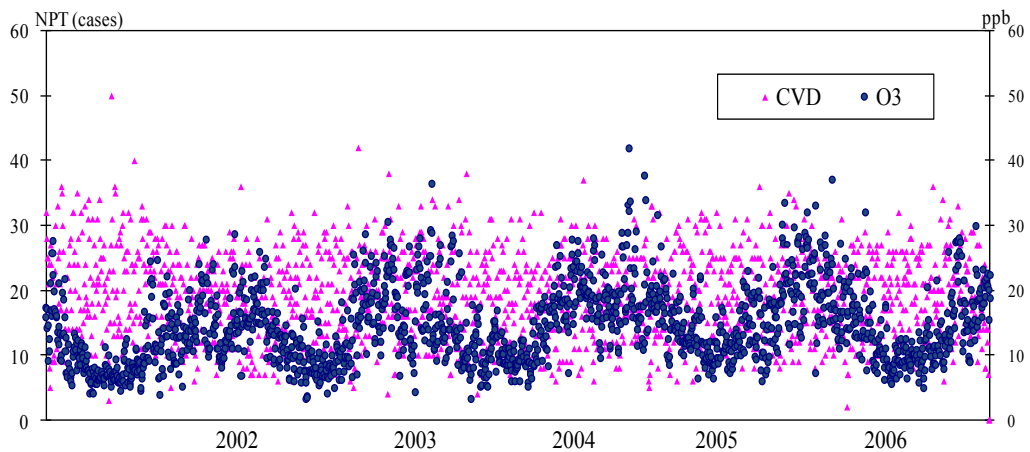
Figure 4.4 Daily average Ozone and daily number of hospital visit with cardiovascular diseases (CVD) patients

Table 4.3 Percentage change in daily hospital visits for cardiovascular diseases (CVD) in association with a 10 µg m^{-3} increase in PM$_{10}$ or increase in O$_3$.

Number of Patients (NPT)	Day	PM$_{10}$		O$_3$	
		NPT change %	95% CI	NPT change %	95% CI
Total CVD; I00-I99	Concurrent	0.01	-0.05, 0.07	-0.01	-0.23, 0.20
	Previous	0.05	-0.01, 0.11	0.23	0.02, 0.44
33,458	2 Cumulative	0.03	-0.03, 0.10	0.17	-0.06, 0.40
	3 Cumulative	0.04	-0.01, 0.09	0.10	-0.15, 0.35
-age < 15 year	Concurrent	-0.27	-0.76, 0.19	-0.49	-2.05, 1.07
	Previous	-0.15	-0.64, 0.34	-1.06	-2.66, 0.54
681	2 Cumulative	-0.24	-0.76, 0.28	-1.00	-2.80, 0.80
	3 Cumulative	-0.09	-0.63, 0.44	-0.82	-2.74, 1.10
-age 15-64 year	Concurrent	-0.02	-0.12, 0.07	-0.16	-0.47, 0.15
	Previous	0.01	-0.08, 0.10	0.01	-0.28, 0.14
16,710	2 Cumulative	-0.01	-0.10, 0.09	-0.08	-0.43, 0.26
	3 Cumulative	0.00	-0.09, 0.10	-0.10	-0.47, 0.27
-age ≥ 65 year	Concurrent	0.06	-0.03, 0.16	0.15	-0.16, 0.46
	Previous	0.10	0.03, 0.19	0.50	0.19, 0.81
16,067	2 Cumulative	0.09	0.00, 0.20	0.48	0.13, 0.83
	3 Cumulative	0.08	-0.01, 0.18	0.36	-0.01, 0.73
Arrhythmia, I46-I49	Concurrent	-0.01	-0.30, 0.29	-0.26	-1.24, 0.72
	Previous	-0.08	-0.37, 0.21	-0.06	-1.00, 0.88
1,557	2 Cumulative	-0.05	-0.36, 0.26	-0.20	-1.27, 0.87
	3 Cumulative	-0.02	-0.34, 0.29	-0.28	-1.43, 0.87
Myocardial Infarction	Concurrent	0.12	-0.11, 0.36	-0.30	-1.08, 0.48
	Previous	0.00	-0.24, 0.24	-0.68	-1.48, 0.12
MI, I21	2 Cumulative	0.06	-0.18, 0.32	-0.68	-1.58, 0.22
2,566	3 Cumulative	-0.02	-0.27, 0.22	-0.97	-1.95, 0.01
Ischemic Heart Disease	Concurrent	0.02	-0.10, 0.14	-0.30	-0.69, 0.09
	Previous	0.07	-0.04, 0.19	0.27	-0.12, 0.66
IHD, I20-I25	2 Cumulative	0.05	-0.07, 0.18	0.00	-0.45, 0.45
10,158	3 Cumulative	0.09	-0.01, 0.20	-0.08	-0.57, 0.41

4.1.4 Effect of Co-Pollutants

This study further investigated the data from the whole study period 2002-2006 presented in Table 4.3 for affected of co-pollutants. CO and O$_3$ were observed low correlation with PM$_{10}$, R^2 = 0.21 and 0.25. These two gaseous may eventually cause no confounding. However, NO$_x$ and PM$_{10}$ data were found some correlation, R^2 = 0.61 which indicated the potential confounding. NO$_x$ could act as a co-pollutant with PM$_{10}$. (Table 4.4)

Table 4.4 The correlation of co-pollutants in ambient air environment, Bangkok: from 1 April 2002 to 31 December 2006. (1,736 days)

Pollutants	Range	Average	Standard	PM_{10} (R^2)	Ozone (R^2)
PM_{10} (μg m^{-3})	19.38-154.93	48.84	120	1.00	0.25
O_3 (ppb)	3.26-41.93	14.43	100	0.25	1.00
NO_x (ppb)	11.4-84.10	33.6	170	0.61	0.29
CO (ppm)	0.44-3.36	1.42	30	0.21	0.001

Source: Pollution Control Department, (PCD), Thailand 2007

As for the other pollutants, the daily NO_x and CO concentrations in Bangkok in 2002-2006 were obtained from Pollution Control Department (PCD) and found that, they were far below the level to cause health effects and does not cause confounding. The study also evaluated the effects of the inclusion of NO_x or CO into the multivariate analysis to look at the relationship between hospital visits and PM_{10}. The changes in % increase of hospital visits by 10 μg m^{-3} increase of PM_{10} were small. (Table 4.5) These provided evidence against the possibility of confounding by NO_x or CO. (Rothman et al., 2008)

Table 4.5 Percentage change in daily hospital visits for cardiovascular diseases (CVD) in association with a 10 µg m^{-3} increase in (a) PM_{10}; (b) PM_{10} and NO_2 ; (c) PM_{10} and CO

Number of Patients (NPT)	Day	PM_{10}		PM_{10} and NO_2		PM_{10} and CO	
		NPT change (%)	95% CI	NPT change (%)	95% CI	NPT change (%)	95% CI
Total CVD; I00-I99 33,458	Concurrent	0.01	-0.05 to 0.07	0.01	-0.01 to 0.05	0.02	0.00 to 0.05
	Previous	0.05	-0.01 to 0.11	0.04	0.00 to 0.09	0.03	0.01 to 0.05
	2 Cumulative	0.03	-0.03 to 0.10	0.04	0.00 to 0.09	0.04	0.02 to 0.06
	3 Cumulative	0.04	-0.01 to 0.09	0.04	0.00 to 0.10	0.04	0.01 to 0.06
-age < 15 681	Concurrent	-0.27	-0.76 to 0.19	-0.15	-0.48 to 0.17	-0.10	-0.25 to 0.05
	Previous	-0.15	-0.64 to 0.34	-0.13	-0.47 to 0.19	-0.12	-0.27 to 0.02
	2 Cumulative	-0.24	-0.76 to 0.28	-0.17	-0.52 to 0.18	-0.13	-0.29 to 0.03
	3 Cumulative	-0.09	-0.63 to 0.44	-0.07	-0.44 to 0.44	-0.12	-0.30 to 0.05
-age15-64 16,710	Concurrent	-0.02	-0.12 to 0.07	0.00	-0.07 to 0.05	0.01	-0.01 to 0.04
	Previous	0.01	-0.08 to 0.10	0.02	-0.04 to 0.08	0.03	0.00 to 0.06
	2 Cumulative	-0.01	-0.10 to 0.09	0.01	-0.05 to 0.07	0.03	0.00 to 0.06
	3 Cumulative	0.00	-0.09 to 0.10	0.02	-0.05 to 0.09	0.03	0.00 to 0.07
-age ≥ 65 16,067	Concurrent	0.06	-0.03 to 0.16	-0.05	-0.12 to 0.00	0.04	0.01 to 0.07
	Previous	0.10	0.03 to 0.19	0.07	0.01 to 0.14	0.06	0.01 to 0.08
	2 Cumulative	0.09	0.00 to 0.20	0.08	0.01 to 0.15	0.06	0.03 to 0.09
	3 Cumulative	0.08	-0.01 to 0.18	0.07	0.00 to 0.14	0.05	0.01 to 0.08
Arrhythmia I46-I49 1,557	Concurrent	- 0.01	-0.30 to 0.29	-0.04	-0.24 to 0.14	-0.05	-0.12 to 0.02
	Previous	-0.08	-0.37 to 0.21	-0.06	-0.25 to 0.13	-0.09	-0.18 to 0.00
	2 Cumulative	-0.05	-0.36 to 0.26	-0.06	-0.27 to 0.14	-0.08	-0.18 to 0.01
	3 Cumulative	-0.02	-0.34 to 0.29	-0.05	-0.27 to 0.16	-0.09	-0.19 to 0.01
MI*, I21 2,566	Concurrent	0.12	-0.11 to 0.36	0.05	-0.10 to 0.13	0.09	0.01 to 0.16
	Previous	0.00	-0.24 to 0.24	-0.04	-0.20 to 0.12	0.05	-0.02 to 0.13
	2 Cumulative	0.06	-0.18 to 0.32	0.00	-0.16 to 0.17	0.08	0.00 to 0.17
	3 Cumulative	-0.02	-0.27 to 0.22	-0.05	-0.23 to 0.12	0.06	-0.02 to 0.15
IHD**, I20-I25 10,158	Concurrent	0.02	-0.10 to 0.14	0.03	-0.04 to 0.11	0.07	0.03 to 0.11
	Previous	0.07	-0.04 to 0.19	0.06	-0.01 to 0.14	0.06	0.02 to 0.10
	2 Cumulative	0.05	-0.07 to 0.18	0.06	-0.02 to 0.14	0.08	0.03 to 0.12
	3 Cumulative	0.09	-0.01 to 0.20	0.07	-0.01 to 0.16	0.09	0.04 to 0.13

*MI= Myocardial Infarction, ** IHD= Ischemic Heart Disease

4.1.5 Discussions

There is substantial epidemiologic literatures indicating an association between air pollution and hospitalization for CVD, most of which was obtained in cold or temperate climates with distinct seasonality. (Zanobetti et al., 2000; Wong et al., 2002 and Dominici et al., 2006) However, few studies have been conducted in tropical areas having little seasonality; therefore, this study in Bangkok is unique in terms of diagnosis of sub coding of CVD patients who might be at particular risks for hospital admission after pollutants exposure. The study used time series data on health

effects of PM_{10} and O_3 concentration associated with hospital visits in inner Bangkok. The results demonstrated that exposure on the previous day to PM_{10} and O_3 had a positive association with hospital visits for CVD in elderly patients.

Resulting from Table 4.3, an increase in PM_{10} of 10 μg m^{-3} was associated with a 0.10% (95% CI: 0.03 to 0.19) increase in daily hospital visits for CVD in elderly patients who had been exposed on the previous day and with 0.09% (95% CI: 0.00 to 0.20) increase in cumulative two days exposure. In addition, an increase in O_3 was associated with the total number of CVD visits also increased by 0.23% (95% CI: 0.02 to 0.44) on the previous day (lag 1) and 0.50% (95% CI: 0.19 to 0.81) increase in daily hospital visits for CVD in the elderly who had been exposed on the previous day. However, the two days cumulative average level of O_3 was found to be a more important parameter for hospital visits with a 0.48% (95% CI: 0.13 to 0.83) increase for CVD in elderly group than the concurrent day exposure values; the latter showed only 0.15% (95% CI: -0.16 to 0.46) increase (Table 4.3) The association between air pollution (PM_{10}) and hospital visit for CVD in the elderly may be explained by the fact that, this group is frailer and may have pre-existing heart problems. (Cowie et al., 1999 and Barnett et al., 2006)

The increase in hospital visits for CVD after a 10 μg m^{-3} increase in PM_{10} in elderly patients was less than that found in cooler climates. For example, Barnett et al studied seven cities in Australia and New Zealand and reported a 1.10% (95% CI: 0.20 to 2.00) increase in hospital visits by the elderly after a 10 μg m^{-3} increase in PM_{10} and a 0.3% (95% CI: 0.10 to 1.00) increase in adult patients. (Barnett et al., 2006) A 2002 European Study (Part of the Air Pollution and Health: A European Approach Project) examined the association between airborne particles and CVD hospital admissions (ICD-9th, 360–429), and found that the percentage increase in hospital admissions for a 10 μg m^{-3} increase in PM_{10} was 0.70% in the elderly (95% CI: 0.40 to 1.00) (Tertre et al., 2002). Unlike the majority of previous studies on air pollution and morbidity conducted in cities in the United States and Western Europe with relatively cold winters and strong seasonal patterns in daily morbidity, the present study was performed in a tropical region and therefore excluded the effects of seasonal variation in climate. The replication in a tropical climate of findings obtained in cooler areas, although to a smaller extent, is still notable. Usually the level of air pollution and its health effects are strongly associated with weather. For example, in

Japan, mortality from CVD is 50% higher in the winter months than in the summer months. (Health and Welfare Statistics Association Tokyo, 2008)

The results of the present study show the net effect of air pollution, excluding the effects of season. On the other hand, human O_3 exposure has been associated with a decrease in HRV (Gold et al., 2000) but there have been conflicting reports on O_3 exposure and hospital admissions for CVD. Koken et al, compared air pollution exposure with the daily CVD hospital admissions among elderly people in Denver, Colorado. (Koken et al., 2003) The results suggested that O_3 is associated with an increase in the risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease. The results show there was no significant association between air pollution (PM_{10} and O_3) and sub coding of arrhythmia, MI and IHD. This may be due to the limited number under sub coding of CVD. In fact IHD, which is the largest component of CVD, was weakly associated with PM_{10} in the previous day.

Wong et al. conducted parallel analyses of the short-term association between air pollution and daily hospital admissions in Hong Kong and London. (Wong et al., 2002) The association between O_3 and cardiac admissions was negative in London but positive in Hong Kong. In general, the effects of gaseous pollutants on CVD have not been systematically examined, and the mechanisms by which pollutants affect cardiovascular health remain speculative.

The present study is limited because it uses environmental monitoring data to represent ambient concentrations. The fact that difference pollutants have not been measured at the same monitoring station can affect the estimated correlations between the pollutants and there were some limitations to the study. First, PM_{10} monitoring data were used in this time series analysis, whereas $PM_{2.5}$, particulate matter with an aerodynamic diameter of less than 2.5 μm, has greater toxicity and should be analyzed in future studies. Second, this time series study considered ambient environmental pollution rather than individual exposure levels as a cross-sectional study in a wide range of populations, which may have omitted some extreme exposure incidents. The use of ambient PM_{10} levels from PCD stations rather than actual personal exposure, with indoor and personal PM_{10} levels, may result in misclassification of exposure. This possible misclassification may not differentiate between those visiting hospitals and those not visiting, so that estimation of the association between air pollution and

hospital visits may be biased toward null and thus underestimate the effects. Despite this possible bias, the study still found effects of PM_{10}; these may be stronger if this study were able to measure the actual level of exposure for each individual. Third, when looking at the acute health effects of air pollution using hospital visits, the availability and accessibility of health services often distort the real picture and this may have happened in the present study. However, in 2001 the primary care unit system (PCUS, fixed at 30 Baht per hospital visit) was introduced in Thailand and this reduced the economic barrier to hospital treatment, allowing the number of hospital visits caused by air pollution to be more directly assessed. There may be other limitations inherent to epidemiological studies using government and hospital statistics; however, believe that the present study showed a credible association between hospital visits for CVD and air pollution.

In conclusions, from this study PM_{10} was associated with CVD, particularly in the elderly patients from inner Bangkok area. A short term association between increases in daily levels of air pollutants and the number of daily emergency hospital visit for CVD, in particular in the subjects aged ≥ 65 years old.

4.2 PM_{10} and HRV Sampling

4.2.1 Demographic and Risk Factor Characteristics

Thai standard cardio-respiratory questionnaires (ATS-DLD and CDQ) were purposively distributed to the elderly based on first diagnosis of CVD (ICD-10th: code, I00-I99). Total pre-existing CVD elderly patient subjects from June to October 2007 were 330 visiting at outpatients department of Medicine (O.P.D. Med), Ramathibodi hospital. From the questionnaire's respond and interviewed, the studied participants were checked and excluded the confounding factors according to the criteria for HRV measurement, studied subjects were described previously in chapter 3 page 58. Figure 4.5 illustrated frame work of the studied subject selection, base on the questionnaires and interview analysis. From 200 completed standard cardio-respiratory questionnaires, only 20 subjects were identified within the criteria for HRV measurement. From 20 HRV measurement qualified subjects, there were 8 participants agreed to perform the personal HRV monitoring.
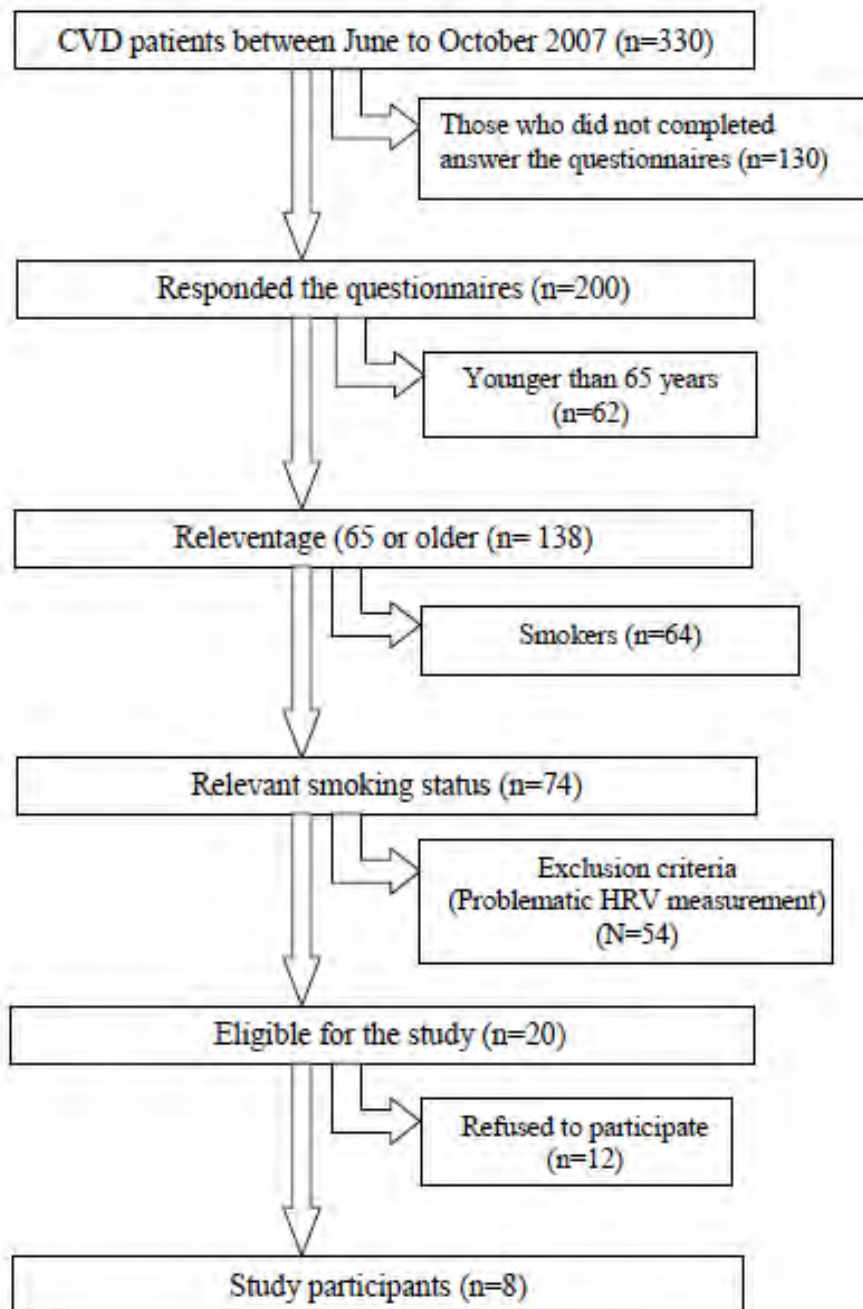
Figure 4.5 Frame work of the studied subject.

There were 8 subjects within the criteria for HRV measurement. Subjects were eligible if they were ambulatory adult ≥65 years of age; not current smokers and they had pre-existing CVD. Exclusion criteria included conditions associated with autonomic dysfunction (e.g., diabetes, chronic renal failure, Parkinsonism, and chronic alcohol abuse), cardiac transplant, cardiac pacemaker, implantable defibrillator, atrial fibrillation, or significant cognitive impairment. The characteristics of HRV study subjects were presented in Table 4.6. Twenty four hour HRV monitoring was digitally recorded for each subject in November 2008, using lightweight Holter monitors with disposable electrodes. During the Holter monitoring, subjects performed their normal daily activities, except those that would interfere with the ECG recording, such as showering. At each session, staff gave the subject a simple 24-hr time-activity diary to record times spent indoors or outdoors, air conditioner (AC) use and whether windows were open during each 2-hr period

Table 4.6 Characteristics of HRV study subjects (N=8)

Characteristics	values
Age (years)	
o 65-70	4
o 71-75	3
o 76-80	1
o ≥81	0
Sex (no.)	
o Male	5
o female	3
Weight (kg.)	71.3±5.7
Height (cm)	162.8±7.2
Smoking status (no.)	
o Never	7
o Former	1
Respiratory symptoms (no.)	
o Cough	1
o Phlegm	1
o Wheezing	0
o Chest tightens	2
Cardiovascular symptoms (no.)	
o Shortness breathing	2
o Awakened by trouble breathing	3
o Feet or ankles swelling	2

4.2.2 Air Pollution and Meteorological data

This study collected hourly ambient PM_{10} concentration from PCD monitoring stations and meteorological variables during the study period nearby the subjects' address. The environment variables (24 hour average) present in table 4.7

Table 4.7 the descriptive statistics for daily PM_{10} and meteorological variables during the study period

Environment variables (24 hour average)	Mean ± SD or total (%)
o Temperature (^{o}C)	29.6±4.6
o Dew point (^{o}C)	23.7±2.8
o Wind (km hr^{-1}.)	4.1±1.8
o 24-hour PM_{10} (μg m^{-3})	57.3±17.7

4.2.3 Heart Rate Variability (HRV)

Twenty-four hour ambulatory HRV was digitally recorded, using lightweight Holter monitors with disposable electrodes, during the Holter Monitoring, all subjects signed a written consent (Appendix D) and performed their normal daily activities, except those that would interfere with the recording (Chapter 3; page 58). Table 4.7 present the descriptive statistics for the pollutants (PM_{10}) and meteorological variables during the study period and Table 4.8 present basal characteristics of heart rate variability (HRV) parameter data for 8 participants in inner Bangkok. Figure 4.6 and 4.7 present an example the data of HRV measurement. (Appendix B)

Table 4.8 Basal characteristics of heart rate variability (HRV) parameter in the study subjects (N=8)

Clinical and ECG characteristics	Mean ± SD or total (%)
Age (years)	70.4±5.2
HRV parameters (N=8)	
○ HR (beats/min)	74.7±12.9
○ SDNN (ms)	94.2±25.6
○ r-MSSD (ms)	26.5±8.0

Abbreviations:

HR   = Heart Rate

NN   = Normal to normal beat interval

SDNN = The standard deviation of normal to normal beat interval

r-MSSD = The square root of the mean of the squared differences between adjacent N-N interval
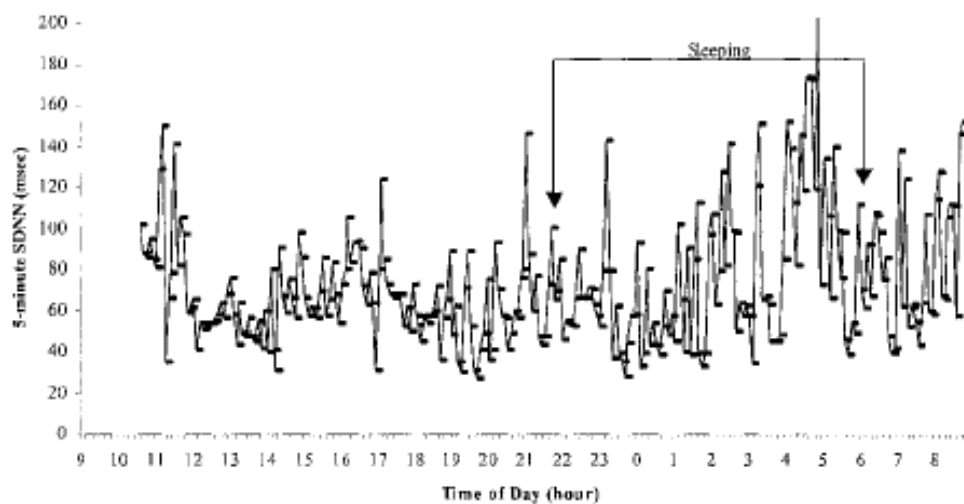
Figure 4.6 An example graph of 5-minute SDNN throughout 24 hour monitoring period, with the time of interest noted from HRV measurement.
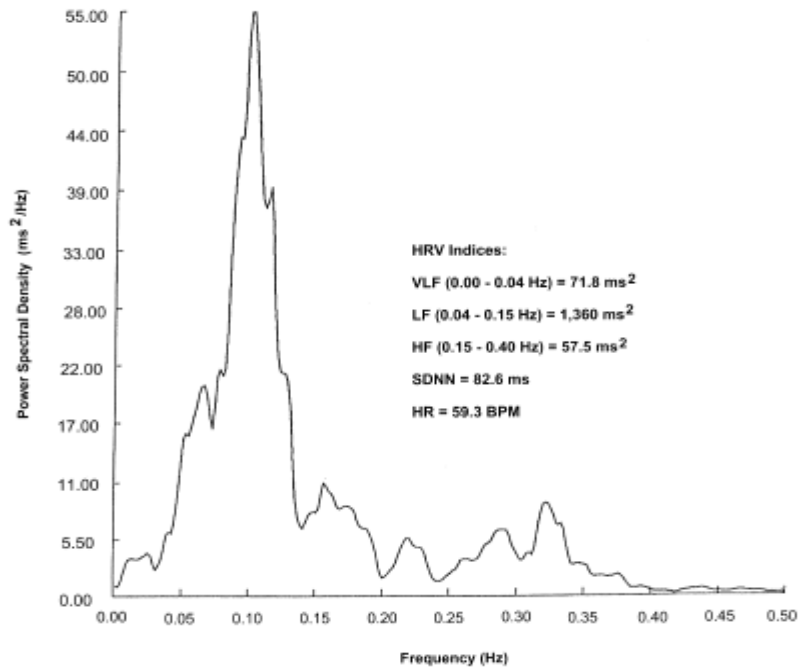
Figure 4.7 An example of a power spectral density curve following fast Fourier transformation of time domain heart rate data. HRV=heart rate variability; VLF=very low frequency; LF=low frequency; HF=high frequency; SDNN=standard deviation of normal R-R intervals; HR= heart rate; BPM=beats per minute.

4.2.4 The association of PM_{10} and Heart Rate Variability (HRV)

Table 4.6 presents the demographic characteristic of the eight study subjects. The time domain, HRV variables used in this analysis and the descriptive statistics for the air pollutant; PM_{10} concentration and meteorological variables during the study period are summarized and presented in Table 4.7 and 4.8

The data in this study existed on multiple level, data such as HRV were measured for the each person, for each observation time. This analysis took into account these multiple level. Most of the HRV variables were log-normally distributed and log-transformed for the analyses. The statistical method applied mixed linear regression models to the continuous HRV variables and PM_{10} concentration, with random-effects parameters to control for inter-individual variation and fixed-effects parameters to estimate relationships between PM_{10} metrics and changes in HRV parameter (SDNN and r-MSSD). This study explored the independent influence

of meteorological factors, temperature, dew point and wind. None of all factors associated with HRV metrics. Then PM_{10} variable was entered into the models; examined the impact of PM_{10} values. For personal HRV variables measured on time domain basis, examined 2-, 4-, and 24-hr PM_{10} moving averages. Because HRV is related inversely to heart rate, the models included the subjects' average heart rate during the monitoring periods. For some of the associations found, the study conducted additional analyses to examine potential impacts of behavioral factors that might influence exposure. For example, for the 2-hr evening period, examined the effects based on responses from the participant's daily diary. Each of these factors was included separately as a dichotomous variable in models that also included PM_{10} metric. Evaluation of potential time-variant confounders through both simple correlation analysis and univariate regressions indicated that the pollutant variables were not confounded by any meteorological variables. Therefore, the results presented are from fixed-effects models that included only the pollutant term and average heart rate as predictor variables. The results of analysis shown the percentage change for HR and HRV variables; SDNN, r-MSSD in association with a 10 µg m^{-3} increase in PM_{10} concentrations presented in Table 4.9

Table 4.9   Percentage change for HRV variables in association with 10 µg m^{-3} increase in PM_{10} concentrations

Parameter	Percent change	95% CI
HR (beats/min)	0.37	-0.01 to 0.73
SDNN (ms)	-1.7	-2.6 to -1.2
r-MSSD (ms)	-2.8	-4.6 to -1.0

Abbreviations: HR, heart rate; SDNN, the standard deviation of normal to normal beat interval; r-MSSD, the square root of the mean of the squared differences between adjacent N-N interval

4.2.5 Discussions

This study found the hourly variation of PM_{10} concentrations and HRV in pre-existing CVD elderly patients ($\geq$65 years) showed an increase in heart rate (HR) and a decrease in heart rate variability (HRV) parameter, SDNN and r-MSSD associated with PM_{10} concentration. These results indicated the association between decrements in SDNN, r-MSSD and increment in HR related to the increasing in PM_{10} concentrations by 10 μg m^{-3} in pre-existing CVD elderly patients in inner Bangkok. The percentage change of heart rate (HR) increasing was 0.37 (95% CI; -0.01 to 0.73) while SDNN and r-MSSD parameter of HRV were decreasing by -1.7% (95% CI; -2.6 to -1.2) and -2.8 % (95% CI; -4.6 to -1.0) respectively. (Table 4.9) The association of PM_{10} with short-term decrements in various HRV parameters in a panel of elderly with pre-existing CVD was consistent. These associations suggest that if there are causal relationships between PM exposures and decreases in HRV, the effects likely occur in close temporal proximity to the exposures.

There were some limitations in this study. First, the information on personal exposure to other air pollutants, such as NO_x, CO, and O_3 are shortage. These co-pollutants may be confounding in the associations between PM_{10} and HRV indices. (Zeger et al., 2000; Zeka and Schwartz, 2004) Therefore, the outcome cannot be entirely ruled out the effects of other air pollutants on HRV. Second, the PM_{10} effects on HRV reduction may be due to the different in particle components rather than particle sizes. Third, the respiration can be the confounding in the association between PM_{10} and HRV. The participants' breathing patterns were not measured. Because the literature suggests that the quantity, periodicity, and timing of vagal cardiac outflow are associated with variations of respiratory dept and interval (Yasuna and Hayano, 2004). Fourth, the technician's presence may also alter the subjects' psychology and autonomic system, and then alter their behaviors, including breathing patterns and heart rates. (Task Force, 1996) Regardless of these limitations, the results generally support conclusion that PM_{10} is an environmental stressor, which may contribute to the fluctuations of HRV indices (decreased SDNN and r-MSSD) and trigger a cascade of events by increasing autonomic function imbalance, and may potentially lead to ischemia or fatal arrhythmia in patients with pre-existing CVD elderly patients are

susceptible to PM_{10} and should be considered a high-risk target group of population in planning future public health abatement measures against particulate matter air pollution.

From the previous reports, for examples, the study of Henneberger et al., in 2005 found the association of the decrease in SDNN and r-MSSD with the increase cardiac risks and Liao et al., in 2004 showed the relationship between increased PM_{10} level and the HR test in elderly subjects. Those reports were similar to this finding. Nevertheless, the results in this study are the first report on the PM_{10} levels effect to impaired HRV in this area, which indicated the high risk of the sensitive elderly CVD patients in inner Bangkok. According to the studied participants and the technique limitations, the studies need to increase the number of subject and the personal monitoring techniques in the future work. However, the implication of this work raised the awareness of the increase air pollution levels effect to population health risks in a big city.

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions Summary

This study was aimed to determine the association between daily average exposure to PM_{10} (particulate matter have diameter less than 10 micron) concentration and the daily hospital visit with cardiovascular disease (CVD) ICD10[th]: I00-I99, and heart function, using the Thai standard cardio-respiratory questionnaires (ATS-DLD and CDQ) and impaired Heart Rate Variability (HRV) function by EKG monitoring among the pre-existing CVD elderly patients ($\geq$65 years) who living in inner part (25/50 districts) of Bangkok. Since this work has involved many social aspects and communities, the ethical issues have been approved by the institutional review board of the Faculty of Medicine; Chulalongkorn University reviewed the protocol based on the International Guidelines for Human Research Protection and International Conference on Harmonization/WHO Good Clinical Practice Standards, ICH/GCP. (Appendix E) Part of this thesis had been published in International Journal of Epidemiology (JOE) and The 11th International Conference on Atmospheric Sciences and Applications to Air Quality (ASAAQ) (Appendix F)

5.1.1 The association between PM_{10} and hospital visit with CVD

In conclusions, from this time-series study air pollution (PM_{10}) associated with the incident of cardiovascular diseases (CVD), particularly in the elderly patients ($\geq$ 65 years) from inner part of Bangkok. A short term association between increases in daily levels of air pollutants and the number of daily emergency hospital visit for CVD, with specificity for all CVD in the subjects aged $\geq$ 65 years old. This part of the study was found no significant association between PM_{10} exposure with total CVD and sub-coding of arrhythmia, MI and IHD on the concurrent day (lag 0) or the previous day (lag 1). However, after controlling for covariate factors, the daily PM_{10} concentrations were positively associated with hospital visits for CVD in the elderly ($\geq$ 65 years). A 0.10% (95% CI: 0.03 to 0.19) increase in CVD visits in this group was

associated with a 10 μg m^{-3} increase in PM$_{10}$. The two cumulative days average of PM$_{10}$ concentration was associated with increased hospital visits for CVD visit in the elderly group of 0.09% (95% CI: 0.00 to 0.20) for each 10 μg m^{-3} increase in PM$_{10}$ (Table 4.3)

5.1.2 The association between PM$_{10}$ and Heart Rate Variability (HRV)

The study found the consistent positive associations between exposures to PM$_{10}$ concentration and impaired the heart functions as heart rate (HR) and heart rate variability (HRV); SDNN, r-MSSD parameters. These results indicated the association between decrements in HRV and increment in HR related to the increasing in PM$_{10}$ concentrations by 10 μg m^{-3} among pre-existing CVD elderly patients (≥ 65 years) in inner part of Bangkok. The percentage change of heart rate (HR) increasing was 0.37% (95% CI; -0.01 to 0.73) while SDNN and r-MSSD parameter of HRV were decreasing by -1.7% (95% CI; -2.6 to -1.2) and -2.8 % (95% CI; -4.6 to -1.0) respectively. (Table 4.9) The association of PM$_{10}$ with short-term the increment in HR and the decrement in various HRV parameters (SDNN, r-MSSD) in a panel of elderly with pre-existing CVD was consistent. These results about the association suggest that, in the inner part of Bangkok elderly patients aged ≥ 65 years old are adverse effect on CVD and impaired HRV increased when particulate matter (PM$_{10}$) concentration increased or chronic health affects increases in high PM$_{10}$ polluted area were associated with reductions in the level of heart function and increased incidence reporting of CVD.

5.2 Recommendations for Future Works

This study aimed as a guide for air quality management in the urban area to for achieve and maintain good air environment is one of the key for protecting of good public health. In addition, suggestions for attempt to reduce adverse impacts on human health and establish strategies to control air pollution are as follows:

5.2.1. Control source emission

- Mobile sources: Formulate a comprehensive control program that includes the setting of stringent fuel or emission standards

such as phase out leaded petrol, vehicular inspection and maintenance systems and enforcement measures.

- Stationary sources: Adopt best available technologies in terms of emission control and fuel efficiency. Industries must have emission equipment in place to reduce particulate pollution.

5.2.2. Zoning or land use concept

- Zone and segregate different types of industries. Construction zones try to wet the area they are working in to avoid particles. At the landfill, the dirt roads are kept wet and the vehicles clean their wheels before going back onto the street again.

- Relocate and centralize industries

5.2.3. Transport and traffic management

- Develop and accelerate other transit systems for convenience to public transport such as sky train, underground train and create an effective bus system. When combined with good public transportation, zoning is a key strategy for reducing vehicular air pollution.

5.2.4. Use of cleaner fuels

- Promote use of cleaner fuels such as natural gas, bio fuels.

5.2.5. Policy

- Accelerate the reduction of air pollutions from vehicles, industries, the construction and transportation. Conducts inspections to ensure that the facility is operating within their limit.

- Maintain air quality standards.

- Controls open burning through education to public community.

- Promote participation among government and private sectors and the general public.

5.2.6. Public participation

- Raise public awareness in pollution reduction through proper maintenance of vehicle engines.

- Promote use of public transportation.

5.3 Suggestions for future health effects researches in Thailand:

a) Examine the relationship between exposure to PM_{10}, prevalence of cardiovascular diseases symptoms, and impaired lung function in other vulnerable groups of population especially, among the residents, adult, elderly and other vulnerable groups of population especially, people with respiratory diseases; asthma, chronic bronchitis, COPD, emphysema and other heart diseases.

b) More through examinations of the relationships between ambient air pollution concentrations and adverse reproductive outcomes, including those involving congenital cardiac anomalies.

c) Determine the relationship between cardio-respiratory healths collected on this cross-sectional study, to long term ambient concentrations of respirable particulate matter (PM_{10}) as well as to conduct multi-pollutant analyses for the other ambient air pollutants such as $PM_{2.5}$, NO_2, SO_2, CO, and O_3 gas co-pollutants by update exposures throughout the period of follow up or cohort study design.

d) Several studies suggested that higher levels of ambient particles are associated with reduced heart rate variability (HRV) (Liao et al., 1999; Pope et al., 1999; Gold et al., 2000; Creason et al., 2001; and Magari et al., 2001) but have not been evaluated systematically in Asia; Bangkok. Therefore, further study should examine the relationship between personal particulate matter exposure and heart rate variability in difference sizes ($PM_{2.5}$ and PM_{10}) and differential toxicity of various constituents and source of air pollution, including:
   - Specific chemical and biological constituents of Particulate matters (e.g., metals, carbon, polycyclic aromatic hydrocarbon, endotoxin)
   - The role of different PM size fractions, including UFPs ($< 0.1\mu m$) and the coarse fraction ($PM_{10\ to\ 2.5}$)
   - The effects of gaseous co-pollutants alone or in combination with particulate matters.

REFERENCES

Anderson, H. R., Bremner, S. A., and Atkinson, R. W. (2001). Particulate matter and daily mortality and hospital admission in the West Midlands conurbation of the United Kingdom: associations with fine and coarse particles, black smoke and sulphate. Occup. Environ. Med. 58: 504-510.

Anderson, H. R., Atkinson, R. W., Bremner, S. A., and Marston, L. (2003). Particulate air pollution and hospital admissions for cardio-respiratory diseases: are the elderly at greater risk ? European Respiratory Journal. 21: 39-46.

Anderson, H. R. (2004). Meta-analysis of time-series studies and panel studies of particulate matter and ozone. Report of a WHO task group. Geneva: World Health Organization.

Arito, H., Uchiyama, I., Arakawa, H., and Yokoyama, E. (1990). Ozone-induced bradycardia and arrhythmia and their relation to sleep-wakefulness in rats. Toxicol Lett. 52: 169-178.

Aschengrau, A., and Seage, G. R. III.. (2003). Essentials of Epidemiology in Public Health. Boston: Jones and Bartlett Publishers Inc.

Aschengrau, A., and Seage, G. R. III. (2008). Essentials of Epidemiology in Public Health. Boston: Jones and Bartlett Publishers Inc.

Ballester, F., Tenias, J. M., and Perez-Hoyos S. (2001). Air pollution and emergency hospital admissions for cardiovascular diseases in Valencia, Spain. Journal of Epidemiology and Community Health. 55: 57-65.

Ballester, F., Rodriguez, P., and Lniguez, C. (2006). Air pollution and cardiovascular admissions association in Spain: results with the EMECAS project. J. Epidemiol Community Health. 60: 328-336.

Bangkok Metropolitan Administration. (2007). Thailand.

Bascom, R. (1996). State of the art: health effects of outdoor air pollution (Part 1) Am. J. Respir. Crit. Care Med. 153: 3-56.

Barnett, A. G., Williams, G. M., Schwartz, J., Best, T. L., and Neller, A. H. (2006). The Effects of Air Pollution on Hospitalizations for Cardiovascular Disease in elderly people in Australian and New Zealand Cities. Environ. Health Perspect. 114: 1018-1023.

Bhatnagar, A. (2004). Cardiovascular pathophysiology of environmental pollutants. Am. J. Physiol Heart Circ Physiol. 286: 479-485.

Bhatnagar, A. (2006). Environmental Cardiology: Studying Mechanistic links between pollution and heart disease. Circulation. 99: 692-705.

Bowerman, B. L., O'Connell, R. T., and Koehler, A. B. (2005). Forecasting, Time series and Regression. Thomson Books/ Cole USA: 279-400.

Brachman, P. S. (2006). Epidemiology [Online]. Available from: http://www.Medmicro Chapter 9.htm [2006, January 20].

Brook, R D., Franklin, B., and Cascio, W. (2004). Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association Circulation. 109: 2655-2671.

Brook, R. D , Brook, J. R., and Urch B. (2002). Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adult. Circulation. 105: 1534-1536.

Burnett, R. T., Smith, D. M., and Stieb, D. (1999). Effects of particulate and gaseous air pollution on cardio-respiratory hospitalizations. Arch Environ Health 54: 130-139.

Burnett, R. T., Smith, D. M., and Stieb D. (2001). Association between Ozone (O_3) and hospitalization for acute respiratory diseases in children less than 2 years of age. Am J. Epidemiol. 153: 444-452.

Burnett, R. T., Cakmak, S., Brook, J. R. (1997). The role of particulate size and chemistry in the association between summer-time ambient air pollution and hospitalizations for cardio-respiratory diseases. Environ Health Perspect. 105: 614-620.

Burnett, R. T., Brook, J. R., and Yung, W. T. (1997). Association between ozone and hospitalization for respiratory diseases in 16 Canadian cities. Environ Resp. 72: 24-31.

Chang, L. V., Chang, L. Y., Huang, Y., and Stockstill, B. L. (1992). Epithelial injury and interstitial fibrosis in the proximal alveolar regions of rats chronically exposed to a simulated pattern of urban ambient ozone. Toxicol Appl. Pharmacol. 115: 241-252.

Colls, J. (2002). Air Pollution: Gaseous air pollution: source and control. Spon Press.: 47-56.

Cowie, M., Wood, D., Coats, A., Thompson, S., Poole-Wilson, P., and Suresh, V. (1999). Incidence and etiology of heart failure: a population-based study. Euro Heart J. 20: 421-428.

Devlin, R. B., Raub, J. A., and Folinsbee, L. J. (1997). Health Effects of Ozone. Sci. Med.: 8-17.

Devlin, R. B., Ghio, A. J., Kehrk, H., Sanders, G., and Cascio, W. Elderly humans exposed to concentrated air pollution particles have decreased heart rate variability. Eur Respir J. 21: 76-80.

Dominici, F., Peng, R. D., Bell, M. L., and Pham, L. (2006). Fine Particulate Air Pollution and hospital admission for cardiovascular and respiratory diseases. JAMA. 295: 1127-1134.

Dominici, F., Zanobetti, A., Zeger, S. L. (2004). Hierarchical bivariate time series models: a combined analysis of the effect of particulate matter on morbidity and mortality. Biostatistics. 5: 41-60.

Dominici, F., Zanobetti, A., Zeger, S. L. (2002). On the use of Generalized Additive Model in time-series studies of air pollution and health. Am. J. Epidemiol. 156: 193-203.

Dominici, F., et al. (2003). Mortality among residents of 90 cities. Revised analyses of time-series studies of air pollution and health. pp. 9-24. Boston: Health Effects Institute.

Donaldson, K., and Macnee, W. (2001). Mini-Review: Potential mechanisms of adverse pulmonary and cardiovascular effects of particulate air pollution (PM_{10}). Int. J. Hyg. Environ. Health. 203: 411-415.

Drew, L., D., et al. (2001). Referent selection in case-crossover analyses of acute health effects of air pollution. Epidemiology. 12: 186-192.

Frischer, T., and Studnicka, M. (1999). Lung Function Growth and Ambient Ozone, A Three-Year Population Study in School Children. Am. J. Resp Crit Care Med. 160: 390-396.

Galan, I., Tobias, A., Banegas, J. R., and Aranguez, E. (2003). Short-term effects of air pollution on daily asthma emergency room admissions. Eur Respir J. 22: 802-808.

Gauderman, W. J., et al. (2002). Association between air pollution and lung
    function growth in Southern California children: Results from a second cohort.
    Am. J. Resp. Crit. Care Med. 166(1): 74-84.

Gold, R. D., Litonjua, A., Schwartz, J., and Lovett, E. (2000). Ambient
    Pollution and Heart Rate Variability. Circulation. 101: 1267-1273.

Gong, H. J. R., Wong, R., Sarma, R. J., Linn, W. S., and Sullivan, E. D.
    (1998). Cardiovascular effects of ozone exposure in human volunteers. Am.
    J. Respir. Crit. Care Med. 158: 538-546.

Hastie, T. J., and Tibshirani, R. J. (1990). Generalized Additive models.
    New York: Chapman and Hall.

Heart Rate Variability: standards of measurement physiological interpretation and
    clinical use. (1996). Task Force of the European Society of Cardiology and
    the North American Society of Pacing and Electrophysiology. Circulation. 93:
    1043-1065.

Henneberger, A., Zareba, W., Mulli, A. I., and Ruckerl, R. (2005).
    Repolarization Changes Induced by Air Pollution in Ischemic Heart Disease
    Patients. Environ Health Perspective. 113: 440-446.

Janssen, N. A., Hoek, G., and Brunekreef, B. (1998). Personal sampling of
    particles in adults: relation among personal, indoor and outdoor air
    concentrations. Am. J. Epidemiol. 147: 537-547.

Jinsart, W., Tamura, K., Loetkamonwit, S., Thepanondh, S., Karita, K., and
    Yano, E. (2002). Roadside Particulate Air Pollution in Bangkok. J. Air &
    Waste Manage Assoc. 52: 1102-1110.

Karita, K., Yano, E., Jinsart, W., Boudoung, D., and Tamura, K. (2001).
    Respiratory symptoms and pulmonary function among traffic policemen in
    Bangkok. Arch Environ Health. 56(5): 467-470.

Karita, K., Yano, E., Tamura, K. and Jinsart, W. (2004). Effect of working and
    residential location areas on air pollution related respiratory symptoms in
    policemen and their wives in Bangkok, Thailand. European Journal of Public
    Health. 14(1): 24-26.

Katsouyanni, K., et al. (2001). Confounding and effect modification in the
    shortterm effects of ambient particles on total mortality: results from 29
    European cities within the APHEA2 project. Epidemiology. 12: 521-531.

Kodanvanti, U. P., Moyer, C. F., and Ledbetter, A. D. (2003). Inhaled environmental combustion particles cause myocardial injury in the Wister Kyoto Rat. Toxicological Sciences. 71: 237-245.

Koken, P. J., Piver, W. T., Ye, F., Elixhauser, A., Olsen, L. M., and Portier, C. J. (2003). Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. Environ Health Perspect. 111: 1312-1317.

Kunzli, N., Ira, B.,Tager. (2005). Air pollution from lung to heart. Swiss Med. 135: 697-702.

Langkulsen, U., Jinsart, W., Karita, K., and Yano, E. (2006). Respiratory symptoms and lung function in Bangkok school children. The European Journal of Public health. 16(6): 676-681.

Last, J. M. (2000). A Dictionary of Epidemiology. 4th Ed., International Epidemiological Association. pp. 228. Oxford: University press.

Liao, D., Creason, J., and Shy, C. M. (1999). Daily variation of particulate air pollution and poor cardiac autonomic control in the elderly. Environ Health Perspect. 107: 521-525.

Liao, D., Duan, Y., Whitsel, E. A., Zheng, Z. J., and Heiss, G. (2004). Association of higher levels of ambient criteria pollutants with impaired cardiac autonomic control: a populationbased study. Am. J. Epidemiol. 159: 768-777.

Lippmann, M., Ito, K., and Nadas, A. (2000). Association of particulate matter component with daily mortality and morbidity in urban populations. Research Report Health Effect Institute. 95: 5-72.

Lipsett, M. J. (2001). Oxides of Nitrogen and Sulfur. In J. B Sullivan., and G. R Krieger (eds.), Clinical Environmental Health and Toxic Exposures. 2nd ed., pp. 818-832. Pennsylvania: Lippincott Williams & Wilkins.

Lipsett, M. J., Tsai, F. C., Roger, L., Woo, M., and Ostro, B. D. (2006). Coarse Particles and Heart Rate Variability among older adults with coronary artery disease in the Coachella Vally, California. Environ Health Perspect. 114: 1215-1220.

Maclure, M. (1991). The case-crossover design: a method for studying transient effects on the risk of acute events. American Journal of Epidemiology. 133: 144-153.

Magari, S. R., Hauser, R., Schwartz, J., Williams, P. L., Smith, T. J., and Christiani, D. C. (2001). Association of heart rate variability with occupational and environmental exposure to particulate air pollution. Circulation. 104: 986-991.

Martins, L. C., and Pereira, L.A. A. (2006). The effects of air pollution on cardiovascular diseases: lag structures. Rev. Saude Publica. 40(4): 677-683.

McConnell, R., Berhane, K., and Gilliland, F. (2007). Asthma in exercising children exposed to ozone: A cohort study. Lancet. 359: 386-391.

Meteorology Department. Bangkok. (2007). Thailand.

Mortimer, K. M., Neas, L. M., Dockery, D. W., Redline, S., and Tager, I. B. (2002). The effect of summer ozone on inner city children with asthma. Eur. Respir. J. 19: 699-705.

Nemmar, A., Nemery, B., and Hoet, P. H. (2003). Pulmonary inflammation and thrombogenicity caused by diesel particles in hamsters: role of histamine. Am. J. Respir. Crit. Care Med. 168: 1366-1372.

Ostro, B. D., Chestnut, L. G., Vadakan, V. N. and Laixuthai, A. (1999). The impact of particulate matter on daily mortality in Bangkok, Thailand. J. Air & Waste Manage. Assoc. 49: 100-107.

Park, S. K., O'Neill, M. S., and Vokonas, P. S. (2005). Effects of Air Pollution on Heart Rate Variability: The VA Normative Aging Study. Environ Health Perspectives. 113: 304-309.

Peter, A., Dockery, D. W., Muller, J. E., and Mittleman, M. A. (2001). Increased particulate air pollution and the triggering of myocardial infarction. Circulation. 103: 2810-2815.

Piver, W. T., Ando, M., Ye, F., and Portier, C. J. (1999). Temperature and air pollution as risk factors for heart stroke in Tokyo, July and August 1980-1995. Environ Health Perspect. 107: 911-916.

Pongsupap, Y., Boonyapaisarncharoen, T., and Lerberghe, W. V. (2005). The Perception of patients using Primary Care Units in comparison with conventional Public Hospital outpatient departments and "Prime Mover Family Practices": An Exit Survey. Journal of Health Science. 14: 475-483.

Pope, C. A. III., Varrier, R. L., Lovett, E. G., and Larson, A. C. (1999). Heart Rate Variability associated with particulate air pollution. American Heart Journal. 138: 890-899.

Rose, G. A., and Blackburn, H. (1986). Cardiovascular Survey Methods. (WHO) World Health Organization Monograph, 56: 1-188.

Rothman, K. J. (2002). Epidemiology, an Introduction. p. 164 Oxford: Oxford University Press.

Routledge, H. C., and Ayres, J. G. (2005). Air Pollution and the Heart. Occupational Medicine. 55: 439-447.

Ruidavets, J. B., Cournot, M., Cassadou, S., and Giroux, M. (2005). Ozone air pollution is associated with acute myocardial infarction. Circulation. 111: 563-569.

Schwartz, J., et al. (1996). Methodological issues in studies of air pollution and daily counts of deaths or hospital admissions. Journal of Epidemiology and Community Health. 50: 3-11.

Schwartz, J. (1993). Air pollution and daily mortality in Birmingham, Alabama. American Journal of Epidemiology, 137: 1136-1147.

Seger, D. L., and Welch, L. W. (2001). Carbon monoxide. . In J. B Sullivan., and G. R Krieger (eds.), Clinical Environmental Health and Toxic Exposures. 2nd ed., pp. 722-727. Pennsylvania: Lippincott Williams & Wilkins.

Shurtleff, D. (1974). Some Characteristics Related to the Incidence of Cardiovascular Disease and Death: Framingham Study, 18-Year Follow-up., Massachusetts: U.S. Department of Health, Education, and Welfare Publication.

Simkhovich, B. Z., Kleinman, M. T., Kloner, R. A. (2008). Air Pollution and cardiovascular injury. J Am Coll Cardiol. 52: 719-726.

Statistics and Information Department, Minister's Secretariat. Ministry of Health, Labour and Welfare. (2006). Vital Statistics of Japan. 3: 402-403.

Sullivan, J. H., Schreuder, A. B., Trenga, C. A., and Liu, S.L. J. (2005). Association between short term exposure to fine particulate matter and heart rate variability in older subjects with and without heart disease. Thorax. 60: 462-466.

Tager, I. B. J., Lurmann, F., Ngo, L., Alcorn, S., and Kunzli, N. (2005). Effect of chronic exposure to Ambient Ozone on lung function in young adults. Epidemiology. 16: 751-759.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). Heart Rate Variability, standards of measurement, physiological interpretation, and clinical use. Circulation. 93: 1043-1065.

Tertre, A. L., Medina, S., Samoli, E., and Forsberg, B. (2002). Short term effects of particulate air pollution on cardiovascular diseases in eight European cities. J. Epidemiology Community Health. 56: 773-779.

Tsuji, H., Larson, M. G., Venditti, J. F. (1996). Impact of reduced heart rate variability on risk for cardiac events: the Framingham Heart Study. Circulation. 94: 2850-2855.

Utell, M. J., Frampton, M. W., Zareba, W., Devlin, R. B., and Cascio, W. E. (2002). Cardiovascular effects associated with air pollution: potential mechanisms and methods of testing. Inhal. Toxicol. 14(12): 1231-1247.

U.S. Environmental Protection Agency. (2006) About AQS Hazardous Air Pollutants. [Online] Available from: http://www.EPA Air Data - About AQS Hazardous Air Pollutants.htm [2006, January 20].

Wellenius, G. A., Bateson, T. F., Mittleman, M. A., and Schwartz, J. (2005). Particulate Air Pollution and the Rate of Hospitalization for Congestive Heart Failure among Medicare Beneficiaries in Pittsburgh, Pennsylvania. Am. J. Epidemiol. 161: 1030-1036.

Wheeler, A., Zanobetti, A., Gold, D. R., Schwartz, J. (2006). The relationship between Ambient Air pollution and Heart Rate Variability differs for individuals with Heart and Pulmonary Disease. Environ Health Perspect. 114: 560-566.

Wong, C. M.,Atkinson, R. W., and Anderson, H. R. (2002). A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared. Environ Health Perspect. 110(1): 67-77.

Wong, T. W., Lau, T. S., Yu, T. S., and Neller, A. (1999). Air pollution and hospital admission for respiratory and cardiovascular disease in Hong Kong. Occup. Environ Med. 56: 679-683.

Wood, S. N., Augustin, H. N. (2002). GAMs with integrated model selection using penalized regression splines and applications to environmental modeling. Ecological Modeling. 157: 157-177

Wangwongwatana, S., and Warapetcharayut, P. (2006). Air pollution management in Thailand [Online] Available from: http://www.asiairnet.org/publications/11-Thailand.pdf [2006, January 20].

Yasuma, F., and Hayano, J. (2004). Respiratory sinus arrhythmia: why does the heartbeat synchronize with respiratory rhythm ? Chest, 125: 683-690.

Zareba, W., Nomura, A., and Couderc, J. P. (2001). Cardiovascular effects of Air Pollution: What to Measure in ECG? Environmental Health Perspectives. 109: 533-538.

Zanobetti, A., Schwartz, J., and Dockery, D. W. (2000). Airborne particles area risk factors for hospital admissions for heart and lung disease. Environmental Health Perspectives. 108: 1071-1077.

Zanobetti, A., and Schwartz, J. (2006). Air pollution and emergency admission in Boston. J. Epidemiol Community Health. 60: 890-895.

Zanobetti, A., and Schwartz, J. (2005). The effect of particulate air pollution on emergency admission for myocardial infarction: a multi-city case-crossover analysis. Environ Health Perspectives. 113: 978-982.

APPENDICES

LIST OF ABBREVIATION

Al	Aluminum
ANOVA	Analysis of variance
AQS	Air quality pollutants system
As	Arsenic
ATS	American Thoracic Society
ATS-DLD	American Thoracic Society Division of Lung Disease
AAR	Autonomic Assessment Report
Ba	Barium
BAL	Broncho-alveolar lavage
BaP	Benzo (a) pyrene
BMA	Bangkok Metropolitan Administration
BMR	Bangkok Metropolitan Region
BTPS	Ambient temperature and pressure, saturated
C	Control area
Ca	Calcium
CI	Confidential interval
Cl	Chlorine
Cl⁻	Chlorine ion
cm	centimeter
CoHb	Carboxyhemoglobin
COPD	Chronic obstructive pulmonary diseases
CO	Carbon monoxide
Cr	Chromium
Cu	Copper
CVD	Cardiovascular diseases
CDQ	Cardiovascular disease questionnaires
DAD	Diffuse alveolar damage
EC	Elemental carbon
ECG	Electro-cartographic monitoring
e.g.	Exempli gratia
ELF	Epithelial lining fluid

EPA	Environmental Protection Agency
ERV	Expiratory reserve volume
etc.	et cetara
Fe	Iron
$FEF_{25-75\%}$	Mean forced expiratory flow during the middle half of the FVC
FEV_1	Forced expiratory volume in one second
FEV_t	Timed forced expiratory volume
FVC	Forced vital capacity
g	gram
g/l	gram per liter
HAPs	Hazardous air pollutants
HC	Hydrocarbon
HG	High-polluted general area
H_2O	Water
HF	High frequency
HR	Heart Rate
HRV	Heart Rate Variability
Hz	Hertz
IC	Inspiratory capacity
ICD10[th]	International Classification of Diseases Tenth Revision
i.e.	id est
IgE	Immunoglobulin E
IgG	Immunoglobulin G
ICH-GCP	International Conference on Harmonization/WHO Good Clinical Practice Standards.
K	Potassium
L	Liter
LDH	lactate dehydrogenase
l/min	Liters per minute
l/s	Liters per second
IHD	Ischemic Heart Diseases
LF	Low frequency
LPG	Liquefied petroleum gas
LSD	Fisher's Least-Significant Difference

MetHb	Met-hemoglobin
MI	Myocardial Infarction
min	minute
mm	milimeter
Mn	Manganese
MR	Moderate-polluted roadside area
Ms	Milliseconds
MSE	Mean square between groups
MST	Mean square within groups
MVV	Maximal voluntary ventilation
NAAQS	National Ambient Air Quality Standards
NH_4^+	Ammonium ion
Ni	Nickel
NIOSH	National Institute of Occupational Safety and Health
NN	Normal to normal beat interval
NO_2	Nitrogen dioxide
NO_3^-	Nitrate ion
NSRD	Non-specific respiratory disease
nu	normalized units
O_3	Ozone
OC	Organic carbon
OR	Odds ratio
P	Phosphorus
PAHs	Polycyclic aromatic hydrocarbons
PCP	Persistent cough and phlegm
Pe	Probability of developing disease, among those exposed to the risk factor
Po	Probability of developing disease, among those not exposed to the risk factor
Pb	Lead
PCD	Pollution Control Department
PCUS	The Primary Care Unit System
PEFR	Peak expiratory flow rate
PFTs	Pulmonary Function Tests

$PM_{2.5}$	Particulate matter less than 2.5 micron in diameter
PM_{10}	Particulate matter less than 10 micron in diameter
ppb	parts per billion
ppm	parts per million
Q	Questionnaire
R	Rural area
r-MSSD	The square root of the mean of the squared differences between adjacent N-N interval
RV	Residual volume
s	second
S	Sulfur
SAS	Statistical Analysis Software
SD	Standard deviation
SE	Standard error
SES	Socioeconomic status
SDNN	The standard deviation of normal to normal beat interval
SO_2	Sulfur dioxide
SO_4^{2-}	Sulfate anion
SPM	Suspended Particulate Matter
SPSS	Statistical package for social science
TEOM	Tapered Element Oscillating Microbalance
TLC	Total lung capacity
TSP	Total suspended particulate matter
TV	Tidal volume
U.S.	United States
USEPA	United States Environmental Protection Agency
VC	Vital capacity
VOC	Volatile organic compound
WHO	World Health Organization
Wt	Weight
Zn	Zinc
$\mu g\ m^{-3}$	Microgram per cubic meter
μm	Micrometer

APPENDIX A

Thai-Standard of Cardio-respiratory Questionnaires
(ATS-DLD and CDQ questionnaires)

แบบสอบถามเพื่อการวิจัย

"ความสัมพันธ์ของฝุ่นละอองขนาดเล็กกับการเกิดโรคของระบบหลอดเลือดหัวใจ

ของประชาชนในเขตกรุงเทพมหานคร"

ผู้ทำการวิจัย

นางสาว ดวงฤทัย บัวด้วง

สหสาขาวิชาวิทยาศาสตร์สิ่งแวดล้อม

จุฬาลงกรณ์มหาวิทยาลัย

คำชี้แจง :   แบบสอบถามนี้เป็นส่วนหนึ่งของการทำวิทยานิพนธ์ในระดับดุษฎีบัณฑิต สหสาขาวิชาวิทยาศาสตร์สิ่งแวดล้อม จุฬาลงกรณ์มหาวิทยาลัย โดยมี   วัตถุประสงค์เพื่อศึกษาความสัมพันธ์ ของฝุ่นละอองขนาดเล็กในอากาศกับการเกิดโรคระบบหลอดเลือดหัวใจของประชาชนในเขต กรุงเทพมหานคร เพื่อให้ทราบสาเหตุหรือปัจจัยเสี่ยงต่อการเกิดโรคระบบหลอดเลือดหัวใจและเป็นประโยชน์ ในด้านการสาธารณสุข เป็นแนวทางให้ประชาชนตระหนักถึงความสำ   คัญของปัญหาสุขภาพอนามัยกับการ เกิดโรคระบบหลอดเลือดหัวใจ และสามารถนำความรู้นั้นไปปฏิบัติเป็นกิจวัตรประจำวันในการดูแลสุขภาพ นอกจากนี้ยังช่วยในการวางแผนการให้การบริการทางการแพทย์สาธารณสุขและการกำหนดนโยบายที่ถูกต้อง เหมาะสมต่อไป คำตอบของท่านมีคุณค่าอย่างยิ่งในง านวิจัย ผู้วิจัยจะเก็บข้อมูลของท่านเป็นความลับ โดยจะ นำไปใช้เพื่อสรุปผลการวิจัยเป็นภาพรวมเท่านั้น ข้อมูลที่ตรงกับความเป็นจริงและสมบูรณ์จะช่วยให้การวิจัย ดำเนินไปด้วยความถูกต้อง ผู้วิจัยจึงใคร่ขอความอนุเคราะห์จากท่านในการตอบแบบสอบถามอย่างรอบคอบ ให้ครบทุกข้อ

แบบสอบถามนี้ มี **43 ข้อ จำนวน 7 หน้า แบ่งออกเป็น 6 ส่วน ดังนี้**

ส่วนที่ 1. (ข้อที่ 1- 14)   แบบสอบถามข้อมูลทั่วไป

ส่วนที่ 2. (ข้อที่ 15- 23)   แบบสอบถามข้อมูลเกี่ยวกับระบบทางเดินหายใจ

ส่วนที่ 3. (ข้อที่ 24- 32)   แบบสอบถามข้อมูลเกี่ยวกับระบบหัวใจและหลอดเลือด

ส่วนที่ 4. (ข้อที่ 33- 40)   แบบสอบถามข้อมูลความเจ็บป่วยอื่นๆ

ส่วนที่ 5. (ข้อที่ 41- 42)   แบบสอบถามข้อมูลประวัติการสูบบุหรี่

ส่วนที่ 6. (ข้อที่ 43)   แบบสอบถามข้อมูลประวัติครอบครัว

หมายเหตุ: เวลาที่ท่านใช้ในการตอบแบบสอบถามประมาณ 15-20 นาที

เลขที่ ☐☐☐☐☐☐

1-6

แบบสอบถามเกี่ยวกับระบบทางเดินหายใจและหลอดเลือดหัวใจ

ขอให้ท่านกรุณากรอกแบบสอบถามโดยตอบคำถามอย่างถูกต้องชัดเจนและเป็นไปได้มาก
ที่สุด ข้อมูลที่ได้ทั้งหมดจากการศึกษานี้ถือเป็นความลับและนำมาใช้เพื่อประโยชน์ทางการวิจัยเท่านั้น (แพทย์
ประจำตัวของท่าน จะได้ทราบผลด้วยหากท่านต้องการ)

วันที่ทำแบบสอบถาม……….. /…………/. …………

(วัน เดือน ปี)

**โปรดทำเครื่องหมาย (✔) หรือเติมข้อความสั้นๆ ลงในช่องว่างหน้าข้อความที่ท่านเห็นว่าเหมาะสมและตรง
กับสภาพความเป็นจริงมากที่สุด**

สำหรับเจ้าหน้าที่กรอก

ส่วนที่ 1. ข้อมูลทั่วไป

1. เพศ 1. ( ) ชาย 2. ( ) หญิง	7	☐
2. วันเกิด …………/……………/………………	8-13	☐☐☐☐☐
(วัน เดือน ปี)		
3. อายุ………………… ปี	14-15	☐☐
4. น้ำหนัก………………กิโลกรัม	16-17	☐☐
5. ส่วนสูง………………เซนติเมตร	18-20	☐☐☐
6. สถานภาพ	21	☐

1. ( ) สมรส   2. ( ) โสด

3. ( ) หม้าย   4. ( ) หย่า

5. ( ) แยก   6. ( ) อื่นๆ โปรดระบุ…………………

7. สถานที่เกิด	22	☐

1. ( ) กรุงเทพมหานคร

2. ( ) ต่างจังหวัด จังหวัด…………………

3. ( ) อื่นๆ โปรดระบุ………………………

8. ที่อยู่ปัจจุบัน ……………………………………..	23	☐
อาศัยในที่อยู่ปัจจุบันมาเป็นเวลา ……..……… ปี	24-25	☐☐

9. ระดับการศึกษา

        1. ( ) น้อยกว่าชั้นประถม   26   ☐

        2. ( ) ชั้นประถม

        3. ( ) ชั้นมัธยมศึกษา

        4. ( ) ชั้นอุดมศึกษา

        5. ( ) สูงกว่าปริญญาตรี

        6. ( ) อื่นๆ โปรดระบุ..

10. อาชีพ (โปรดระบุ)..   27   ☐

11. A. ในบ้านของท่านมีห้องทั้งหมด .... ห้อง (ไม่รวมห้องน้ำ)   28-29   ☐☐

    B. ในบ้านของท่านมีสมาชิกอาศัยอยู่ทั้งหมด........... คน (จำนวนคน)   30-31   ☐☐

12. ในบ้านของท่านใช้เตาและอุปกรณ์ประกอบอาหารประเภทใด   32   ☐

      1. ( ) แก๊ส   3. ( ) ถ่าน

      2. ( ) ไฟฟ้า   4. ( ) อื่นๆ ระบุ…………………...

13. ในบ้านท่านมีเครื่องปรับอากาศ เครื่องดูดความชื้นหรือเครื่องฟอกอากาศหรือไม่   33   ☐

    (ถ้ามี โปรดระบุ)

        0. ( ) ไม่มีเลย

        1. ( ) เครื่องปรับอากาศ

        2. ( ) เครื่องดูดความชื้น

        3. ( ) เครื่องฟอกอากาศ

        4. ( ) เครื่องปรับอากาศ + เครื่องดูดความชื้น

        5. ( ) เครื่องปรับอากาศ + เครื่องฟอกอากาศ

        6. ( ) เครื่องดูดความชื้น + เครื่องฟอกอากาศ

        7. ( ) เครื่องปรับอากาศ + เครื่องดูดความชื้น + เครื่องฟอกอากาศ

14. ท่านมีสัตว์เลี้ยงไว้ในบ้านของท่านหรือไม่ (ถ้ามี โปรดระบุ)   34   ☐

        0. ( ) ไม่มี   4. ( ) แมว

        1. ( ) สุนัข   5. ( ) นก

        2. ( ) แมว + สุนัข   6. ( ) แมว + นก

        3. ( ) สุนัข +นก   7. ( ) แมว + สุนัข +นก

ส่วนที่ 2. คำถามต่อไปนี้ส่วนใหญ่เกี่ยวกับระบบทางเดินหายใจ

กรุณาตอบใช่หรือไม่ใช่ แต่ถ้าคำตอบใดไม่เกี่ยวกับท่าน กรุณาเลือกคำตอบ ไม่เข้าข่าย

อาการไอ

15. A. ท่านมักจะมีอาการ ไอเมื่อเป็นหวัด 1) ใช่……....2) ไม่ใช่………. 35 ☐

   B. ท่านมีอาการ ไอเนื่องจากสาเหตุอื่นที่ไม่ใช่หวัด 1) ใช่……. 2) ไม่ใช่…….. 36 ☐

   <u>ถ้าตอบใช่ ในข้อ (15.A) หรือ (15.B)</u>

   C. ท่านมีอาการ ไอเป็นเวลานาน 1) ใช่……. 2) ไม่ใช่………. 37 ☐

   (มากกว่า 4 วันต่อสัปดาห์) หรือไอเป็นเวลามากกว่า 3 เดือนต่อปี

   D. ท่านมีอาการไอเป็นเวลา………………..……………ปี 38-39 ☐☐

อาการมีเสมหะ

16. A ท่านมักจะมีอาการแน่นหน้าอกหรือ 1) ใช่……. 2) ไม่ใช่……...... 40 ☐
   มีเสมหะเนื่องจากหวัด

   B. ท่านมักจะมีอาการแน่นหน้าอกหรือมีเสมหะ 1) ใช่……. 2) ไม่ใช่……...... 41 ☐
   เนื่องจากสาเหตุอื่นที่ไม่ใช่หวัด

   <u>ถ้าตอบใช่ ในข้อ (16.A) หรือ (16.B)</u>

   C. ท่านมีอาการอึดอัด มีเสมหะ มีเสลด 1) ใช่……. 2) ไม่ใช่……...... 42 ☐
   คัดจมูกจากอาการแน่นหน้าอกหลายวัน

   (มากกว่า 4 วันต่อสัปดาห์) นานกว่า 3 เดือนต่อปี

   D. ท่านมีอาการอึดอัดหรือเริ่มมีเสมหะ มีเสลดหรือมี………………. …ปี 43-44 ☐☐
   อาการคัดจมูกซึ่งมาจากอาการแน่นหน้าอกเป็นเวลา

17. A. ท่านมีอาการ ไอหรือแน่นหน้าอกหรือมีเสมหะ 1) ใช่……....2) ไม่ใช่…….. 45 ☐
   ครั้งสุดท้ายเป็นเวลานานกว่า 1 สัปดาห์

   <u>ถ้าตอบใช่ ในข้อ (17.A)</u>

   B. ท่านมีอาการเหล่านี้เป็นเวลา……………………….. ……….ปี 46-47 ☐☐

   C.ท่านมีอาการแน่นหน้าอกเนื่องจากเป็นหวัดโดยเฉลี่ย…………….ครั้ง/ ปี 48-49 ☐☐

อาการหายใจมีเสียง

18. ท่านมีอาการหายใจมีเสียงในช่วงเวลาใด

   A. ขณะเป็นหวัด 1) ใช่……. 2) ไม่ใช่……...... 50 ☐

   B. เป็นบางครั้งและไม่ได้มาจากการเป็นหวัด 1) ใช่……. 2) ไม่ใช่……...... 51 ☐

C. ตลอดทั้งวันทั้งคืน   1) ใช่…….. 2) ไม่ใช่….…….   52   ☐

<u>ถ้าตอบใช่ ในข้อ (18.B) หรือ (18.C)</u>

D. ท่านมีอาการหายใจมีเสียงเป็นเวลา……………….. ……..ปี   53-54   ☐☐

19.   A. ท่านมีอาการหายใจมีเสียง   1) ใช่…….. 2) ไม่ใช่….……..   55   ☐

ซึ่งเป็นสาเหตุให้เกิดอาการหายใจช่วงสั้นๆ

<u>ถ้าตอบใช่ ในข้อ (19.A)</u>

B. ท่านมีอาการคราวละ 2 ครั้งหรือมากกว่า   1) ใช่…….. 2) ไม่ใช่………   56   ☐

C. ท่านต้องการยาหรือการบำบัดอาการนี้   1) ใช่…….. 2) ไม่ใช่….…….   57   ☐

D. ท่านมีอาการนี้ครั้งแรกเมื่ออายุ...ปี   58-59   ☐☐

E. ในระหว่างการหายใจเป็นปกติมีอาการ   1) ใช่…….. 2) ไม่ใช่….…….   60   ☐

       หายใจที่มีเสียงเกิดขึ้น

20.   ท่านเคยเกิดอาการหายใจมีเสียงหลังจากที่   1) ใช่…….. 2) ไม่ใช่….…….   61   ☐

      มีการออกกำลังกายมาก ๆ

<u>อาการแน่นหน้าอก</u>

21.   A. ในช่วงระยะเวลา 3 ปีที่ผ่านมา ท่านเคย   1) ใช่…….. 2) ไม่ใช่….…….   62   ☐

มีอาการแน่นหน้าอกจนเป็นสาเหตุให้ต้องหยุดพักถึง 3วัน

<u>ถ้าตอบใช่ ในข้อ (21.A)</u>

B. ท่านมีเสมหะร่วมกับอาการเจ็บหน้าอก   1) ใช่…….. 2) ไม่ใช่….…….   63   ☐

C. ท่านมีอาการเจ็บป่วยข้างต้นกี่ครั้งในช่วงระยะ 3 ปีที่ผ่านมา   64   ☐

         1. ( ) น้อยกว่า 1 ครั้งต่อปี

         2. ( ) 1 ครั้งต่อปี

         3. ( ) 2-5 ครั้งต่อปี

         4. ( ) มากกว่า 5 ครั้งต่อปี

D. ความเจ็บป่วยเหล่านี้เกิดขึ้นจำนวนกี่ครั้งที่มีเวลา   65-66   ☐☐

นานกว่า 7 วัน   จำนวนที่เกิดขึ้น ....ครั้ง

22. ท่านเคยมีประวัติการป่วยทางทรวงอกภายในระยะเวลา 2 ปีหรือไม่   67   ☐

     1. ( ) ใช่ 1 ครั้ง   3. ( ) ใช่ 3 ครั้งหรือมากกว่า

     2. ( ) ใช่ 2 ครั้ง   4. ( ) ไม่เคยเลย

23. ที่ผ่านมาท่านเคยมีปัญหาความเจ็บป่วย   1) ใช่……….2) ไม่ใช่….…….   68   ☐

     ทางทรวงอกอื่นๆ

ส่วนที่ 3. คำถามต่อไปนี้ส่วนใหญ่เกี่ยวกับระบบหัวใจและหลอดเลือด
กรุณาตอบใช่หรือไม่ใช่ แต่ถ้าคำตอบใดไม่เกี่ยวกับท่าน กรุณาเลือกคำตอบ ไม่เข้าข่าย

24. ท่านเคยหายใจขัด, เหนื่อยขณะเดิน   1) ใช่........ 2) ไม่ใช่............   69   ☐
อย่างเร็วในที่ราบหรือเดินในทางลาดขึ้นหรือไม่

25. ท่านเคยรู้สึกเหนื่อย, หายใจขัด   1) ใช่........ 2) ไม่ใช่............   70   ☐
ขณะเดินกับผู้อื่นในทางราบปกติหรือไม่
         <u>ถ้าไม่ใช่ ให้ข้ามไปทำ (ข้อ 28)</u>

26. ท่านเคยหยุดเดินเพื่อพักให้หายใจ   1) ใช่........ 2) ไม่ใช่............   71   ☐
ขณะเดินในทางราบหรือไม่

27. ท่านเคยหยุดเดินเพื่อพักหายใจ   1) ใช่........ 2) ไม่ใช่............   72   ☐
(ขณะเดินในระยะทาง 10 เมตร หรือ
หลังจากเดิน 4-5 นาทีในทางราบ) หรือไม่

28. ท่านเคยถูกทำให้ตื่นเนื่องจากหายใจขัด   1) ใช่........ 2) ไม่ใช่............   73   ☐
มากกว่าเมื่อเปรียบเทียบกับตอนท่านเป็นหวัดหรือไม่
         <u>ถ้าตอบไม่ใช่ ให้ข้ามไปทำ (ข้อ 30)</u>

29. ท่านเคยต้องตื่นลุกขึ้นมานั่งข้างเตียงหรือไม่   1) ใช่........ 2) ไม่ใช่............   74   ☐

30. ท่านเคยนอนหนุนหมอน 2 ใบหรือมากกว่า   1) ใช่........ 2) ไม่ใช่............   75   ☐
เพื่อช่วยในการหายใจหรือไม่

31. ท่านเคยมีอาการบวมที่เท้าหรือข้อเท้าหรือไม่   1) ใช่........ 2) ไม่ใช่............   76   ☐
    (ไม่รวมอาการขณะตั้งครรภ์)
<u>ถ้าตอบใช่ ใน (ข้อ 31)</u>

32. ท่านมีอาการดังกล่าวในช่วงระหว่างวันและ   1) ใช่........ 2) ไม่ใช่............   77   ☐
ลดลงขณะหัวค่ำใช่หรือไม่

ส่วนที่ 4. ความเจ็บป่วยอื่นๆ
33. ท่านเคยเจ็บป่วยด้วยโรคต่างๆ ดังต่อไปนี้หรือไม่ ถ้าเคย เกิดขึ้นเมื่อท่านมีอายุเท่าใด
                                                 <u>*การวินิจฉัยโรคครั้งแรกจากแพทย์*</u>

     A. หัด (ยกเว้นหัดเยอรมัน)   1)ใช่ .... เมื่ออายุ .... 2) ไม่ใช่   78   ☐

     B. ปัญหาไซนัส   1)ใช่ ....เมื่ออายุ .... 2)ไม่ใช่   79   ☐

     C. หลอดลมอักเสบ   1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่   80   ☐

     D. หลอดลมเล็กอักเสบ   1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่   81   ☐

E. หอบหืด	1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่	82	☐
F. ปอดอักเสบ	1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่	83	☐
G.ไอกรน	1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่	84	☐
H.โรคซาง (แพ้ฝุ่นเกสรดอกไม้)	1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่	85	☐
I. โรคระบบทางเดินหายใจอื่นๆ	1)ใช่ .... เมื่ออายุ ....2)ไม่ใช่	86	☐

34. ท่านเคยมีปัญหาในเรื่องหูชั้นนอกอักเสบ 1)ใช่ .... 2)ไม่ใช่ ...... 87 ☐

35. ท่านเคยได้รับการรักษาทางหู 1)ใช่ .... 2)ไม่ใช่ ...... 88 ☐

36. ท่านเคยได้รับการผ่าตัดทอนซิล 1)ใช่ .... 2)ไม่ใช่ ...... 89 ☐

37. A. ท่านเคยได้รับการวินิจฉัยจากแพทย์ว่าเป็นหอบหืด 1)ใช่ ......2)ไม่ใช่..... 90 ☐

    <u>ถ้าตอบใช่ ใน (ข้อ 37.A)</u>

    B. ท่านเริ่มเป็นหอบหืดเมื่ออายุ ……......................………ปี 91-92 ☐☐

    C. ในปัจจุบันท่านยังคงเป็นหอบหืด 1)ใช่ .... 2)ไม่ใช่ ...... 93 ☐

    D. ท่านยังคงรับการรักษาเรื่องหอบหืด 1)ใช่ .... 2)ไม่ใช่ ...... 94 ☐

<u>ถ้าตอบไม่ใช่ ใน (ข้อ 37.C)</u>

    E. ท่านหายจากหอบหืดเมื่ออายุ …………………....…… ปี 95-96 ☐☐

38. ท่านเคยได้รับการผ่าตัดทรวงอกหรือไม่ 1)ใช่ .... 2)ไม่ใช่ .... 97 ☐

    ถ้าเคย โปรดระบุประเภทของการผ่าตัด …………………......…………………..

39. ท่านเคยได้รับการวินิจฉัยจากแพทย์ว่าเป็น 1)ใช่ .... 2)ไม่ใช่ .... 98 ☐

    โรคหัวใจหรือไม่ ถ้าใช่โปรดระบุ ….....………………………………………

<u>ภูมิแพ้</u>

40. A. ท่านเคยได้รับการตรวจจากแพทย์และวินิจฉัยว่าท่านเป็นโรคภูมิแพ้ 99 ☐

1. ( ) ใช่ แพ้อาหาร 2. ( ) ใช่ แพ้ยา

3. ( ) ใช่ แพ้ทั้งอาหารและยา 4. ( ) ไม่ใช่

    B. แพทย์เคยบอกว่าท่านแพ้ฝุ่นละออง 1)ใช่ .... 2)ไม่ใช่ ...... 100 ☐

    C. แพทย์เคยบอกว่าท่านแพ้สารเคมี 1)ใช่ .... 2)ไม่ใช่ ...... 101 ☐

    D. ท่านเคยได้รับการทดสอบภูมิแพ้ 1)ใช่ .... 2)ไม่ใช่ ...... 102 ☐

ส่วนที่ 5. ประวัติการสูบบุหรี่

41. A. ท่านเคยสูบบุหรี่หรือไม่　　　　　　　　1 ( ) ไม่สูบ 2. ( ) สูบ　　103　□

　　　　　ถ้าตอบใช่ (สูบ)ในข้อ (41.A)

　　B. ปัจจุบันท่านยังคงสูบบุหรี่　　　　　　1) ใช่ ……. 2) ไม่ใช่ ……　104　□

　　　　(ภายใน 1 เดือนที่ผ่านมา)

　　C. ท่านเริ่มสูบบุหรี่ครั้งแรกเมื่อท่านอายุ..............................ปี　　105-106 □□

　　D. จำนวนบุหรี่ที่ท่านสูบในแต่ละวันในปัจจุบันเฉลี่ย...................มวน/วัน　　107-108 □□

　　E. นับตั้งแต่ท่านเริ่มสูบบุหรี่โดยเฉลี่ยแล้วท่านสูบบุหรี่.................มวน/วัน　　109-110 □□

　　　　　　สมาชิกหรือบุคคลอื่นๆ

42. มีบุคคลในบ้านท่านสูบบุหรี่หรือไม่　　　　1. ( ) มี　 2. ( ) ไม่มี　　111　□

　　　ถ้ามี (ไม่นับรวมผู้ตอบ) มีจำนวน.....................................คน　　112-113 □□

ส่วนที่ 6. ประวัติครอบครัว

43. บิดามารดาของท่านเคยได้รับการตรวจและวินิจฉัยจากแพทย์ว่ามีอาการเจ็บป่วยด้วยโรคเกี่ยวกับโรคต่าง ๆ ดังนี้หรือไม่

	บิดา			มารดา			
	1) ใช่	**2) ไม่ใช่**	**3) ไม่ทราบ**	**1) ใช่**	**2) ไม่ใช่**	**3) ไม่ทราบ**	
A. โรคหลอดลมเรื้อรัง	………	………	………	…………	………	………	114-115 □□
B. โรคเยื่อหุ้มปอดเป็นหนอง	……	………	………	…………	………	………	116-117 □□
C. โรคหอบหืด	………	………	………	…………	………	………	118-119 □□
D. โรคมะเร็งปอด	………	………	………	…………	………	………	120-121 □□
E. โรคปอดอื่นๆ	………	………	………	…………	………	………	122-123 □□
F. โรคหัวใจ	………	………	………	…………	………	………	124-125 □□
G. โรคเบาหวาน	………	………	………	…………	………	………	126-127 □□
H. โรคความดันโลหิตสูง	………	………	………	…………	………	………	128-129 □□

APPENDIX B

Heart Rate Variability (HRV) Monitoring

Hunter Kane

HEART RATE VARIABILITY - HRV

Twenty-Four-hour Monitoring

Heart Rate Variability (HRV)

Heart Rate Variability (HRV) is a very sophisticated measure of physiological health. It can predict risks of major disease and underpins vitality and performance.

In learning to master the physiology the most important physiological signal of which to gain control is the one generated by the heart. This is because the heart is the most powerful signal generator in the human body and the stream of information entering the brain from the heart is constantly changing. This beat-to-beat change in the heart rate is called Heart Rate Variability (HRV) and it can be measured continuously throughout an individual's day.
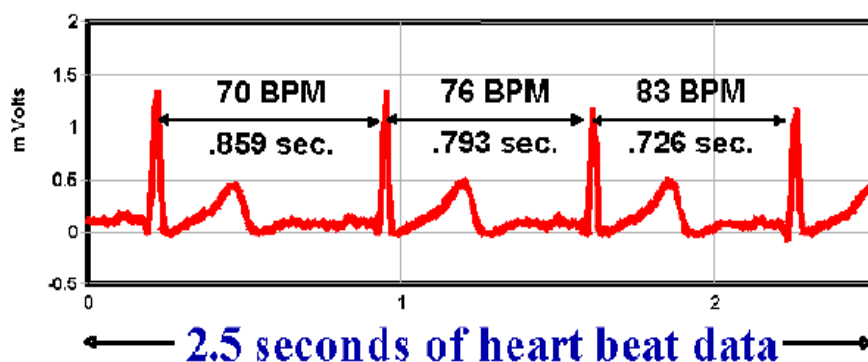
Heart Rate Variability (HRV):

1. Underpins energy and dynamism

indicates ageing rate	*Umetani, et al, J. Am. Coll. Cardiol. 1998*
indicates fitness levels	*Gallagher, et al, Clin. Auton. Res. 1992*
Autonomic nervous system (ANS) function	*Wood, et al, J Cardiopulm Rehabil. 1998*

2. Can be used to predict risk of ill health and major disease

3. Underpins performance

indicates nervous system balance	*Friedman, et al, J Psychosom. Res. 1998*

Health Risk Prediction

HRV can be used to detect early warning signs of any dysfunction long before routine medical investigation detects a problem or before any symptoms arise. HRV can also be used to track the progress of any training intervention and monitor the degree of improvement.

Performance

HRV early warning

Poor Performance

Breakdown

most medical testing

Pressure / Challenge / Stress
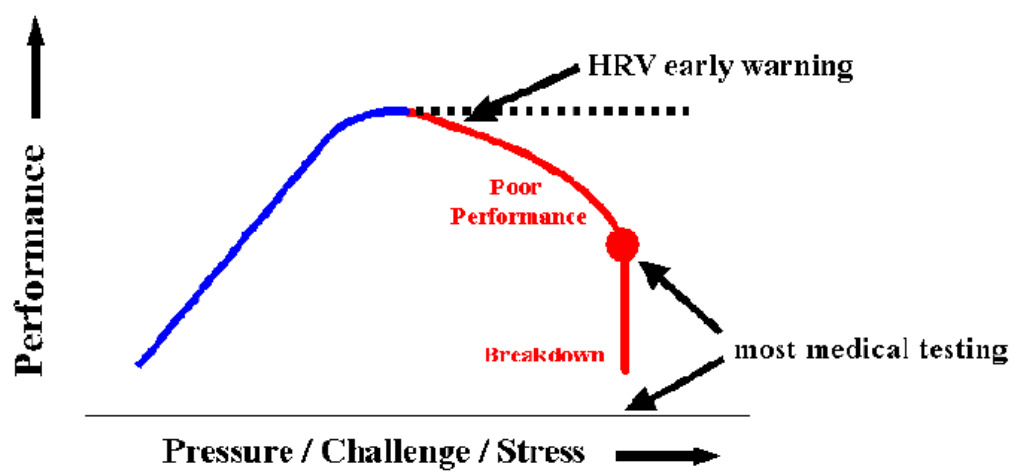
HRV throughout the day

If we look at HRV patterns throughout the day we can start to identify the events and situations where an individual expends energy. It is therefore very useful to compare this trace to an individual's diary to see where the major energy expenditures really were.
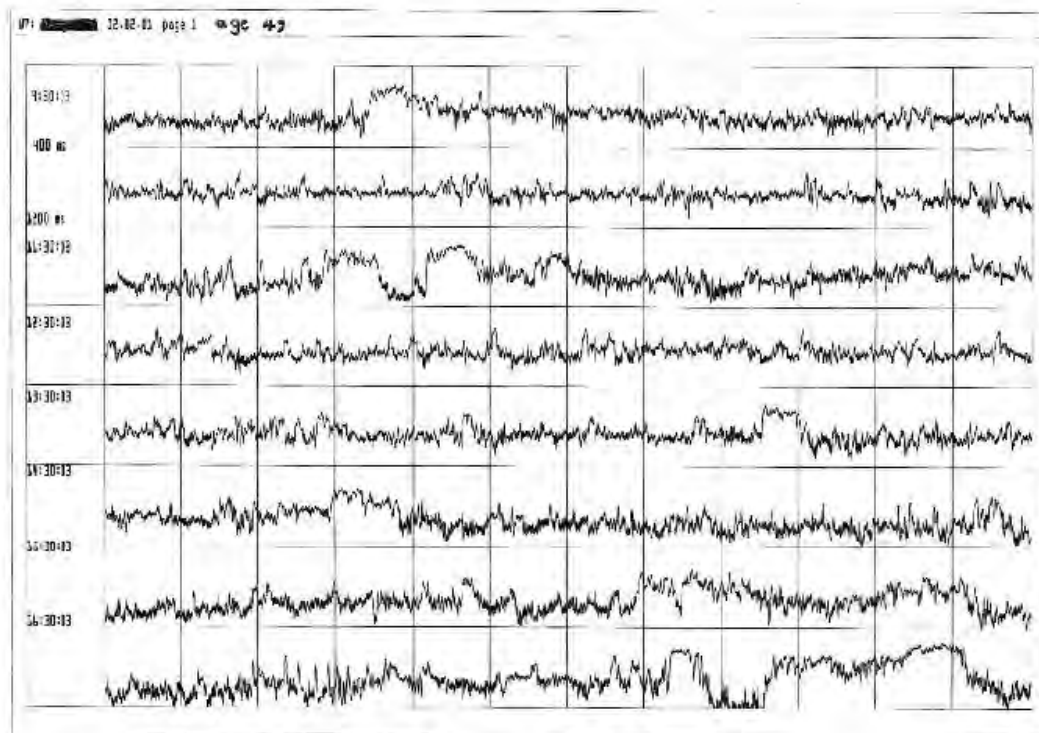
HRV and Emotional State – Good Days and Bad Days

When individuals are having a bad day and they feel negative emotion, for example frustration, their HRV signal is chaotic (top panel below).

In contrast, when individuals are having a good day and they feel positive emotion, for example appreciation, their HRV signal is coherent (lower panel).
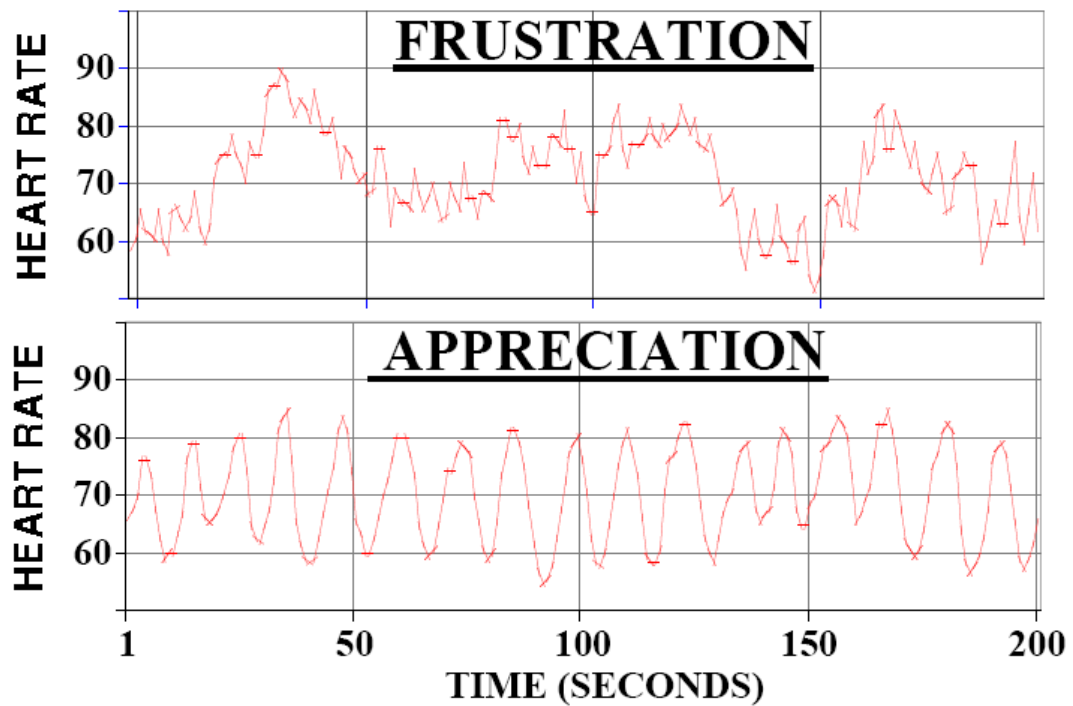
The Impact of Physiological Mastery

The rhythms generated by the heart, whether chaotic or coherent, are sent to the brain, via the vagus and spinal nerves, and profoundly influence the operation of a number of key brain centres.
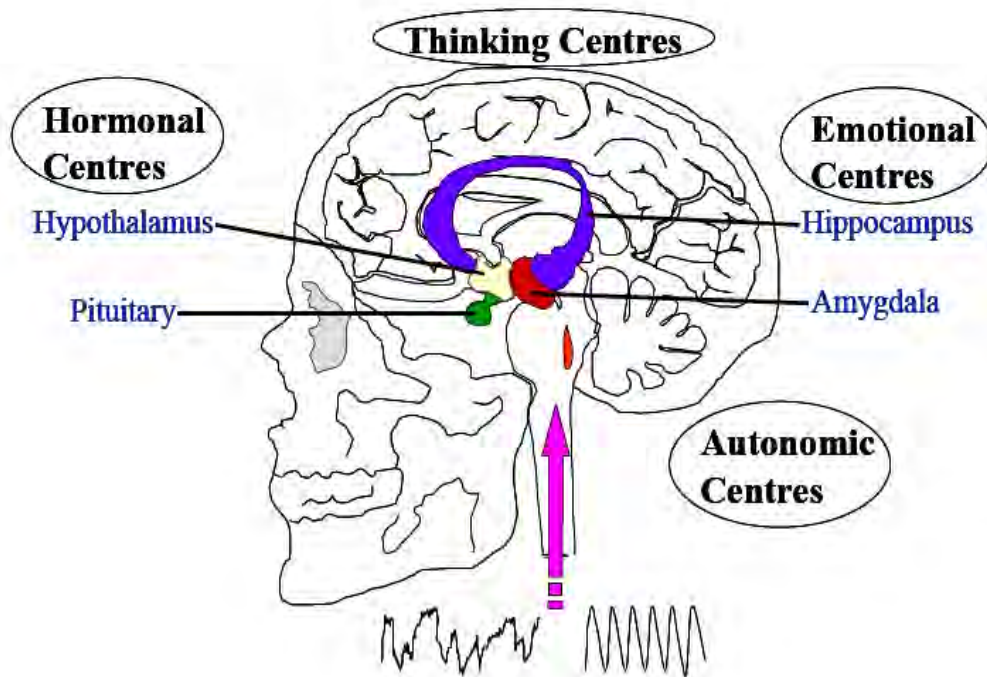
Signal:	Chaotic	Coherent
Effect:	Stop	Start
	Confusion	Clarity
	Inhibition	Facilitation

Monitoring Process

The HRV monitor is a small piece of digital recording technology about the size of a mobile phone which clips onto a waistband. In order to comply with the Medical Records Act, a consent form must be signed by anyone being monitored. Three self-adhesive electrodes are attached to the body, one on the upper chest and one either side of the lower ribcage. Whilst wearing the monitor, the individual cannot bath or shower (strip wash only) and is advised to keep away from microwaves and electric blankets (since this affects the signal and is not dangerous to the person being monitored.

Indicators of HRV measurement

HRV measurement (units)	Description
SDNN* (msec)	SD of all N-N intervals an estimate of overall variability
HF ($msec^2$)	High frequency power (0.15-0.4Hz), a marker of parasympathetic (vagal) modulation
HFnom (nu)	HF power in normalized units, HF/total power-very low frequency power ×100.
LF(ms^2)	Low frequency power (0.04-0.15Hz),a marker of both sympathetic and vagal modulations
LFnom (nu)	LF power in normalized units, LF/(total power-very low frequency power)×100, a marker of sympathetic modulation
LF/HF*	Ratio LF (ms2)/HF (ms2), sympathovagal balance or the sympathetic modulation

SDNN = Standard deviation of normal RR interval
LF = Low frequency
HF = High frequency

Conclusion

In conclusion an HRV monitoring trace shows a twenty-four hour snapshot of the current state of an individual's physiology. This will give an indication of current state of physical health including sleep pattern and quality and also what affect any stress is having on emotional and physical wellbeing. The trace should indicate which areas should be concentrated on to improve physiology.

APPENDIX C

SPSS Results

Regression

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	O3[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: PM10

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.251[a]	581.340	1	1734	.000

a. Predictors: (Constant), O3

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	NO2[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: PM10

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.617[a]	2797.820	1	1734	.000

a. Predictors: (Constant), NO2

Variables Entered/Removed^b

Model	Variables Entered	Variables Removed	Method
1	COPPB[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: PM10

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.217[a]	481.419	1	1734	.000

a. Predictors: (Constant), COPPB

Regression

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	PM10[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: O 3

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.251[a]	581.340	1	1734	.000

a. Predictors: (Constant), PM10

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	NO2[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: O 3

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.293[a]	717.002	1	1734	.000

a. Predictors: (Constant), NO2

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	CO[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: O 3

Model Summary

Model	Change Statistics				
	R Square Change	F Change	df1	df2	Sig. F Change
1	.001[a]	1.350	1	1734	.245

a. Predictors: (Constant), CO

APPENDIX D

Certificate of Ethic Approval

No. 302/2007
REC. No. 021/50

Certificate of Approval

The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, has approved the following study which is to be carried out in compliance with the ICH/GCP according to the protocol of the principal investigator

The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University reviewed the protocol based on the international guidelines for human research protection and ICH-GCP

Study Title : ASSOCIATION OF RESPIRABLE PARTICLATE MATTER WITH CARDIOVASCULAR DISEASE IN BANGKOK

Study Code :

Center : Chulalongkorn University

Principal Investigator : Ms. Dongruethai Buadong

Document Reviewed :

: ....
(Emeritus Professor Anek Aribarg, M.D.)
Chairman of Institutional Review Board

: ....
(Associate Professor. Vilai Chentanez, M.D.)
Associate Dean for the Research Affairs
With Representative of Dean

Date of Approval : April 19, 2007

Approval Expire Date : April 19, 2008

Approval is granted subject to the following conditions: (see back of this Certificate)

หนังสือยินยอมโดยได้รับการบอกกล่าวและเต็มใจ

(Informed Consent Form)

ชื่อโครงการ ความสัมพันธ์ของฝุ่นละอองกับโรคระบบหลอดเลือดหัวใจในกรุงเทพมหานคร
ชื่อผู้วิจัย นางสาวดวงฤทัย บัวด้วง
*ชื่อผู้เข้าร่วมการวิจัย ....
อายุ ....เลขที่เวชระเบียน ....

คำยินยอมของผู้เข้าร่วมการวิจัย

        ข้าพเจ้า นาย/นาง/นางสาว .... ได้ทราบรายละเอียด
ของโครงการวิจัยตลอดจนประโยชน์ และข้อเสี่ยงที่จะเกิดขึ้นต่อข้าพเจ้าจากผู้วิจัยแล้วอย่างชัดเจน ไม่มี สิ่งใด
ปิดบังซ่อนเร้นและยินยอมให้ทำการวิจัยในโครงการที่มีชื่อข้างต้น และข้าพเจ้ารู้ว่าถ้ามีปัญหาหรือข้อสงสัย
เกิดขึ้นข้าพเจ้าสามารถสอบถามผู้วิจัยได้ และข้าพเจ้าสามารถไม่เข้าร่วมโครงการวิจัยนี้เมื่อใดก็ได้ โดยไม่มี
ผลกระทบต่อการรักษาที่ข้าพเจ้าพึงได้รับ นอกจากนี้ผู้วิจัยจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับ
และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆที่
เกี่ยวข้อง กระทำได้เฉพาะกรณีจำเป็นด้วยเหตุผลทางวิชาการเท่านั้น

        ลงชื่อ..(ผู้เข้าร่วมการวิจัย)

        ....(พยาน)

        ....(พยาน)

        วันที่ ....

คำอธิบายของแพทย์หรือผู้วิจัย

        ข้าพเจ้าได้อธิบายรายละเอียดของโครงการ ตลอดจนประโยชน์ของการวิจัย รวมทั้งข้อเสี่ยงที่อาจจะ
เกิดขึ้นแก่ผู้เข้าร่วมการวิจัยทราบแล้วอย่างชัดเจนโดยไม่มีสิ่งใดปิดบังซ่อนเร้น

        ลงชื่อ..(แพทย์หรือผู้วิจัย)

        วันที่.............................

หมายเหตุ : กรณีผู้เข้าร่วมการวิจัย ไม่สามารถอ่านหนังสือได้ ให้ผู้ วิจัยอ่านข้อความในหนังสือยินยอมฯ นี้
ให้แก่ผู้เข้าร่วมการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้เข้าร่วมการวิจัยลงนามหรือพิมพ์ลายนิ้วหัวแม่มือรับทราบใน
การให้ความยินยอมดังกล่าวข้างต้นไว้ด้วย

        * ผู้เข้าร่วมการวิจัย หมายถึง ผู้ยินยอมตนให้ทำวิจัย

APPENDIX E

SAS program

SAS 9.0, 9.1, 9.1.2, and 9.1.3 Highlights

The Cornerstones of SAS

SAS®9 is built on four cornerstones: Scalability, Interoperability, Manageability, and Usability. These cornerstones are the foundation for the future of SAS.

Scalability

- SAS now runs in many 64-bit operating environments, which allows SAS to scale in-memory processes.
- Parallel processing takes advantage of multiple CPUs by dividing processing among the available CPUs, which provides performance gains for two types of SAS processes: threaded I/O and threaded application processing. Some areas that use parallel processing include:

  Indexing

  When creating an index that requires sorting, SAS attempts to sort the data using the thread-enabled sort. By dividing the sorting task into separately executable processes, the time needed to sort the data can be reduced.

  Selected analytic procedures
  The following are thread-enabled:

  Base SAS procedures
  MEANS, REPORT, SORT, SQL, SUMMARY, TABULATE

  SAS/STAT procedures
  GLM, LOESS, REG, ROBUSTREG

  SAS/SHARE procedure
  SERVER (with the experimental THREADEDTCP option)

  Enterprise Miner procedures
  DMINE, DMREG

  SAS/ACCESS engines

The following engines use multiple threads to access data from the DBMS server:

- Oracle
- Sybase
- DB2 (UNIX and PC)
- ODBC
- SQL Server
- Teradata

Scalable Performance Data (SPD) Engine

The Scalable Performance Data Engine provides parallel I/O by using multiple CPUs to read SAS data and deliver it rapidly to applications.

SAS/CONNECT

MP CONNECT gives you the ability to exploit SMP (Symmetric Multi-Processing) hardware as well as network resources to perform parallel processing and easily coordinate all the results into a single client SAS session.

SAS Metadata Server

The SAS Metadata Server uses threads to enable the best response time for delivering metadata as requested by any number of clients.

SAS OLAP Server

The SAS OLAP Server provides a new multi-threaded data storage and server functionality that provides faster cube performance. The data can be stored in a multidimensional form (MOLAP) or in a form that includes existing aggregations from presummarized data sources.

- SAS/CONNECT supports pipeline parallelism, which allows multiple DATA steps or procedures to execute in parallel and to pipe the output from one process as the input to the next process in a pipeline. Piping improves performance and reduces the demand for disk space.
- The time required for transferring large amounts of data when using SAS/CONNECT has been significantly reduced as a result of improvements to the file compression algorithm.

Interoperability

- SAS Open Metadata Architecture provides common metadata services to all SAS applications, which improves communication among applications.
- The SAS Add-In for Microsoft Office is an integral part of a complete end-to-end business intelligence solution that enables you to harness the power of SAS analytics, access relational data sources directly from Microsoft Word and Microsoft Excel, and create reports within Microsoft Office.
- SAS/CONNECT libref inheritance eliminates the need to duplicate data for use in multiple SAS sessions. Server sessions can inherit client-defined librefs, which allows multiple sessions to read and write data in a single library.
- SAS Integration Technologies now includes support for creating Web services that enable cross-platform integration, an enhanced publishing framework that supports the generation and publication of explicit and implicit events, and a new set of core infrastructure services that Java programmers can use to write applications that are integrated with the SAS platform.
- The XML LIBNAME engine imports and exports a broader variety of XML documents.

Manageability

- SAS Management Console provides a single point-of-control for SAS administrative tasks.
- SAS ETL Studio is a thin-client system, developed by using Java technology that enables you to manage the Extraction, Transformation, and Loading (ETL) of data.
- SAS Personal Login Manager is an application that enables you to manage the metadata that describes your user accounts. You can use the SAS Personal Login Manager to add, update, and remove your logins.
- Application Response Measurement (ARM) enables you to check the availability and the transaction rates of SAS applications.
- Secure Sockets Layer (SSL) provides network security and privacy. SSL is used in Base SAS, SAS/CONNECT SAS/SHARE, and Integration Technologies.
- The new Integration Technologies Windows Object Manager and Java Connection Service create and manage workspace objects that support new types of IOM servers.
- New IOM options are provided to support load balancing.

Usability

- SAS Information Map Studio is an application that enables you to create, manage, and view *SAS Information Maps*—business metadata about your physical data. Information maps are user-friendly metadata definitions of physical data sources that enable your business users to query a data warehouse in order to meet specific business needs.
- SAS Web Report Studio is a Web-based application that enables you to create, view, and organize reports.
- The MIGRATE procedure simplifies the process of migrating your libraries.
- New SAS/GRAPH styles provide a consistent look for output created by the Output Delivery System (ODS), which enhances readability and usability.
- The metadata LIBNAME engine enables you to read and create metadata in a SAS Metadata Repository. By incorporating metadata, this engine makes it easier to control access to the data.
- The Output Delivery System writes to more destinations and provides a greater variety of formatting selections, which enables you to select an output destination and format that best meets your reporting needs.
- User-created formats and informats can have names that are longer than eight characters, which allow you to provide names that are more descriptive.
- New SAS functions improve how you can search for character strings and regular expressions, which makes it easier for you to search your data for specific results.
- SAS Data Quality Server has been re-engineered to add increased accuracy and usability to your data.
- All help and reference documentation is accessible within a SAS session. Selecting SAS Help and Documentation from the Help menu enables you to view both online Help information and the full SAS reference library. Prior to SAS 9.0, the reference library was available only on the SAS Online Doc CD-ROM or in hard-copy format.
- SAS has been enhanced with accessibility features for SAS users who have disabilities.
- National Language Support (NLS) enhancements enable customers in regions around the world to process data successfully in their native languages and environments.

The GAM Procedure -- <u>Experimental</u>

Overview

The GAM procedure fits generalized additive models as those models are defined by Hastie and Tibshirani (1990). This procedure provides an array of powerful tools for data analysis, based on nonparametric regression and smoothing techniques.

Nonparametric regression relaxes the usual assumption of linearity and enables you to uncover structure in the relationship between the independent variables and the dependent variable that might otherwise be missed. The SAS System provides many procedures for nonparametric regression, such as the LOESS procedure for local regression and the TPSPLINE procedure for thin-plate smoothing splines. The generalized additive models fit by the GAM procedure combine

- an additivity assumption (Stone,1985) that enables relatively many nonparametric relationships to be explored simultaneously with
- the distributional flexibility of generalized linear models (Nelder, 1972)

Thus, you can use the GAM procedure when you have multiple independent variables whose effect you want to model non-parametrically, or when the dependent variable is not normally distributed. See the "Nonparametric Regression" section for more details on the form of generalized additive models.

The GAM procedure

- provides nonparametric estimates for additive models
- supports the use of multidimensional data
- supports multiple SCORE statements
- fits both generalized semi-parametric additive models and generalized additive models
- enables you to choose a particular model by specifying the model degrees of freedom or smoothing parameter

Nonparametric Regression

Nonparametric regression relaxes the usual assumption of linearity and enables you to explore the data more flexibly, uncovering structure in the data that might otherwise be missed.

However, many forms of nonparametric regression do not perform well when the number of independent variables in the model is large. The sparseness of data in this setting causes the variances of the estimates to be unacceptably large unless the sample size is extremely large. The problem of rapidly increasing variance for increasing dimensionality is sometimes referred to as the "curse of dimensionality." Interpretability is another problem with nonparametric regression based on kernel and smoothing spline estimates. The information these estimates contain about the relationship between the dependent and independent variables is often difficult to comprehend.

To overcome these difficulties, Stone (1985) proposed additive models. These models estimate an additive approximation to the multivariate regression function. The benefits of an additive approximation are at least twofold. First, since each of the individual additive terms is estimated using a univariate smoother, the curse of dimensionality is avoided, at the cost of not being able to approximate universally. Second, estimates of the individual terms explain how the dependent variable changes with the corresponding independent variables.

To extend the additive model to a wide range of distribution families, Hastie and Tibshirani (1990) proposed generalized additive models. These models enable the mean of the dependent variable to depend on an additive predictor through a nonlinear link function. The models permit the response probability distribution to be any member of the exponential family of distributions. Many widely used statistical models belong to this general class; they include additive models for Gaussian data, nonparametric logistic models for binary data, and nonparametric log-linear models for Poisson data.

APPENDIX F

Journal Publication and Conference

February 24, 2009

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Title: Association between PM_{10} and O_3 and hospital visits for cardiovascular diseases in Bangkok, Thailand

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 IKUKO FUNATAGAWA, KANAE KARITA, EIJI YANO

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Association between PM$_{10}$ and O$_3$ and hospital visits for cardiovascular diseases in Bangkok, Thailand

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The association between air pollution and cardiovascular diseases is well known, but previous studies only assessed mortality and hospital admissions in North America, Europe, and Northeast Asia. Few studies have been conducted in less-developed countries in regions with a tropical climate. This study aimed to evaluate the association between short-term exposure to fine particulate matter (PM$_{10}$) and ozone (O$_3$) in relation to hospital visits for cardiovascular diseases (CVD: ICD-10th, I00–I99) in the inner part of Bangkok. Data from hospital records were obtained from three major government hospitals. All hospital visits were stratified by age group and category of CVD. Daily PM$_{10}$ and O$_3$ levels reported by the Pollution Control Department (PCD) from April 2002 to December 2006 (1,736 days) were used in time series analysis with a Generalized Additive Model (GAM) procedure in the Statistical Analysis System (SAS) program. Exposure on the previous day to PM$_{10}$ and O$_3$ had positive association with hospital visits for CVD in the elderly ($\geq$ 65 years). The increase in CVD hospital visits in this age group was 0.10% (95% CI: 0.03, 0.19) with increase in PM$_{10}$ by 10 µg m^{-3} and 0.50% (95% CI: 0.19, 0.81) with an increase in O$_3$.PM$_{10}$ and O$_3$ were associated with cardiovascular diseases, particularly in the elderly patients from inner Bangkok areas. A short term association between increases in daily levels of air pollutants and the number of daily emergency hospital visit for CVD, in particular in the subjects aged $\geq$ 65 years old.

Keywords: PM$_{10}$, ozone, cardiovascular diseases, hospital visits, Bangkok, air pollution.

PM$_{10}$ AND HEART RATE VARIABILITY AMONG ELDERLY PATIENTS WITH CARDIOVASCULAR DISEASES IN INNER BANGKOK, THAILAND

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Previous epidemiological studies on an association between air pollution and cardiovascular diseases (CVD) mortality have been reported, but the underlying mechanisms are unknown. In this study, the short-term associations between PM$_{10}$ levels and alterations in cardiac autonomic control were examined by Heart Rate Variability (HRV). 330 existing CVD patients visit Ramathibodi hospital from June to October 2007 was investigated. Initially, the studied subjects were screened by the American Thoracic Society's Division of Lung Diseases Questionnaire (ATS-DLD) and Cardiovascular Diseases Questionnaire (CDQ). After adjusting all confounding by questionnaires, there were 8 qualified subjects conducted HRV measurement for 24 hours. The hourly PM$_{10}$ concentrations were assessed from nearby Pollution Control Department (PCD) monitoring stations. The multiple logistic regression analysis was carried out to evaluate the relationships between PM$_{10}$ and several HRV metrics. The magnitude associations (-1.7 to -2.8 % decrease in HRV per 10 μg m^{-3} increase in PM$_{10}$) was comparable with those observed in other studies. Elevated levels of ambient PM$_{10}$ may adversely affect HRV in elderly subjects with existing CVD patients in inner Bangkok.

Key words: Air pollution, PM$_{10}$, Cardiovascular diseases, Heart rate variability (HRV), Bangkok

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PM$_{10}$ AND HEART RATE VARIABILITY AMONG ELDERLY PATIENTS WITH CARDIOVASCULAR DISEASES IN INNER BANGKOK, THAILAND

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Abstract

Previous epidemiological studies on an association between air pollution and cardiovascular diseases (CVD) morbidity have been reported, but the underlying mechanisms are unknown. In this study, the short-term associations between PM$_{10}$ levels and alterations in cardiac autonomic control were examined by Heart Rate Variability (HRV). 330 existing CVD patients visit Ramathibodi hospital from June through October 2007 was investigated. Initially the studied subjects were screened by the American Thoracic Society's Division of Lung Diseases (ATS-DLD) and Cardiovascular Diseases Questionnaire (CDQ). After adjusting all confounding by questionnaires, there were 8 qualified subjects conducted HRV measurement for 24 hours. The hourly PM$_{10}$ concentrations were assessed from nearby Pollution Control Department (PCD) monitoring stations. The multiple logistic regression analysis was carried out to evaluate the relationships between PM$_{10}$ and several HRV metrics. The magnitude associations (-1.7 to -2.6 % decrease in HRV indices per 10 µg m^{-3} increase in PM$_{10}$) was comparable with those observed in other studies. Elevated levels of ambient PM$_{10}$ may adversely affect HRV in elderly subjects with existing CVD patients in inner Bangkok.
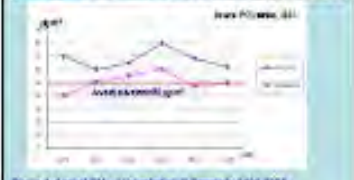
Introduction

Bangkok, Thailand

Figure-1 Annual PM$_{10}$ Concentration in Bangkok, 2001-2005
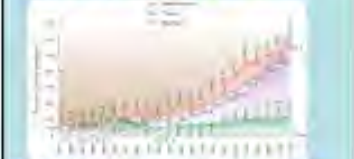
Figure-2 Rate of Hospitalization of patient with heart disease, census and deaths, 1995-2005. (Thailand Health Profiles, 2005-2007) Source: Ministry of Public Health 2007

Bangkok is the capital city of Thailand with the population more than 6 millions. Due to the high number of residents who live in Bangkok, traffic congestion and constructions are commonly seen. In particular, air pollution from dusts and fine particles are frequently high in heavy traffic and construction areas. Air pollutions in Bangkok have been monitored considerably for many years. Particularly, particulate matters those diameters less than 10 microns (PM$_{10}$) annual average concentrations were frequently above 50 µg m^{-3} (Figure-1). PM$_{10}$ could associated to the pulmonary functions and cardiovascular impairments in long term exposures. There have been many reports indicating the relation between particulate matter (PM$_{10}$) and cardiovascular diseases (CVD)

Objective:

To determine the degree of correlation between PM$_{10}$ and the impairment of cardiovascular function; Heart Rate Variability (HRV) in pre-existing CVD patients inner Bangkok.

Hypothesis:

High level of PM$_{10}$ concentration is associated with impaired Heart Rate Variability (HRV) parameters among people with pre-existing cardiovascular diseases (CVD) patients in inner Bangkok.

Methodology:

1. Subjects are pre existing cardiovascular diseases (CVD) elderly patients (≥65 years), only living in inner Bangkok, from OPD medicine, Ramathibodi hospital in June to October 2007

Figure-3 Map of Bangkok area divided by the district. Source: BMA 2007

2. The standard Thai questionnaires and interviewed screen confounding factors. (Figure-4)
   - A modified standard ATS-DLD & CDQ Thai version of cardio-respiratory questionnaires.
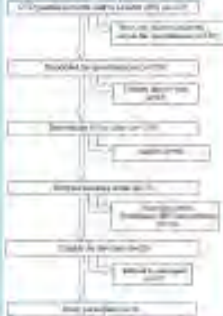
Figure-4 Flows work of the subjects selection

3. Health examination in studied subjects
   - HRV sampling by specialists, electrocardiograph (EKG) 24-hr for HRV parameters and related to average ambient PM$_{10}$ concentration. (N=8)

Farasid Holter monitor

Figure-5 Example of a power spectral density curve following fast Fourier transformation of the Green's heart rate data.

4. Ambient PM$_{10}$ concentration were assessed at nearby fixed-site Pollution Control Department (PCD) monitoring stations.
5. Data analysis : Multiple logistic regression analysis.

Result and Discussion:

Table-1 Basal characteristics of heart rate variability (HRV) parameter in pre-existing cardiovascular disease patients and environmental variables (N=8)

Clinical and ECG characteristics	Mean , SD
HRV parameters (N=8)	
HR (beats/min)	14.7/12.9
SDNN (ms)	94.3/35.8
r-MSSD (ms)	26.5/8.6
age (year)	53.5/13.5
Environment variables (24hr average)	
Temperature (°C)	29.8/2.6
Dew point (°C)	23.7/2.6
Wind (km hr^{-1})	4.5/1.9
24-hr PM$_{10}$ (µg m^{-3})	57.5/17.1

Table-2 Percentage change for HRV variables in association with a 10 µg m^{-3} increase in PM$_{10}$ concentrations

Parameter	% Change	95% CI
HR (beats/min)	0.3	0.0 to 0.7
SDNN (ms)	-1.7	-2.6 to -1.2
r-MSSD (ms)	-2.6	-4.6 to -1.0

Abbreviations:
HR = Heart Rate
SDNN = The standard deviation of normal to normal beat interval
r-MSSD = The square root of the mean of the squared differences between adjacent NN interval

The study found the consistent positive association between exposures to PM$_{10}$ concentration and impaired the heart functions on heart rate (HR) and heart rate variability (HRV) indices, SDNN, r-MSSD. These results indicated the association between decrements in HRV and increment in HR related to the increasing in PM$_{10}$ concentrations by 10 µg m^{-3} among pre-existing CVD elderly patients (≥ 65 years) in inner part of Bangkok. The percentage change of heart rate (HR) increasing was 0.3% (95% CI: 0.0 to 0.7) while SDNN and r-MSSD parameter of HRV were decreasing by -1.7% (95% CI: -2.6 to -1.2) and -2.6 % (95% CI: -4.6 to -1.0) respectively (Table-2)

Conclusion:

The exposure to PM$_{10}$ was associated with a decrease HRV, by higher ambient PM$_{10}$ concentrations are associated with lower cardiac autonomic control (impaired HRV function) so, elevated levels of ambient PM$_{10}$ may adversely affect HRV in elderly subjects with pre-existing CVD patients in inner Bangkok, Thailand.

BIOGRAPHY

Ms. Dongruethai Buadong was born on February 19, 1972 in Bangkok, Thailand. She obtained her B.N. degree from Faculty of Nursing, Mahidol University in 1993 and working as a nurse at Ramathibodi Hospital. She received her M.Sc. degree in Environmental Science, Graduate School, Chulalongkorn University in 2000. She began her Doctor Degree studies in Inter-Department of Environmental Management, Graduate School, Chulalongkorn University in May 2004. She also received a Thailand Research Fund scholarship under the Royal Golden Jubilee Ph.D. Program. She finished her Doctor Degree of Philosophy in Environmental Science in May 2008.