Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure

Douglas W. Dockery, C. Arden Pope III, Richard E. Kanner, G. Martin Villegas, and Joel Schwartz

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Includes the Commentary of the Institute’s Health Review Committee

Research Report Number 83
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The Health Effects Institute, established in 1980, is an independent and unbiased source of information on the health effects of motor vehicle emissions. HEI studies all major pollutants, including regulated pollutants (such as carbon monoxide, ozone, nitrogen dioxide, and particulate matter), and unregulated pollutants (such as diesel engine exhaust, methanol, and aldehydes). To date, HEI has supported more than 170 projects at institutions in North America and Europe.

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Synopsis of Research Report Number 83

Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure

BACKGROUND

A number of epidemiologic studies have shown an association between exposure to particulate air pollution and mortality, especially from respiratory and cardiovascular causes. The elderly and people with existing cardiovascular disease are considered to be among the groups most at risk. Although the results of these studies have not been accepted by all scientists, the U.S. Environmental Protection Agency (EPA) has considered the evidence of adverse health effects caused by exposure to particulate matter (PM) to be of sufficient concern that it has promulgated National Ambient Air Quality Standards (NAAQS) for PM with a mean average diameter of up to 10 micrometers (PM$_{10}$) and, more recently, for PM with a mean average diameter of up to 2.5 micrometers (PM$_{2.5}$).

The mechanism or mechanisms by which PM may affect human health remains a critical, unresolved issue. Dockery and Pope speculated that exposure to PM might lead to a transient drop in blood oxygenation, which might have serious consequences in humans with heart or lung problems. The Health Effects Institute funded their study to determine whether exposure to PM affected blood oxygenation and clinical symptoms. In addition, the investigators tested the effects of PM on pulse rate, which is another important cardiovascular parameter.

STUDY DESIGN

The one-year study described in this report was conducted by a group led by Drs. Douglas Dockery at the Harvard School of Public Health and C. Arden Pope III at Brigham Young University. The investigators designed the study to increase the possibility of observing PM effects by testing a potentially at-risk group (the elderly) at a time of year that historically had experienced relatively high levels of PM (the winter). They also conducted the study in residents of the Utah Valley, because at this altitude (4,000 feet above sea level) greater declines in oxygen saturation would be expected than at sea level.

Twice a day subjects used a small medical device called an oximeter to measure their blood oxygen saturation. The instrument also provided information on pulse rate. One group of subjects also kept a diary of their clinical symptoms. Information about daily PM level was collected from fixed, outdoor monitors in the Utah Valley. Other weather variables, such as temperature and barometric pressure, were measured at a nearby weather station.

RESULTS AND IMPLICATIONS

Dockery and Pope established the feasibility of measuring oxygen saturation in a community setting, and their approach may be useful in future air pollution epidemiology studies. They found no evidence of an association of ambient PM with oxygen saturation in an elderly population living at high altitude, except for a subset of the population—men over 80 years of age. Although the subjects were generally healthy and the air pollution episodes were not as high as expected, the findings of this preliminary study do not support oxygen desaturation as a possible mechanism for particle-induced health effects.

In a post hoc analysis, the investigators obtained pulse rate data from the three-minute oximetry measurements. They reported a small increase in daily pulse rate associated with exposure to PM on the previous 1 to 5 days. These findings are intriguing and warrant further investigation using continuous monitoring techniques with careful control of medications and other potential confounding factors.

This Statement, prepared by the Health Effects Institute and approved by its Board of Directors, is a summary of a research project sponsored by HEI from 1995 to 1996. This study was conducted by Drs. Douglas W. Dockery of the Harvard School of Public Health and C. Arden Pope III of Brigham Young University. The following Research Report contains both the detailed Investigators' Report and a Commentary on the study prepared by the Institute's Health Review Committee.
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I. **STATEMENT** Health Effects Institute

This Statement, prepared by the HEI and approved by the Board of Directors, is a nontechnical summary of the Investigators' Report and the Health Review Committee's Commentary.

II. **INVESTIGATORS' REPORT**

When an HEI-funded study is completed, the investigators submit a final report. The Investigators' Report is first examined by three outside technical reviewers and a biostatistician. The Report and the reviewers' comments are then evaluated by members of the HEI Health Review Committee, who had no role in selecting or managing the project. During the review process, the investigators have an opportunity to exchange comments with the Review Committee and, if necessary, revise the report.

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III. **COMMENTARY** Health Review Committee

The Commentary on the Investigators' Report is prepared by the HEI Health Review Committee and staff. Its purpose is to place the study into a broader scientific context, to point out its strengths and limitations, and to discuss the remaining uncertainties and the implications of the findings for public health.

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ABSTRACT

Epidemiologic studies have linked fine particulate air pollution with increases in morbidity and mortality rates from cardiopulmonary complications. Although the underlying biologic mechanisms responsible for this increase remain largely unknown, potential pathways include transient declines in blood oxygenation and changes in pulse rate following exposures to particulate air pollution episodes. This study evaluated potential associations between daily measures of respirable particulate matter (PM)* with pulse rate and oxygen saturation of the blood. Pulse rate and oxygen saturation (SpO2) using pulse oximetry were measured daily in 90 elderly subjects living near air pollution monitors during the winter of 1995–96 in Utah Valley. We also evaluated potential associations of oxygen saturation and pulse rate with barometric pressure. Small but statistically significant positive associations between day-to-day changes in SpO2 and barometric pressure were observed. Pulse rate was inversely associated with barometric pressure. Exposure to particulate pollution was not significantly associated with SpO2 except in male participants 80 years of age or older. Increased daily pulse rate, as well as the odds of having a pulse rate 5 or 10 beats per minute (bpm) above normal (normal is defined as the individual’s mean pulse rate throughout the study period), were significantly associated with exposure to particulate pollution on the previous 1 to 5 days. The medical or biologic relevance of these increases in pulse rate following exposure to particulate air pollution requires further study.

INTRODUCTION

Increases in respiratory and cardiovascular morbidity and mortality that accompanied episodes of extreme air pollution earlier in this century demonstrated that air pollution can adversely affect human health (Firket 1931; Logan 1953; Ciocco and Thompson 1961; Gore and Shadick 1968). Since the 1970s, epidemiologic studies have provided additional quantification of the health effects associated with much lower levels of PM air pollution. Observed health effects include increased respiratory symptoms, decreased lung function, increased use of asthma medication, increased hospitalizations and other health care visits for respiratory and cardiovascular disease, increased respiratory morbidity as measured by absenteeism from work or school or other restrictions in activity, and increased mortality (Dockery and Pope 1994; Lipfert 1994).

Investigations of the health effects of particulate air pollution include daily time-series studies that observed changes in daily mortality associated with short-term changes in particulate air pollution. These pollution-mortality associations have been observed in various communities across the United States, including Santa Clara, CA (Fairley 1990); Steubenville, OH (Schwartz and Dockery 1992b); Detroit, MI (Schwartz 1991); St. Louis, MO (Dockery et al. 1992); Kingston/Harriman, TN (Dockery et al. 1992); Philadelphia, PA (Schwartz and Dockery 1992a); Los Angeles, CA (Kinney et al. 1995), Utah Valley (Pope et al. 1992), and Birmingham, AL (Schwartz 1993). Several reviews of these studies noted the consistency of the results and suggested that it is unlikely that the overall results could be due to methodologic bias, or to confounding by season, weather, or other nonpollution variables (Ostro 1993; Dockery and Pope 1994; Schwartz 1994a; Samet et al. 1995).

Cause of death was evaluated in studies of four of these communities: Santa Clara (Fairley 1990), Philadelphia.
Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure

(Schwartz and Dockery 1992a), Utah Valley (Pope et al. 1992), and Birmingham (Schwartz 1993). Particulate air pollution was associated with both respiratory and cardiovascular mortality but not with mortality due to other causes. Two recent prospective cohort studies also observed that long-term exposure to fine particulate air pollution was associated with an increased risk of mortality, primarily cardiopulmonary mortality (Dockery et al. 1993; Pope et al. 1995).

A series of epidemiologic investigations observed associations between particulate air pollution and respiratory hospitalizations in various places, including Utah Valley (Pope 1989, 1991); Birmingham, AL (Schwartz 1994b); and Detroit, MI (Schwartz 1994c). In addition, sulfate ion concentrations, a marker for fine-particle mass in the eastern United States, have been associated with respiratory hospital admissions in several cities in New York (Thurston et al. 1992) and in Ontario (Bates and Sitzo 1987; Burnett et al. 1994; Thurston et al. 1994). Recently, associations of particulate air pollution with cardiovascular admissions have been observed in Minneapolis, MN (Schwartz 1994d) and Ontario (Burnett et al. 1995). The largest apparent effects of particulate exposure were found for congestive heart failure.

Although the epidemiologic evidence linking particulate air pollution with increased cardiopulmonary mortality and morbidity has been reasonably consistent and coherent (Bates 1992), the underlying mechanisms of particle-induced mortality and morbidity remain unknown. Why an increased cardiovascular mortality is associated with particulate air pollution is unclear. A detailed examination of cardiovascular deaths on days with high particulate air pollution showed that most of the increases in cardiovascular deaths were in patients who had respiratory disease as a contributing factor (Schwartz 1994e).

Two recent studies reported associations between increased particulate pollution exposures and small transient decreases in peak expiratory flow measured daily in panels of children and asthmatic patients (Pope et al. 1991; Pope and Dockery 1992). These studies were designed to observe very small changes in peak expiratory flow. In fact, the estimated pollution effect on peak expiratory flow in these studies was statistically significant, but it was too small to be considered clinically significant. Nonetheless, the results of the studies suggest that a decline in lung function may be part of the pathophysiological pathway for respiratory disease.

Potential pathways for the observed cardiovascular mortality include transient declines in blood oxygenation or increase in pulse rate following exposures to particulate air pollution episodes. In persons with severe cardiopulmonary disease, episodes of acute but small decreases in blood oxygenation can be clinically significant and in extreme cases might be fatal. In most individuals, small declines in oxygenation may have little if any effect on overall well being but, in an adequately designed study, these declines may be measurable. The role of pulse rate in cardiopulmonary disease is not fully understood. Recent research suggests that elevated heart rate is a risk factor for hypertension, coronary heart disease, and mortality (Dyer et al. 1980; Kannel et al. 1987; Gillum 1988, 1992; Hjalmarson et al. 1990; Gillman et al. 1991; Gillman et al. 1993; Goldberg et al. 1996). Furthermore, a recent study observed increases in the heart rates of rats following exposure to elevated levels of particulate air pollution (Nadziejko et al. 1997).

The primary objective of our study was to evaluate potential associations of daily measurements of respirable particulate air pollution with both pulse rate and acute changes in oxygen saturation of the blood in panels of elderly adults. The performance of the pulse oximeters and the daily changes in oxygen saturation and pulse rate associated with changes in barometric pressure were also evaluated.

METHODS

STUDY PERIOD AND AREA

The primary data collection period for this study was from November 18, 1995, through March 15, 1996. This study was conducted in Utah Valley in central Utah. A population of approximately 200,000 reside in several contiguous cities situated on the valley floor (Figure 1). Only about 6% of the area’s adults smoke. This valley has histories of respiratory hospital admissions in several cities in New York (Thurston et al. 1992) and in Ontario (Bates and Sitzo 1987; Burnett et al. 1994; Thurston et al. 1994). Recently, associations of particulate air pollution with cardiovascular admissions have been observed in Minneapolis, MN (Schwartz 1994d) and Ontario (Burnett et al. 1995). The largest apparent effects of particulate exposure were found for congestive heart failure.

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the oxyhemoglobin dissociation curve, relatively small declines in \( P_{\text{aO}_2} \) will cause greater declines in \( S_{\text{PO}_2} \) than would be seen at lower altitudes.

**SUBJECT SELECTION AND RECRUITMENT**

Two panels were selected for the study. The first panel was a "private home panel," which was composed of participants who were solicited from retired Brigham Young University faculty, staff, and spouses living in private homes in Utah County. This list was obtained from Brigham Young University's Alumni Association for the sole purpose of recruitment. An introductory letter describing the study was sent to potential participants. This was followed by a phone call intended to explain the purpose of study, to describe possible benefits, and to determine demographic characteristics and eligibility. Preselected potential participants were visited for additional evaluation and recruitment by a research assistant and the study coordinator.

Final participation in the home panel was limited to elderly persons who met the following eligibility requirements. Each participant: (1) lived with his or her spouse; (2) had a spouse who also was willing to be a participant; (3) lived in Orem or Lindon near PM air pollution monitors (Figure 1); (4) lived in a home without a special air filtration system (i.e., other than a furnace filter); (5) was a nonsmoker and had smoked less than 10 packs of cigarettes in his or her lifetime; and (6) had no serious medical condition that would preclude participation, including mental illness, currently undergoing oxygen therapy, or having a history of heart failure in the prior six months. Twenty-five retired Brigham Young University faculty or staff and their spouses were enrolled according to the study protocol, plus two additional volunteer participants who also met the eligibility requirements. This brought the total of home sites to 26, with 52 participants in the private home panel (Table 1).

The second panel was a "retirement home panel" consisting of residents of a retirement home, located east of the steel mill and the Orem PM monitor (Figure 1). All residents of this home were nonsmokers. They were retired elderly individuals who were relatively independent and not in need of regular medical or nursing care. Residents lived in one large building as couples or individually in separate units, each of which included bedrooms, a bathroom, a kitchen/dining area, and a living room. Although they could eat in their own units, most of the residents ate together in a common dining area. This retirement home was visited several times by the study coordinator and local principal investigator to establish the study protocol, to solicit cooperation from the management, to brief management and residents on study design and procedures, and to solicit participation from the residents. The study was described to small groups of three to five residents during the evening meal. Potential participants were evaluated and later selected based on their status as nonsmokers, their willingness to participate, and the absence of any medical condition that would preclude participation, including mental illness or being currently under oxygen therapy. Thirty-eight residents of this retirement home were eventually selected (Table 1).

**MATERIALS AND METHODS**

Research protocols and consent forms were approved by institutional review boards for human subjects at Brigham Young University, University of Utah School of Medicine, and Harvard School of Public Health. For the private home panel, on or about November 17, 1995, the research coordinator and an assigned research assistant visited each home and obtained from each participant informed written consent to participate in the study and to obtain medical records. Each home received a Nellcor N-20P pulse oximeter with a finger sensor and printer (Nellcor Incorporated, Hayward, CA). This pulse oximeter measures oxygen saturation (\( S_{\text{PO}_2} \)) based on the transmission of light in two wavelengths through a vascular bed, in this case the finger.
Table 1. Summary Information About the Participants in the Two Panels\textsuperscript{a}

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<th>Private Home Panel</th>
<th>Retirement Home Panel</th>
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<tbody>
<tr>
<td>Original number of participants</td>
<td>52</td>
<td>38</td>
</tr>
<tr>
<td>Final number of participants</td>
<td>50</td>
<td>36</td>
</tr>
<tr>
<td>Average number participating on any given study day</td>
<td>46</td>
<td>28</td>
</tr>
<tr>
<td>Mean age (at time of enrollment)</td>
<td>74</td>
<td>81</td>
</tr>
<tr>
<td>Age range</td>
<td>61-89</td>
<td>49-96</td>
</tr>
<tr>
<td>Female (%)</td>
<td>50</td>
<td>68</td>
</tr>
<tr>
<td>History of respiratory\textsuperscript{b}, but no cardiac\textsuperscript{c}, conditions (%)</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>History of cardiac, but no respiratory, conditions (%)</td>
<td>44</td>
<td>50</td>
</tr>
<tr>
<td>History of both respiratory and cardiac conditions (%)</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>No history of respiratory or cardiac conditions (%)</td>
<td>42</td>
<td>32</td>
</tr>
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\textsuperscript{a} For 37 of the private home participants, the health status from the entry questionnaire could be verified by medical records. However, health status for the remaining private home participants and all of the retirement home participants is based entirely on information given on entry questionnaires.

\textsuperscript{b} Chronic respiratory conditions: chronic obstructive pulmonary disease, asthma, chronic bronchitis, and emphysema.

\textsuperscript{c} Cardiac conditions: heart attack, heart failure, angina, and hypertension.

The pulsatile flow of blood through the tissue bed modulates the light reaching the detector. Some measurement error can be produced by dyshemoglobins, such as carboxyhemoglobin, or by conditions that reduce the amplitude of the arterial pulsations, such as hypertension or ischemia. The pulse oximeter also measures pulse rate and prints out both $\text{SpO}_2$ and pulse rate.

Each of the participants in each home also received a customized bound folder that included the following: (1) instructions about daily data collection procedures and about the operation of the pulse oximeter; (2) daily health diaries to record the pulse oximeter readings and various health symptoms; (3) an envelope for copies of the oximeter printouts; (4) copies of the consent forms; and (5) telephone numbers for the research assistant assigned to the home, the study coordinator, and principal investigators. Participants were instructed to measure their oxygen saturation and pulse rate twice daily: shortly after rising in the morning and before breakfast, and before retiring to bed. Participants were also instructed to complete their health diaries each night before retiring to bed, indicating the presence during the day of trouble breathing, runny nose, wheezing, fever, sore throat, cough, sputum, or upset stomach. They were not to take oxygen saturation readings or record symptoms if they were out of town.

When measuring the oxygen saturation and pulse rate, participants were instructed to sample in the continuous operating mode for approximately three minutes. In this mode the sampler prints out the date, time, integrated pulse rate, and oxygen saturation (to the nearest integer) every thirty seconds. At the end of the sample, the average pulse rate and $\text{SpO}_2$ over the entire interval are printed. After writing their name or an identification number on the printout, they placed the results in the envelope attached to their diary. Before starting each test, participants were instructed to remain sitting at rest for one minute and to remain still throughout the test. They were also instructed to use the left index finger to keep uniformity and to avoid the presence of bright light sources, such as direct sunlight, surgical lamps, infrared warming lamps, and phototherapy lights. Some female participants were advised to remove fingernail polish, especially blue, green, black, and brown nail polish.

Approximately seven days following the initial visit, the research assistant assigned to the home made a follow-up visit to interview the participants, evaluate compliance, test the performance of the oximeter, check for adequate paper in the oximeter printer, identify any problems, and collect the printouts from the oximeters. Regular follow-up visits approximately every two weeks were conducted throughout the study period, which ended on March 15, 1996. Participants were instructed to call the research assistant if any problems arose. The research assistants were sometimes called before the scheduled visit to help add new printing paper in the oximeter.

Similar protocols were used for measuring oxygen saturation levels and pulse rates of participants at the retirement home. The primary differences in protocols were that these participants took measurements only once each day, between 5 and 7 p.m., and they were always assisted by a research assistant assigned to the retirement home. The research assistant set up three pulse oximeters in a room adjacent to the dining area and participants stopped in before or after their evening meal. The subjects were seated...
and had the three-minute measurement taken. The oximeter printout was then labeled and filed by the research assistant. Symptom diaries were not completed for the retirement home panel.

QUALITY CONTROL

Depending on the manufacturer, pulse oximeters are calibrated against functional or fractional saturation. The Nellcor N-20P determines pulse rate and functional oxygen saturation, that is, oxygenated hemoglobin expressed as a percentage of the hemoglobin that is capable of transporting oxygen. The Nellcor N-20P is automatically calibrated each time it is turned on or whenever a new sensor is connected. The oximeter sets sensor-specific calibration coefficients by reading a calibration resistor in the sensor. Therefore, there is no additional method for calibrating these pulse oximeters in the field. For this reason, two quality control approaches to evaluate the performance of the oximeter were used. Each pulse oximeter was tested for accuracy once each month with an SRC-2 pulse oximeter tester (Nellcor Incorporated). The Nellcor SRC-2 tests the light-emitting diode drive circuits and internal detection circuits of the Nellcor N-20P pulse oximeter. Four tests that simulated different pulse rates (38, 112, 201 bpm), oxygen saturation (80%), and light intensity (low, high1, high2) were conducted using this tester.

In addition, at each visit, a control pulse oximeter was brought to each home by the assigned research assistant. A three-minute test was run on each participant using the control oximeter on the right-hand index finger, and the participant's oximeter on the left-hand index finger. Both oximeter readings were printed and compared for consistency.

Data were collected approximately every two weeks by a research assistant. They were sorted, checked, and photocopyied by the assigned research assistant. Photocopied data were filed; the original data were used for data entry and then filed. One research assistant performed initial data entry; these data were double checked by a second assistant. A computer data printout was proofread by a third research assistant. Finally, the data were graphed and checked by computer for consistency and congruity with known parameters.

POLLUTION AND WEATHER DATA

Daily monitoring of PM$_{10}$ (particulate matter 10 μm or smaller in aerodynamic diameter) was conducted by the Utah State Department of Health in accordance with the EPA's reference method (U.S. Environmental Protection Agency 1987) at three sites in the valley—Lindon, Provo, and Orem monitoring sites (Figure 1). Samples for each 24-hour period were collected starting at midnight. Daily measurements of PM$_{10}$ concentrations were mostly complete for the study period, with measurements available for 85%, 90%, and 94% of the days at the monitoring sites in Lindon, Orem, and Provo, respectively. Monitoring of carbon monoxide (CO) was conducted by the Utah State Department of Health at five sites in the valley. Daily 24-hour-average and maximum daily 8-hour mean CO values for each of these monitors were collected.

Because concentrations of sulfur dioxide, nitrogen dioxide, and ozone are so low, the state conducts very limited monitoring of these pollutants. Even when PM$_{10}$ levels are elevated, sulfur dioxide concentrations averaged less than 0.01 parts per million (ppm) (26 μg/m$^3$), with maximum one-hour concentrations never exceeding 0.04 ppm (104 μg/m$^3$). During hot summer middays, ozone levels occasionally approach 0.12 ppm (240 μg/m$^3$), but during winter months (when this study was conducted), ozone levels are relatively low because conditions necessary for substantial ozone formation do not exist (see Pope et al. 1991; Pope 1996).

Weather data were obtained from the Botany Pond weather station at Brigham Young University (Figure 1). High and low temperatures, high and low relative humidity, and barometric pressure at 5 p.m. local time were collected for each day in the study period. Barometric pressure readings were reported by the weather station in inches of mercury adjusted to sea level. Barometric pressure values were then converted to millimeters of mercury (mm Hg) to indicate actual barometric pressure at the valley floor (i.e., not adjusted to sea level values).

STATISTICAL METHODS

Key variables were plotted together over time. Pearson correlation coefficients between Spo$_2$, pulse rate, the pollution variables, and the weather variables were calculated to evaluate simple pairwise correlations. The PM$_{10}$ levels at the three different monitoring sites were very similar and highly correlated over the study period. Therefore, in most of the analytic plots and statistical analyses, PM$_{10}$ levels averaged across available data from the three sites were used except for two days for which no monitor data were obtained. On those two days, PM$_{10}$ was estimated by simple linear extrapolation.

Fixed-effects autoregressive multiple regression models were estimated as follows. Ninety individuals were observed over a period of 119 days, yielding (assuming no missing data) a maximum of 10,710 possible nighttime or evening observations. When participants from the retire-
ment home were combined with participants in private homes, a total of approximately 8,760 nighttime or evening $\text{SpO}_2$ and pulse rate values were available for analysis (82% complete). The data were stacked, with observations for participant 1 followed by observations for participant 2, and so on. Values of $\text{SpO}_2$ and pulse rate were then regressed on indicator (dummy) variables for each participant and the time-dependent covariates, including pollution, barometric pressure, and other weather variables. Temperature and relative humidity were divided into quintile ranges, and indicator (dummy) variables for quintiles of temperature and relative humidity were included in the models.

To evaluate more fully the potential lagged relationships between $\text{SpO}_2$, pulse rate, $\text{PM}_{10}$, and barometric pressure, we estimated single-period and various lagged-moving-average models. Because we observed statistically significant ($p < 0.05$) autocorrelation, we estimated first-order autoregressive models using the maximum likelihood estimation method (SAS Institute 1988). Models were estimated after stratifying the data by health status, sex, and age, and also with CO included.

The effects of particles on the measured outcome variables (oxygen saturation and heart rate) are assumed to be additive—that is, an incremental change in exposure leads to an incremental increase in the outcome measure. The effects of particles on binary outcome variables (respiratory symptoms and indicators of large changes in heart rate) are assumed to be multiplicative—that is, an incremental change in exposure leads to a relative increase in the odds of the outcome variable.

The mean pulse rate across the full study period was calculated for each participant. Binary variables were created to indicate days when pulse rate was 5 or 10 bpm higher than the study period mean for the participant. These binary high-pulse-rate event variables were analyzed by estimating fixed-effects logistic regression models (Cox and Snell 1989).

The binary symptom variables were also analyzed by estimating fixed-effects logistic regression models (Cox and Snell 1989). For $\text{PM}_{10}$, single-period and lagged-moving-average models (the mean of the nonmissing values of $\text{PM}_{10}$ for the concurrent day and previous 6 days) were used. Each of the respiratory symptom variables was analyzed. In addition, a binary variable was created that indicated the presence of any one of the lower respiratory illness symptoms of trouble breathing, wheeze, cough, or sputum. Because repeated daily observations were made on each subject, serial correlation in reported symptoms needed to be addressed in the analysis. Therefore, the conditional expectation of the binary-dependent symptom variables given previous observations was modeled. This approach used autoregressive logistic models as described by Bonney (1987).

RESULTS

COMPLIANCE AND OXIMETER PERFORMANCE

Table 1 describes the participants in both panels. The participants were elderly and the majority suffered from heart and/or lung disease. A summary of the collected

Table 2. Summary of Primary Variables Used in Analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>n&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{SpO}_2$, night, combined (%)</td>
<td>8,777</td>
<td>94.7</td>
<td>1.6</td>
<td>87–100</td>
</tr>
<tr>
<td>Pulse rate, night, combined (bpm)</td>
<td>8,760</td>
<td>73.1</td>
<td>10.4</td>
<td>32–132</td>
</tr>
<tr>
<td>$\text{PM}_{10}$, Lindon ($\mu g/m^3$)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>101</td>
<td>43</td>
<td>34</td>
<td>5–147</td>
</tr>
<tr>
<td>$\text{PM}_{10}$, Orem ($\mu g/m^3$)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>107</td>
<td>42</td>
<td>29</td>
<td>9–128</td>
</tr>
<tr>
<td>$\text{PM}_{10}$, Provo ($\mu g/m^3$)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>111</td>
<td>35</td>
<td>26</td>
<td>5–120</td>
</tr>
<tr>
<td>CO (8-hour), South Orem (ppm)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>119</td>
<td>2.91</td>
<td>1.30</td>
<td>0.89–7.62</td>
</tr>
<tr>
<td>CO (24-hour), South Orem (ppm)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>119</td>
<td>1.76</td>
<td>0.74</td>
<td>0.57–4.70</td>
</tr>
<tr>
<td>Barometric pressure (mm Hg)</td>
<td>119</td>
<td>647</td>
<td>4</td>
<td>635–661</td>
</tr>
<tr>
<td>Low relative humidity (%)</td>
<td>119</td>
<td>45</td>
<td>17</td>
<td>15–98</td>
</tr>
<tr>
<td>Low temperature (°C)</td>
<td>119</td>
<td>28</td>
<td>8</td>
<td>3–43</td>
</tr>
<tr>
<td>High temperature (°C)</td>
<td>119</td>
<td>49</td>
<td>11</td>
<td>28–73</td>
</tr>
</tbody>
</table>

<sup>a</sup> For the $\text{SpO}_2$ and pulse rate data, $n$ represents the total number of values available from all participants. For the pollution and weather data, $n$ represents the number of days during the study period for which data were available (total of 119 days).

<sup>b</sup> 24-Hour mean value.

<sup>c</sup> Maximum daily 8-hour mean value.
Table 3. Quality Control Comparisons of the Pulse Oximeters Used in the Study with a Control Oximeter and with the SRC-2 Tester

<table>
<thead>
<tr>
<th>Quality Control Instrument</th>
<th>Number of Comparisons</th>
<th>Percentage of Coreadings with Differences Equal to</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Spo2</strong></td>
<td><strong>Control oximeter</strong></td>
<td>165</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 1)</strong></td>
<td>116</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 2)</strong></td>
<td>119</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 3)</strong></td>
<td>114</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 4)</strong></td>
<td>119</td>
</tr>
<tr>
<td><strong>Pulse Rate</strong></td>
<td><strong>Control oximeter</strong></td>
<td>165</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 1)</strong></td>
<td>116</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 2)</strong></td>
<td>119</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 3)</strong></td>
<td>114</td>
</tr>
<tr>
<td></td>
<td><strong>SRC-2 (test 4)</strong></td>
<td>119</td>
</tr>
</tbody>
</table>

*Tests 1 through 4 were identical tests conducted at one-month intervals throughout the study period for quality control purposes.

b When the difference is 0, the readings of the study instrument and the quality control instrument were identical. The difference of 1, 2, or 3, indicates that the study instrument and the quality control instrument differed by 1, 2, or 3 percent for Spo2 and 1, 2, or 3 bpm for pulse rate.

Spo2, pulse rate, air pollution, and weather data is presented in Table 2. Throughout the study period there was excellent compliance by the participants in both panels. Daily compliance, in terms of completing the Spo2 and pulse rate measurements, was confirmed by the printouts from the pulse oximeters. Oxygen saturation and pulse rate measures for the private home panel were 88% complete. Measures for the retirement home panel were 74% complete. There was never an occasion during the study period when there was evidence that any one of the oximeters failed to operate properly. The only performance problem with the oximeters was that some of the participants were unable to change the printer paper. Occasionally a research assistant would not be available until the next day and a reading would be missed.

A summary of the quality control comparisons is provided in Table 3. As reported in this table, when coreadings of Spo2 and pulse rate with the study oximeters and the control oximeter were compared, the readings were identical or differed by only one digit 93% of the time. Never did the Spo2 control comparisons differ by more than 3%. Table 3 also presents similar comparisons of the study oximeter readings using the Nellcor SRC-2 pulse oximeter tester at four intervals throughout the study period. The readings were nearly always identical or differed by only one digit. Based on manufacture's specifications, none of the oximeters failed the quality control tests for either Spo2 or pulse rates.

LEVELS AND VARIABILITY OF AIR POLLUTION AND BAROMETRIC PRESSURE

Figure 2 presents plots of daily concentrations of PM10 at each of the three monitors and CO concentrations at the South Orem monitor over the days in the study period. Also presented in this figure are barometric pressure and the mean nighttime or evening Spo2 readings for participants in both panels. Episodes of high concentrations of particulate pollution typically occur when there is snow cover in the valley and a near stationary high pressure system over the western Rocky Mountains. The winter of the study period began relatively warm and dry. Early in the winter there were high pressure systems, but without snow cover there were no major pollution episodes. Midway through the study period there were two minor episodes followed by two weeks that were very clean, with maximum PM10 less than 15 μg/m3. In late January there was a shift in the weather pattern with heavy snows and colder temperatures. Air pollution concentrations built up over the first two weeks of February, reaching a maximum daily PM10 concentrations of 147 μg/m3 on the 14th of February. There was substantial improvement in air quality after the 15th of February.

As can be seen in Figure 2, the PM10 levels at the three monitoring sites were very highly correlated. Pearson correlation coefficients (r) for PM10 levels at the three sites
Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure

Figure 2. PM$_{10}$, CO, barometric pressure, and mean $\text{SpO}_2$ values (all participant data) plotted against barometric pressure.
Table 4. Regression Coefficients (± SE) for \( \text{SpO}_2 \) on PM and on Concurrent-Day Barometric Pressure Using Different Lagged Models for PM\(^{10} \)

<table>
<thead>
<tr>
<th>PM Measure Used in the Model</th>
<th>PM(^{b} ) (x 100)</th>
<th>Concurrent-Day Barometric Pressure (x 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concurrent day</td>
<td>0.06 ± 0.05</td>
<td>0.59 ± 0.08***</td>
</tr>
<tr>
<td>Previous day</td>
<td>-0.01 ± 0.04</td>
<td>0.62 ± 0.08***</td>
</tr>
<tr>
<td>2-Day-lagged moving average</td>
<td>0.02 ± 0.05</td>
<td>0.61 ± 0.08***</td>
</tr>
<tr>
<td>3-Day-lagged moving average</td>
<td>0.02 ± 0.05</td>
<td>0.61 ± 0.08***</td>
</tr>
<tr>
<td>4-Day-lagged moving average</td>
<td>-0.00 ± 0.05</td>
<td>0.62 ± 0.08***</td>
</tr>
<tr>
<td>5-Day-lagged moving average</td>
<td>-0.03 ± 0.05</td>
<td>0.63 ± 0.08***</td>
</tr>
<tr>
<td>6-Day-lagged moving average</td>
<td>-0.05 ± 0.05</td>
<td>0.63 ± 0.08***</td>
</tr>
</tbody>
</table>

* Other covariates included in the models are quintile indicator variables for temperature and relative humidity, and subject-specific indicator variables for each participant. Statistical significance of \( p < 0.10 \), \( p < 0.05 \), and \( p < 0.01 \) are indicated by * , ** , and *** , respectively.

\( ^{b} \) Average PM\(_{10} \) levels from the Lindon, Orem, and Provo sites were used except for the two days with no monitor data. On these two days, PM\(_{10} \) levels were estimated by simple linear extrapolation.

Ranged from 0.92 to 0.96, PM\(_{10} \) was less strongly correlated with carbon monoxide levels (\( r = 0.61 \) to 0.76) and barometric pressure (\( r = 0.38 \) to 0.48).

**ASSOCIATIONS WITH OXYGEN SATURATION**

Based on the values shown in Figure 2, there is no obvious association between mean \( \text{SpO}_2 \) levels and air pollution. An association between mean \( \text{SpO}_2 \) and barometric pressure, however, is clearly observable (Figures 2 and 3). Table 4 presents the results of various fixed-effects autoregressive multiple regression models where PM\(_{10} \) is included in the models as concurrent-day PM\(_{10} \), previous-day PM\(_{10} \), and 2- to 6-day-lagged moving averages of PM\(_{10} \). For example, the 5-day-lagged moving average of PM\(_{10} \) is the average of the PM\(_{10} \) concentrations for the concurrent day and the previous 4 days. Table 5 presents regression results after stratifying by sex, age, housing, health status, and medication use.

The most consistent result from the regression models is the positive highly statistically significant relationship between \( \text{SpO}_2 \) and barometric pressure. This association was highly consistent across models and different stratification. The estimated effect of barometric pressure was not affected by the inclusion of other covariates in the models. The estimated effect of barometric pressure (25 mm Hg) without any pollution variable was 0.69 (SE = 0.07), nearly the same as the estimated effect reported in Table 4. Also, no clear lag structure was observed for barometric pressure. Barometric pressure’s estimated effect on \( \text{SpO}_2 \) appeared to be due to the concurrent day’s barometric pressure.

Weaker, less consistent associations between \( \text{SpO}_2 \) and PM\(_{10} \) were observed. Significant contemporaneous negative association between \( \text{SpO}_2 \) and PM\(_{10} \) were generally not observed. In fact, the concurrent day PM\(_{10} \) levels were often positively associated with \( \text{SpO}_2 \). As can be seen in Table 5, however, \( \text{SpO}_2 \) is generally negatively associated with previous-day and 5-day-lagged moving average PM\(_{10} \). For some of the strata, most notably male participants 80 years old or older, the negative association between \( \text{SpO}_2 \) and PM\(_{10} \) was statistically significant.

Controlling for weather variables in the regression models had little impact on the estimated effects of PM\(_{10} \) or barometric pressure on \( \text{SpO}_2 \). The regression models were reestimated using data from all the participants but excluding the temperature and relative humidity indicator variables. The regression coefficients (± SE) from these models for concurrent-day barometric pressure, previous-day PM\(_{10} \), and 5-day-lagged moving average PM\(_{10} = 0.68 \) (± 0.07), -0.00 (± 0.04), and -0.01 (± 0.05), respectively.
Figure 4. Daily mean pulse rates (all participant data) (top panel) and the proportion of the participants with pulse rates more than 10 bpm above their study-period mean (bottom panel) plotted against the previous day's PM$_{10}$ levels across all days in the study period.
Table 5. Regression Coefficients ($\times 100 \pm SE$) for $S_{P2}$ on PM (Previous-Day and 5-Day-Lagged Moving Average) Stratified by Sex, Age, Housing, and Health Status

<table>
<thead>
<tr>
<th></th>
<th>Previous-Day PM</th>
<th>5-Day-Lagged Moving Average PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants ($n = 90$)</td>
<td>$-0.01 \pm 0.04$</td>
<td>$-0.03 \pm 0.05$</td>
</tr>
<tr>
<td>Male ($n = 38$)</td>
<td>$-0.01 \pm 0.06$</td>
<td>$-0.06 \pm 0.08$</td>
</tr>
<tr>
<td>Male, age $\geq 80$ ($n = 14$)</td>
<td>$-0.21 \pm 0.10**$</td>
<td>$-0.33 \pm 0.12***$</td>
</tr>
<tr>
<td>Male, age $&lt; 80$ ($n = 24$)</td>
<td>$0.10 \pm 0.08$</td>
<td>$0.10 \pm 0.10$</td>
</tr>
<tr>
<td>Female ($n = 52$)</td>
<td>$-0.01 \pm 0.06$</td>
<td>$-0.01 \pm 0.07$</td>
</tr>
<tr>
<td>Female, age $\geq 80$ ($n = 20$)</td>
<td>$-0.06 \pm 0.08$</td>
<td>$-0.06 \pm 0.10$</td>
</tr>
<tr>
<td>Female, age $&lt; 80$ ($n = 32$)</td>
<td>$0.01 \pm 0.08$</td>
<td>$0.00 \pm 0.09$</td>
</tr>
<tr>
<td>Private homes ($n = 52$)</td>
<td>$0.06 \pm 0.06$</td>
<td>$0.03 \pm 0.07$</td>
</tr>
<tr>
<td>Retirement home ($n = 38$)</td>
<td>$-0.13 \pm 0.07^*$</td>
<td>$-0.13 \pm 0.08^*$</td>
</tr>
<tr>
<td>History of respiratory$^b$, but no cardiac$^c$, conditions ($n = 4$)</td>
<td>$-0.16 \pm 0.17$</td>
<td>$-0.43 \pm 0.20**$</td>
</tr>
<tr>
<td>History of cardiac, but no respiratory, conditions ($n = 42$)</td>
<td>$0.07 \pm 0.06$</td>
<td>$0.08 \pm 0.07$</td>
</tr>
<tr>
<td>History of both respiratory and cardiac conditions ($n = 10$)</td>
<td>$-0.09 \pm 0.14$</td>
<td>$-0.10 \pm 0.16$</td>
</tr>
<tr>
<td>No history of respiratory or cardiac conditions ($n = 34$)</td>
<td>$-0.06 \pm 0.07$</td>
<td>$-0.09 \pm 0.09$</td>
</tr>
</tbody>
</table>

$^a$ Other covariates included in the models are barometric pressure, quintile indicator variables for temperature and relative humidity, and subject-specific indicator variables for each participant. Statistical significance of $p < 0.10$, $p < 0.05$, and $p < 0.01$ are indicated by *, **, and ***, respectively. Average PM$_{10}$ levels from the Lindon, Orem, and Provo sites were used except for the two days with no monitor data. On these two days, PM$_{10}$ levels were estimated by simple linear extrapolation.

$^b$ Chronic respiratory conditions: chronic obstructive pulmonary disease, asthma, chronic bronchitis, and emphysema.

$^c$ Cardiac conditions: heart attack, heart failure, angina, and hypertension.

Figure 5. Daily mean pulse rates (all participant data) plotted against the previous day's PM$_{10}$.

Including CO in the regression models resulted in slightly larger estimated effects of PM$_{10}$ on $S_{P2}$. For example, when daily 8-hour maximum CO levels from the South Orem monitor were also included in the regression model, the regression coefficients ($\pm SE$) for barometric pressure, previous-day PM$_{10}$, and 5-day-lagged moving average PM$_{10}$ = 0.59 ($\pm 0.08$), $-0.05$ ($\pm 0.05$), and $-0.08$ ($\pm 0.06$), respectively. Coefficients on CO were positive, but small (0.02) and statistically insignificant ($p > 0.10$). Exposure to CO

Figure 6. Proportion of the participants with pulse rates more than 5 bpm (or 10 bpm) above their normal rates, plotted across the previous day's PM$_{10}$ levels.
should falsely raise $\mathrm{SpO}_2$, slightly, as the oximeter cannot read carboxyhemoglobin and ignores it. In addition, CO shifts the oxyhemoglobin dissociation curve to the left, which increases $\mathrm{SpO}_2$ for a given $\mathrm{Paco}_2$.

**ASSOCIATIONS WITH PULSE RATE**

Figure 4 presents daily mean pulse rate for all the participants and the proportion of the participants with pulse rates more than 10 bpm above their study-period mean pulse rate. These are both plotted with the previous day's PM$_{10}$ levels across the day in the study period. Figure 5 presents daily mean pulse rate for all the participants plotted against the previous day's PM$_{10}$. Figure 6 presents the proportion of the participants with pulse rates more than 5 bpm (and more than 10 bpm) higher than their normal pulse rates plotted against the previous day's PM$_{10}$. A careful examination of Figures 4 through 6 indicates that there is high variability in pulse rate but also suggests that a small subtle positive association between pulse rate and PM$_{10}$ levels may exist.

**Table 6.** Regression Coefficients (± SE) for Pulse Rate on PM and Concurrent-Day Barometric Pressure Using Different Lagged Models for PM$^b$

<table>
<thead>
<tr>
<th>PM Measure Used in the Model</th>
<th>PM$^b$ (x 100)</th>
<th>Concurrent-Day Barometric Pressure (x 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concurrent-day</td>
<td>0.31 ± 0.29</td>
<td>-1.39 ± 0.49***</td>
</tr>
<tr>
<td>Previous-day</td>
<td>0.78 ± 0.27***</td>
<td>-1.50 ± 0.48***</td>
</tr>
<tr>
<td>2-Day-lagged moving average</td>
<td>0.63 ± 0.30**</td>
<td>-1.48 ± 0.49***</td>
</tr>
<tr>
<td>3-Day-lagged moving average</td>
<td>0.67 ± 0.31**</td>
<td>-1.49 ± 0.49***</td>
</tr>
<tr>
<td>4-Day-lagged moving average</td>
<td>0.66 ± 0.31**</td>
<td>-1.48 ± 0.49***</td>
</tr>
<tr>
<td>5-Day-lagged moving average</td>
<td>0.69 ± 0.32**</td>
<td>-1.47 ± 0.48***</td>
</tr>
<tr>
<td>6-Day-lagged moving average</td>
<td>0.70 ± 0.33**</td>
<td>-1.44 ± 0.48***</td>
</tr>
</tbody>
</table>

$^a$ Other covariates included in the models are quintile indicator variables for temperature and relative humidity, and subject-specific indicator variables for each participant. Statistical significance of $p < 0.10$, $p < 0.05$, and $p < 0.01$ are indicated by *, **, and *** respectively.

$^b$ Average PM$_{10}$ levels from the Lindon, Orem, and Provo sites were used except for the two days with no monitor data. On these two days, PM$_{10}$ levels were estimated by simple linear extrapolation.

**Table 7.** Regression Coefficients (x 100 ± SE) for Pulse Rate on PM (Previous-Day and 5-Day-Lagged Moving Average) Stratified by Sex, Age, Housing, and Health Status$^a$

<table>
<thead>
<tr>
<th></th>
<th>Previous-Day PM</th>
<th>5-Day-Lagged Moving Average PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>0.78 ± 0.27***</td>
<td>0.69 ± 0.32**</td>
</tr>
<tr>
<td>Male (n = 38)</td>
<td>0.51 ± 0.42</td>
<td>0.26 ± 0.50</td>
</tr>
<tr>
<td>Male, age ≥ 80</td>
<td>0.89 ± 0.74</td>
<td>0.17 ± 0.87</td>
</tr>
<tr>
<td>Male, age &lt; 80</td>
<td>0.29 ± 0.51</td>
<td>0.29 ± 0.62</td>
</tr>
<tr>
<td>Female (n = 52)</td>
<td>1.00 ± 0.35***</td>
<td>1.03 ± 0.42**</td>
</tr>
<tr>
<td>Female, age ≥ 80</td>
<td>1.05 ± 0.59*</td>
<td>0.71 ± 0.68</td>
</tr>
<tr>
<td>Female, age &lt; 80</td>
<td>0.96 ± 0.44**</td>
<td>1.28 ± 0.53**</td>
</tr>
<tr>
<td>Private homes (n = 52)</td>
<td>0.37 ± 0.34</td>
<td>0.06 ± 0.41</td>
</tr>
<tr>
<td>Retirement home (n = 38)</td>
<td>1.44 ± 0.45***</td>
<td>1.64 ± 0.53***</td>
</tr>
<tr>
<td>History of respiratory$^b$, but no cardiac$^c$, conditions (n = 4)</td>
<td>-0.35 ± 2.01</td>
<td>-3.64 ± 2.39</td>
</tr>
<tr>
<td>History of cardiac, but no respiratory, conditions (n = 42)</td>
<td>0.43 ± 0.39</td>
<td>0.47 ± 0.46</td>
</tr>
<tr>
<td>History of both respiratory and cardiac conditions (n = 10)</td>
<td>1.74 ± 1.01*</td>
<td>1.93 ± 1.22</td>
</tr>
<tr>
<td>No history of respiratory or cardiac conditions (n = 34)</td>
<td>1.08 ± 0.38***</td>
<td>1.15 ± 0.44***</td>
</tr>
</tbody>
</table>

$^a$ Other covariates included in the models are barometric pressure, quintile indicator variables for temperature and relative humidity, and subject-specific indicator variables for each participant. Statistical significance of $p < 0.10$, $p < 0.05$, and $p < 0.01$ are indicated by *, **, and *** respectively. Average PM$_{10}$ levels from the Lindon, Orem, and Provo sites were used except for the two days with no monitor data. On these two days, PM$_{10}$ levels were estimated by simple linear extrapolation.

$^b$ Chronic respiratory conditions: chronic obstructive pulmonary disease, asthma, chronic bronchitis, and emphysema.

$^c$ Cardiac conditions: heart attack, heart failure, angina, and hypertension.
Table 8. Logistic Regression Coefficients (x 100 ± SE) for Pulse Rate 5 or 10 bpm Above Normal on PM (Previous-Day and 5-Day-Lagged Moving Average) Stratified by Sex, Age, Housing, and Health Status*

<table>
<thead>
<tr>
<th></th>
<th>5 bpm Above Normal</th>
<th>10 bpm Above Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Previous-Day PM</td>
<td>5-Day-Lagged Moving Average PM</td>
</tr>
<tr>
<td>All participants (n = 90)</td>
<td>0.26 ± 0.11***</td>
<td>0.23 ± 0.13*</td>
</tr>
<tr>
<td>Male (n = 38)</td>
<td>0.21 ± 0.17</td>
<td>0.20 ± 0.20</td>
</tr>
<tr>
<td>Male, age ≥ 80 (n = 14)</td>
<td>0.26 ± 0.29</td>
<td>0.35 ± 0.33</td>
</tr>
<tr>
<td>Male, age &lt; 80 (n = 24)</td>
<td>0.18 ± 0.22</td>
<td>0.11 ± 0.25</td>
</tr>
<tr>
<td>Female (n = 52)</td>
<td>0.29 ± 0.14**</td>
<td>0.25 ± 0.17</td>
</tr>
<tr>
<td>Female, age ≥ 80 (n = 20)</td>
<td>0.13 ± 0.24</td>
<td>−0.12 ± 0.28</td>
</tr>
<tr>
<td>Female, age &lt; 80 (n = 32)</td>
<td>0.40 ± 0.18**</td>
<td>0.46 ± 0.21**</td>
</tr>
<tr>
<td>Private homes (n = 52)</td>
<td>0.23 ± 0.14</td>
<td>0.22 ± 0.16</td>
</tr>
<tr>
<td>Retirement home (n = 38)</td>
<td>0.29 ± 0.18</td>
<td>0.23 ± 0.20</td>
</tr>
<tr>
<td>History of respiratory*, but no cardiac*, conditions (n = 4)</td>
<td>−0.26 ± 0.49</td>
<td>−0.81 ± 0.60</td>
</tr>
<tr>
<td>History of cardiac, but no respiratory, conditions (n = 42)</td>
<td>0.16 ± 0.17</td>
<td>0.16 ± 0.20</td>
</tr>
<tr>
<td>History of both respiratory and cardiac conditions (n = 10)</td>
<td>0.22 ± 0.31</td>
<td>0.17 ± 0.36</td>
</tr>
<tr>
<td>No history of respiratory or cardiac conditions (n = 34)</td>
<td>0.46 ± 0.18***</td>
<td>0.50 ± 0.20**</td>
</tr>
</tbody>
</table>

* Other covariates included in the models are barometric pressure, quintile indicator variables for temperature and relative humidity, and subject-specific indicator variables for each participant. Statistical significance of p < 0.10, p < 0.05, and p < 0.01 are indicated by *, **, and ***, respectively. Average PM10 levels from the Lindon, Glenn, and Provo sites were used except for the two days with no monitor data. On these two days, PM10 levels were estimated by simple linear extrapolation.

b Chronic respiratory conditions: chronic obstructive pulmonary disease, asthma, chronic bronchitis, and emphysema.

c Cardiac conditions: heart attack, heart failure, angina, and hypertension.

Regression analysis confirms the existence of a small but statistically significant association between pulse rate and PM10 exposure. Table 6 presents the results of various fixed-effects autoregressive multiple regression models for pulse rate where PM10 is included in the models as concurrent-day PM10, previous-day PM10, and 2- to 6-day-lagged moving averages of PM10. Table 7 presents regression results for pulse rate after stratifying by sex, age, housing, health status, and medication use. Similarly, Table 8 presents the stratified logistic results for pulse rates 5 or 10 bpm above normal.

A relatively consistent result from the regression models presented in Table 6 is the negative statistically significant relationship between pulse rate and barometric pressure. A 25-mm Hg increase in barometric pressure was associated with an average decrease in pulse rate equal to about 1.4 bpm. The estimated effect of barometric pressure on pulse rate was not highly affected by the inclusion of pollution variables in the models. The estimated effect of barometric pressure (25 mm Hg) without any pollution variable was −1.27 (SE = 0.47). No clear lag structure was observed for barometric pressure. Barometric pressure's estimated effect on pulse rate appeared to be due to the concurrent day's barometric pressure.

Positive associations between pulse rate and PM10 were observed. Daily pulse rate was associated with exposure to particulate pollution on the previous 1 to 6 days (Tables 6 and 7). A 100-μg/m³ increase in previous-day PM10 was associated with an average increase of 0.78 bpm. Also, the odds of having a pulse rate 5 or 10 bpm above normal was associated with exposure to particulate air pollution on the previous 1 to 5 days. Based on the logistic regression coefficients presented in Table 8 for all participants, a 100-μg/m³ increase in previous-day PM10 was associated with an increase of 30% or 95% in the odds of experiencing a pulse rate of 5 or 10 bpm above normal, respectively.

As with the analysis for SpO2, controlling for weather variables in the regression models had little impact on the estimated effects of PM10 on barometric pressure on pulse rate. The regression models for pulse rate were reestimated using data from all the participants but excluding the temperature and relative humidity indicator variables. The regression coefficients (± SE) from these models for
concurrent-day barometric pressure, previous-day PM10, and 5-day-lagged moving average PM10 = -1.33 (± 0.43), 0.74 (± 0.26), and 0.66 (± 0.32), respectively.

Including CO in the regression models resulted in mostly unchanged or slightly larger estimated effects of PM10 on pulse rate. When daily 8-hour maximum CO levels from the South Orem monitor were also included in the regression model, the regression coefficients (± SE) for barometric pressure, previous-day PM10, and 5-day-lagged moving average PM10 = -1.43 (± 0.49), 0.88 (± 0.31), and 0.70 (± 0.36), respectively. Coefficients on CO were not statistically significant (p > 0.10).

RESPIRATORY SYMPTOMS

Because only the participants in the private home panel completed symptom diaries, the analysis of symptoms and PM10 was restricted to this panel. Across all of the participants in this panel there were a total of 5,682 completed daily entries in the diaries. This total number of entries represented approximately 94% overall compliance. Unlike the pulse oximeter readings for Spo2 and pulse rate that were confirmed by printouts, the only information about the quality of this self-reported symptom data was completed entries and stated compliance. Based on the symptoms reported in these diaries, the average frequency of trouble breathing, wheeze, cough, or sputum was 3.4%, 1.0%, 15.4%, and 10.4%, respectively. An average of 19.1% of all entry days included a report of one or more of these symptoms. Based on the logistic regressions of symptoms, statistically significant positive associations between the symptoms and concurrent or lagged PM10 were not consistently observed.

DISCUSSION

Over the last several years, a number of studies specific to Utah Valley have evaluated the health effects of air pollution (Pope 1996). Apparent health effects of elevated particulate pollution observed in the valley include (1) decreased lung function, as measured by expiratory flow rates, and increased incidences of respiratory symptoms (Pope et al. 1991; Pope and Dockery 1992); (2) increased school absenteeism (Ransom and Pope 1992); (3) increased respiratory hospital admissions (Pope 1989; 1991); (4) increased mortality, especially respiratory and cardiovascular mortality (Archer 1990; Pope et al. 1992); and (5) possibly increased incidence of lung cancer (Archer 1990; Lyon et al. 1981; Blindauer et al. 1993).

As with the present study, all of these previous studies have used central fixed-site monitors to measure air pollution. In general, if the observed associations between these health endpoints and air pollution are not strictly spurious, it is concluded that fixed-site monitoring at least partly reflects differences in personal exposures over time. The pollution levels at the PM10 monitoring sites are highly correlated, suggesting that the fine particulate air pollution is dispersed across the study area. Because most of the elderly participants would spend most of their time in their homes, the largest difference in personal exposures would probably be due to outdoor/inhome differences in particulate concentrations. These differences were lessened by including only homes without any smokers (including the retirement home) and homes without special air filtration systems.

This study attempted to evaluate declines in blood oxygenation or increases in pulse rate as potential pathways for previously observed increased cardiovascular mortality associated with particulate air pollution. Within the context of this basic objective, this study provides preliminary information regarding at least four questions of interest as outlined below. These questions are:

1. How usable and reliable are the data?
2. Is the study designed to be capable of observing very small changes in SpO2?
3. Are there observable declines in SpO2 following exposure to PM10?
4. Are there observable increases in pulse rate following exposure to PM10?

1. How usable and reliable are the data from pulse oximetry in a study of this type?

The performance and usability of the pulse oximeters were excellent. The oximeters were relatively easy to use and were generally well received by the elderly participants in this study. The printouts provided a ready way to check for compliance and collect hard copies of the results. Quality control comparisons with control readings and test readings suggested that the SpO2 measures were consistent and reproducible.

2. Is the study designed to be capable of observing very small changes in SpO2, such as those associated with small daily changes in barometric pressure?

The results of this study indicate remarkable power to observe small day-to-day changes in SpO2 and pulse rate associated with changes in barometric pressure by using pulse oximeters and this type of study design. The range of barometric pressure that occurred during the study period was only 26 mm Hg (635 to 661). Based on the estimated regression coefficients for barometric pressure presented in Table 4, the mean increase in SpO2 that would be expected
for an increase in barometric pressure equal to 26 mm Hg would be less than 1% (about 0.6%). This is approximately what would be expected at this point on the oxygen-hemoglobin dissociation (saturation) curve, given a comparable relative change in $P_{aO_2}$ in the blood (approximately 2 mm Hg or about 0.12 vol% of oxygen).

Although the direction and size of the observed association between barometric pressure and $S_{pO_2}$ are reasonable, care must be taken not to overinterpret the results. As noted in Table 2, mean $S_{pO_2}$ measured by the oximeters was approximately 95%. However, most oximeters, including Nellcor, read too high at the upper end of the oxygen dissociation curve. Between 70% and 90%, the Nellcor oximeters read most accurately, but at the expected mean $S_{pO_2}$ levels of 91% to 93%, the Nellcor oximeters may be recording readings closer to 95% (Severinghaus and Naifeh 1987; Severinghaus et al. 1989). Furthermore, monitoring of oxygen saturation was conducted only once or twice a day rather than continuously. It is possible that the times of day with the largest changes in oxygen saturation were missed.

Also, the differences in $S_{pO_2}$ across this range of barometric pressure is much smaller than the differences in $S_{pO_2}$ across individuals in the study (Table 2). However, by looking at daily means across an entire cohort of participants, or by estimating fixed-effects regression models, individual differences could be averaged out or controlled for in the analysis. By using such approaches, the subtle association between daily changes in $S_{pO_2}$ and daily changes in barometric pressure was observed. This observation suggests that barometric pressure should possibly be included as a potentially important weather variable in daily time-series studies of morbidity and mortality rates and air pollution. This observation also suggests that if a negative association of similar or larger size existed with PM$_{10}$ at levels that occurred during the study period, then it should also be observable. However, because barometric pressure is generally positively associated with particulate air pollution, not including it in the analysis would most likely result in underestimating adverse effects of particulate pollution.

3. Are there observable declines in $S_{pO_2}$ following exposure to differing daily concentrations of PM pollution?

Oxygen saturation represents an integrated measure of cardiopulmonary function. Pulse oximetry is commonly used clinically to manage patients with respiratory disorders. Given the epidemiological findings of relationships between elevated cardiopulmonary mortality and hospitalizations with urban particulate air pollution, and given that small declines in lung function as measured by expiratory flow rates have also been associated with particulate pollution, it is reasonable to hypothesize that a negative association between $S_{pO_2}$ and particulate pollution might be observed. This hypothesis implies that transient declines in blood oxygenation following exposures to particulate air pollution episodes may be a pathway for observed cardiopulmonary mortality.

In individuals with coronary artery disease, the delivery of oxygen to the myocardium may already be precarious. Thus, for these individuals, a slight decrease of $S_{pO_2}$ may have a significant effect on overall cardiac function. Similar reasoning can be used for individuals with arteriosclerosis of the carotid arteries. Most of the previous epidemiologic studies of cause-specific mortality rates and particulate pollution have observed that overall cardiovascular disease mortality, including deaths due to cerebrovascular accident, are associated with pollution. Although acute hypoxemia can be clinically significant and in extreme cases might be fatal, it is unlikely that exposure to particulate pollution, by itself, can result in large declines in oxygenation in most individuals.

The hypothesized negative association with $S_{pO_2}$ and contemporaneous PM$_{10}$ was not observed. Contemporaneous exposure to PM pollution was not consistently associated with declines in $S_{pO_2}$. Small negative associations between $S_{pO_2}$ and 1- to 6-day-lagged PM levels were typically observed, but for analysis that included all participants, observed associations between $S_{pO_2}$ and even lagged PM were not statistically significant. It is possible that the study population, on average, was too young or too healthy for such potential changes in oxygen saturation to be observed. It was observed, in stratified analysis, that there were statistically significant associations between $S_{pO_2}$ and lagged PM levels for male participants 80 years old or older—suggesting that the effects may be larger in older, less healthy individuals. Baseline testing of cardiac or pulmonary function may have provided more guidance about the most sensitive subjects.

These results may be seen as providing weak evidence of a possible lagged or cumulative negative association between $S_{pO_2}$ and PM exposures. Even allowing for the potential of these observed lagged negative associations with particulate air pollution to be causal, the associations were very small, even when compared with the effects of small changes in barometric pressure.

4. Are there observable increases in pulse rate following exposure to differing daily concentrations of PM pollution?

Increased daily pulse rate, as well as the odds of having a pulse rate elevated by more than 5 or 10 bpm above normal, were associated with exposure to particulate air pollution on the previous 1 to 5 days. The association between pulse rate and PM is small compared with the overall variability in pulse rate. In this study, however, pulse rate was obtained as integrated pulse rate over ap-
proximately three minutes using a pulse oximeter for 90 participants measured repeatedly over 119 days. The use of aggregated data across the entire cohort of participants and the use of fixed-effects regression models provided the opportunity to peer through the expected variability and observe and evaluate the subtle associations between pulse rate and PM.

The importance of pulse has been emphasized in medicine for many centuries (Baldry 1971; Gillum 1988). Recent studies have observed that a high pulse rate is associated with hypertension, coronary heart disease, and mortality (Dyer et al. 1980; Kannel et al. 1987; Gillum 1988, 1992; Hjalmarsen et al. 1990; Gillum et al. 1991, 1993; Gillman et al. 1993; Goldberg et al. 1996). A recent study observed increases in pulse rates of rats following exposure to elevated levels of particulate air pollution (Nadziejko et al. 1997). ECG abnormalities in dogs were observed following exposure to PM (Godeski 1997). We are unaware of any previous studies that have evaluated potential associations between particulate air pollution and pulse rate in humans. However, air pollution was linked to elevated levels of plasma viscosity in both men and women living in Augsburg, Germany, during an air pollution episode (Peters et al. 1997). The authors speculated that “altered blood rheology due to inflammatory processes in the lung which induce an acute phase reaction might therefore be part of the pathological mechanisms linking air pollution to mortality” (Peters et al. 1997). Within the context of treating plasma viscosity as an indicator for impaired blood flow properties, these results may be relevant to the present study. The results of this study suggest a lag structure of 1 to 5 days. These results may also be consistent with the hypothesis that inflammatory responses to particulate pollution are involved and that it takes a day or so before the inflammatory response is apparent.

The observed associations between pulse rate and previous exposure to PM are probably the most intriguing findings of this study. Nevertheless, the medical or biological relevance of these observed increases in pulse rate following exposure to particulate air pollution remains unclear. If there is a nonspurious association between particulate air pollution and pulse rate, it is almost certainly only a part of substantially complex pathological mechanisms linking air pollution to cardiopulmonary mortality.

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REFERENCES


Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure


PUBLICATIONS RESULTING FROM THIS RESEARCH


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ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>bpm</td>
<td>beats per minute</td>
</tr>
<tr>
<td>CO</td>
<td>carbon monoxide</td>
</tr>
<tr>
<td>(P_{aO_2})</td>
<td>partial pressure of (O_2) in arterial blood</td>
</tr>
<tr>
<td>PM</td>
<td>particulate matter</td>
</tr>
<tr>
<td>PM(_{10})</td>
<td>particulate matter 10 (\mu)m or smaller in aerodynamic diameter</td>
</tr>
<tr>
<td>(r)</td>
<td>correlation coefficient</td>
</tr>
<tr>
<td>(Sp_{aO_2})</td>
<td>oxygen saturation level obtained by pulse oximetry</td>
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INTRODUCTION

Many epidemiologic studies have suggested that exposure to particulate matter (PM)*, a general term for chemically and physically heterogeneous substances that exist as discrete particles, is associated with both increased respiratory disease morbidity and increased respiratory and cardiovascular disease mortality (Pope et al. 1992; Schwartz and Dockery 1992a,b; Ostro 1993; Dockery and Pope 1994). The results and interpretation of these studies, however, have not been accepted throughout the scientific community (Moolgavkar et al. 1994; Gamble and Lewis 1996). The U.S. Environmental Protection Agency (EPA) has considered the evidence of health effects of PM to be of sufficient concern (U.S. Environmental Protection Agency 1996a,b) for it to promulgate a National Ambient Air Quality Standard (NAAQS) for PM with a mean average diameter of up to 10 micrometers (PM10). In 1987, the NAAQS was set at 50µg/m³ as the annual average and 150µg/m³ as the 24-hour average, with no more than one expected exceedance per year (Federal Register 1987). In 1997, after a lengthy evaluation, the EPA decided to retain the current 24-hour and annual standards for PM10. Because of concerns about the potential health effects of PM of even smaller diameter, the EPA added 24-hour and annual standards for PM with a mean average diameter of up to 2.5 micrometers (PM2.5) (Federal Register 1997).

Major issues about the effects of PM remain unresolved. These include the question of whether some groups of people, such as the elderly or those with preexisting cardiopulmonary conditions, are at greater risk than the general population, and the problem of the mechanistic link between PM and clinical endpoints (U.S. Environmental Protection Agency 1996b). In an attempt to address these issues, the Health Effects Institute issued Request for Applications (RFA) 94-2, Particulate Air Pollution and Daily Mortality: Identification of Populations at Risk and Underlying Mechanisms of Effects, in 1994.

In response to this RFA, Drs. Dockery and Pope, who had previously reported that long-term exposure to PM was associated with an increased risk of cardiopulmonary mortality (Dockery et al. 1993, Pope et al. 1995), submitted a proposal, "Does Particulate Pollution Induce Hypoxemia?" to study the short-term effects of PM on an elderly population with cardiopulmonary disease. To account for the association of particle pollution with increased cardiovascular mortality, Drs. Dockery and Pope and their co-investigators Drs. Schwartz, Kanner, and Villegas hypothesized that episodes of exposure to particulate matter might lead to drops in blood oxygenation—that is, to acute hypoxemia. Changes in oxygenation might be particularly hazardous in patients with congestive heart failure whose oxygen saturation might be impaired. To increase the likelihood of detecting changes in oxygen saturation, Dockery and Pope proposed to study subjects living at moderately high altitude (1,400 meters above sea level) because comparatively greater changes in oxygen saturation would be expected at this altitude than at sea level. In support of their hypothesis, the investigators described in their application the results of a preliminary study with a limited number of retirement community residents in the Utah Valley. This preliminary study suggested a small, negative association between oxygen saturation in the blood and the previous day's PM10 levels. Dockery and Pope proposed to conduct a larger study to determine whether exposure to PM affected (1) the level of oxygen saturation in the blood and (2) symptoms of respiratory illness in these elderly subjects.

The application of Dockery and Pope was one of the six studies funded under RFA 94-2 by the HEI Research Committee. (Reports from the other five studies, Bailar and Wichmann [Epidemiology Studies], and Godleski, Gordon, and Oberdörster [Experimental Studies] are due in the next year.) During the review of the study, the HEI Review Committee and the investigators exchanged comments and clarified issues in the Investigators' Report and in the Review Committee’s Commentary. This Commentary is intended to aid HEI sponsors and the public by highlighting the strengths of the study, pointing out alternative interpretations, and placing the report into scientific perspective.

* A list of abbreviations appears at the end of the Investigators’ Report for your reference.

† Drs. Douglas W. Dockery and C. Arden Pope's one-year study, Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure, began in September 1995 and had total expenditures of $189,779. The Investigators’ Report was received for review in December 1996. A revised report, received in August 1997, was accepted for publication in October 1997. During the review process, the HEI Review Committee and the investigators had the opportunity to exchange comments and to clarify issues in the Investigators’ Report and in the Review Committee’s Commentary.

This document has not been reviewed by public or private-party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views of these parties, and no endorsements by them should be inferred.
SCIENTIFIC BACKGROUND

Episodes of extreme air pollution earlier this century have been associated with increased respiratory and cardiovascular morbidity and mortality (Firket 1931; Giocco and Thompson 1961; Logan 1953; Gore and Shaddick 1968). More recent time-series studies in several U.S. localities have suggested a small but statistically significant association between daily mortality and short-term changes in particulate air pollution at much lower levels than was observed in the early reports (Fairley 1990; Schwartz 1991; Dockery et al. 1992; Pope et al. 1992; Schwartz and Dockery 1992a,b; Kinney et al. 1995). In studies in which the cause of death was evaluated, particle air pollution was associated with both respiratory and cardiovascular mortality but not with mortality due to other causes (Fairley 1990; Pope et al. 1992; Schwartz and Dockery 1992b; Schwartz 1994b). Two recent prospective cohort studies also observed that increased long-term average levels of fine particulate air pollution were associated with an increased risk of mortality, primarily cardiopulmonary mortality (Dockery et al. 1993; Pope et al. 1995).

In addition to studies linking the effects of PM with excess mortality, a number of epidemiologic studies have observed associations between particulate air pollution and hospitalizations due to respiratory causes (Pope 1989, 1991; Schwartz 1994b,c). Sulfate ion, a marker for fine particle mass in eastern North America, has been associated with respiratory health admissions in several cities in New York (Thurston et al. 1992) and Ontario (Bates and Sitzo 1987; Thurston et al. 1994, Burnett et al. 1994). An association of PM and hospital admissions due to cardiovascular causes was found in Minneapolis, MN (Schwartz 1994d), and Ontario, Canada (Burnett et al. 1995). The largest estimated effects were found for congestive heart failure.

One of the major problems in trying to determine whether elevated levels of PM cause human health effects or how such effects may occur is that the physiological responses to PM have not been clarified. Seaton and colleagues hypothesized that the deposition of particles in the airways results in the release of acute inflammatory mediators, such as tumor necrosis factor alpha, which in turn induce or increase levels of circulating hematologic factors (Seaton et al. 1995). Thus, the effects of PM on the cardiovascular system are seen to occur as a consequence of the induction of an inflammatory response in the airways. In support of this hypothesis, it is known that levels of several clotting factors—such as fibrinogen, factor VII, and plasminogen activator inhibitor—are increased in inflammatory responses. Fibrinogen is also an important determinant of plasma viscosity; thus, release of mediators such as fibrinogen could increase plasma viscosity and affect the coagulability of blood.

Studies in rats have shown that PM<sub>10</sub> particles eluted from filters at a monitoring site in Edinburgh, Scotland, cause proinflammatory effects (such as increases in bronchoalveolar lavage [BAL] neutrophils and total protein, and increased epithelial permeability) 6 hours after intratracheal instillation into the lungs (Li et al. 1997). In addition, BAL leukocytes from PM<sub>10</sub>-treated rats produced greater amounts of nitric oxide and tumor necrosis factor alpha in culture than control cells produced (Li et al. 1997). Preliminary results from the ongoing animal studies of Godleski and colleagues (normal and compromised dogs and rats) and Gordon and colleagues (normal and compromised rats) also support the notion that exposure to particles concentrated from ambient air induces an inflammatory response in the airways and may alter cardiovascular parameters such as electrocardiogram pattern (Godleski et al. 1996, 1997) and pulse rate (Gordon et al. 1997; Nadziejko et al. 1997). In addition, inhalation or instillation of fuel oil fly ash, a combustion-generated urban particulate, has been shown to induce inflammation and death in compromised rat models with cardiorespiratory disease (Costa et al. 1994; Killingsworth et al. 1997; Watkinson et al. 1998).

Few studies have explored the possible links between particle pollution and cardiovascular endpoints in humans. A recent cross-sectional epidemiologic study by Peters and colleagues found that residents of Augsburg, Germany, showed elevated plasma viscosity during a major air pollution episode. This response suggests that PM might have induced an acute inflammatory response in the airways resulting in the release of mediators that affected the viscosity of blood, thus implying a possible association between particulate air pollution and the human cardiovascular system (Peters et al. 1997). HEI funded the study ofDockery and Pope and colleagues to determine whether exposure to episodes of particulate air pollution resulted in transient declines in blood oxygenation and changes in clinical symptoms; the investigators went further and checked the effects of PM on pulse rate in the data already gathered.

TECHNICAL EVALUATION

STUDY OBJECTIVES

The original objective of this one-year study was to evaluate the association of daily measures of particulate air pollution (PM<sub>10</sub>) with acute changes in blood oxygen satu-
ration and symptoms of respiratory illness in an elderly population living at moderately high altitude. During the course of HEI’s review of the investigators’ draft report, other researchers reported preliminary data suggesting that exposure to PM might be associated with changes in heart rate in humans (Peters et al. 1997) and animals (Godleski et al. 1997; Gordon et al. 1997). As the instruments used to measure oxygen saturation—pulse oximeters—had also collected pulse rate information, Dockery and Pope subsequently evaluated the effects of PM$_{10}$ on pulse rate in their study population.

STUDY DESIGN

The investigators conducted the study in the Utah Valley during the winter of 1995-1996. The site was chosen because this area has historically experienced relatively high levels of PM$_{10}$ resulting from point source emissions from a steel mill, together with motor vehicle emissions and wood smoke, and compounded by temperature inversions during the winter. Another reason for the choice of site is that the valley is approximately 1,400 meters above sea level. Because of the shape of the oxyhemoglobin dissociation curve, relatively small declines in the partial pressure of oxygen in the blood at this altitude cause greater declines in oxygen saturation than occur at sea level.

To study the effects of exposure to PM$_{10}$ on oxygen saturation and pulse rate, and on symptoms of respiratory distress, the investigators recruited two panels of nonsmoking elderly people living near air pollution monitors. One group of participants lived at home with their spouses; the other group lived in a retirement home. An intriguing aspect of this study was its focus on a potentially sensitive population. Although the subjects were elderly and most had a history of heart and/or lung disease, all were healthy enough to live relatively independently, and the small changes in oxygen saturation and pulse rate described in the study did not lead to significant clinical problems. A study of elderly subjects in even more precarious health might have shown changes not seen in this study population.

A research coordinator and assistant visited each private home and instructed the subjects on the use of a Nellcor N20-P pulse oximeter, which measured oxygen saturation (and also provided measurements of pulse rate). For this population, three-minute oximeter measurements were made shortly after arising and before going to bed. At night, the subjects completed a health diary for symptoms they had experienced during the day. Following the initial visit, the assistant returned 7 days later and then every 2 weeks during the study period. For subjects living in the retirement home, oximeter measurements were made only once a day, between 5 and 7 p.m. One limitation of this approach is that the largest changes in an individual’s oxygen saturation occur during night sleep (American Thoracic Society 1995). Thus, as noted by the investigators, the “snapshot” measurement protocol described in the study might have missed the times of the day at which large changes in oxygen saturation occurred. Continuous monitoring would provide measurements of oxygen saturation at the times of expected greatest variation.

QUALITY CONTROL

Each pulse oximeter was tested for accuracy once each month. In addition, at each visit, a control pulse oximeter was run simultaneously with the individual’s oximeter and readings were compared. The investigators found that the reproducibility among the oximeters was very high. The levels of oxygen saturation recorded by the oximeters in this study were over 90%, however, which is above the range of greatest accuracy (between 70% and 90%) for the Nellcor N-20P and other oximeters (Severinghaus and Naifeh 1987; Severinghaus et al. 1989). Thus, as noted by Dockery and Pope, it is possible that the use of oximeters at high oxygen saturation levels may have been a source of measurement error in the study. It is not clear whether this may have biased the comparison of outcomes at different saturation levels or merely compressed the scale of the oximeter readings.

POLLUTION AND WEATHER DATA

The Division of Air Quality, Utah State Department of Environmental Quality, monitored PM$_{2.5}$ daily at three sites in the valley. Samples for each 24-hour period were collected starting at midnight. Daily 24-hour average and 8-hour high carbon monoxide (CO) levels were monitored by the Utah State Department of Health at five sites in the valley. Data on temperature, humidity, and barometric pressure were collected each day at a weather station located at Brigham Young University, approximately 5 miles from the participants’ residences.

Although most studies of PM health effects have relied on ambient fixed-site monitors, there is concern that readings from outdoor monitors may not reflect personal exposure accurately. As noted by the investigators, subjects over 70 years old may reasonably be expected to spend a considerable part of the winter season indoors. Thus, the study participants might have been exposed to pollutants or levels of particle pollution indoors that differed from those measured by the fixed outdoor monitors. In the future, personal exposure monitors, although they are more diffi-
cult to use and more expensive than fixed monitors, should be considered because they provide a more accurate measurement of individual exposures to PM.

**STATISTICAL METHODS**

The investigators plotted key variables together over time. To evaluate simple pairwise comparisons, they calculated Pearson correlation coefficients between oxygen saturation, pulse rate, pollution variables, and the weather variables. They then estimated fixed-effects autoregressive multiple regression models.

To evaluate potential lagged relationships between oxygen saturation, pulse rate, PM, and barometric pressure, the investigators estimated both single-period models and lagged moving average models with a lag structure of up to 7 days. Because the investigators observed statistically significant autocorrelation, they estimated first-order autoregressive models, using the maximum likelihood estimation method (SAS Institute 1988). The investigators also estimated models after stratifying data by health status, age, and sex, and by including CO levels.

The investigators analyzed binary symptom variables by estimating fixed-effects logistic regression models. For PM$_{10}$, single-period and 7-day-lagged moving average models were used to analyze each respiratory symptom. In addition, the investigators created a binary variable indicating the presence of any one of the lower respiratory illness symptoms. To address the issue of serial correlation in reported daily symptoms for each subject, they used an autoregressive logistic approach to model the conditional expectation of the binary dependent symptom variables. These approaches seem appropriate, although the implied statistical models have yet to be validated.

Other approaches to data analysis may also be appropriate for this data set, for example, in the investigators’ analysis of the association of previous-day PM$_{10}$ concentration and pulse rate. Figure 5 of the Investigators’ Report depicts the data and the best-fitting linear model, but it is hard to tell whether the data points are truly linear or nonlinear. Furthermore, the investigators assumed that the scatter around the straight line in Figure 5 was Gaussian, but it is not clear that this was correct, and Dockery and Pope apparently did not check the distribution of the residuals to see whether the inclusion of covariates might have substantially improved fit.

In addition, the investigators did not discuss residuals or outliers, either of which might have revealed bias in the data, and might have led to new analyses with increased precision, by a) using a more accurate model or b) setting aside data points that did not fit the model. Moreover, although there was a high degree of compliance by subjects in the study, the investigators do not discuss how missing data were handled.

**RESULTS AND DISCUSSION**

The investigators successfully achieved their stated objectives: measuring the effects of PM on oxygen saturation and clinical symptoms in an elderly population. In addition, they analyzed the accumulated pulse oximeter data to assess the effects of PM on pulse rate.

The key results of the study are summarized and discussed in the following sections.

**Oxygen Saturation**

*No consistent association was found between ambient PM$_{10}$ levels and mean arterial blood oxygen saturation.*

Analysis of the entire cohort indicated that there was no association between oxygen saturation and either contemporaneous or lagged (previous-day’s or 5-day-lagged moving average) PM$_{10}$ levels. When the data were stratified, the investigators did find a statistically significant negative association between oxygen saturation and the previous-day’s or 5-day-lagged moving average PM$_{10}$ for males over 80 years old. Controlling for weather variables had little impact on the estimated effects of PM$_{10}$ on oxygen saturation.

As discussed by the investigators, these findings do not support their original hypothesis that increases in PM levels may lead to changes in blood oxygen saturation. It is possible that a group in more precarious health might have shown different effects. Nonetheless, within the range of PM values assessed, the negative findings of PM on oxygen saturation of the arterial blood at high altitude makes it unlikely that PM would produce physiologically significant reductions at lower altitudes.

**Symptoms**

*Based on symptom diaries kept by private home residents, the investigators found no associations between symptoms reported and concurrent or lagged PM$_{10}$.*

Although the investigators found no association between PM and clinical symptoms based on the use of self-reported symptom diaries, in future studies changes in symptoms could be assessed more accurately by evaluating the participants at the start of and during the study; for example, by performing tests of pulmonary function or by making objective measurements of respiratory symptoms or heart disease.
Pulse Rate

In a post hoc analysis, the investigators found a small but statistically significant positive association between daily pulse rate and PM10 exposure up to 6 days previously.

During the write up of their report, Dockery and Pope examined the oximeter data they had collected for effects on pulse rate. The investigators found a positive association between PM10 exposure and daily pulse rate, expressed in two different ways: an increase in heart beats per minute, and an increased odds ratio of having a pulse rate higher than the individual's average pulse rate over the study period. They reported that a 100μg/m³ increase in the previous day's PM10, for example, was associated with an estimated increase of 0.8 beats per minute. They also reported that the probability of an increase in pulse rate (5 or 10 beats per minute above an individual average) was associated with average PM10 over the previous 1 to 5 days. Each 100μg/m³ increase in PM10 was associated with a 30% increased relative odds of having a pulse rate 5 beats per minute higher on the succeeding day, and a 95% increased relative odds of a pulse rate 10 beats per minute higher. Including CO in the models resulted in either unchanged or slightly larger estimated effects of PM10 on pulse rate, depending on the model; controlling for weather variables had little impact on the estimated effects.

This association of PM and changes in pulse rate is consistent with data from epidemiologic studies (Peters et al. 1997), and from preliminary toxicologic studies that indicate effects of PM on the cardiopulmonary system (Godleski et al. 1996; Godleski et al. 1997; Gordon et al. 1997; Nadziejko et al. 1997). The overall effect reported in Dockery and Pope's study was small, however, and might be explained by uncontrolled confounding or other biases. In addition, as indicated in Table 7 of the Investigators’ Report, the association between pulse rate and PM was driven largely by effects on the retirement home residents.

Barometric Pressure

The investigators found a negative association between daily barometric pressure and pulse rate, and a positive association between barometric pressure and oxygen saturation.

The association of barometric pressure with both oxygen saturation and pulse rate appeared to be due to the concurrent day’s barometric pressure, with no evidence for a lagged relationship. Including pollution variables in the models had little effect on the level of association. This is an intriguing finding, but perhaps it is not unexpected as atmospheric inversions occur and levels of pollutants increase with periods of high barometric pressure.

All results observed in this study need to be interpreted in the context that the air pollution episodes were quite small. The atmospheric conditions associated with episodes of high concentrations of particulate pollution (snow cover in the Utah Valley accompanied by a near stationary high pressure system over the western Rocky Mountains) did not occur during the study period.

IMPLICATIONS FOR FUTURE RESEARCH

Dockery and Pope found that their study subjects’ level of compliance in taking readings of oxygen saturation and pulse rate was 87% to 88% for the private home panel, and 74% for the retirement home panel, suggesting that their approach—allowing individuals to take their own oxygen saturation and pulse rate measurements in a home setting, rather than in a laboratory or clinic—may be useful in future epidemiologic studies of particulate pollution effects. Modifications of the study design and statistical approaches used in the current study may improve the ability to detect associations between particulate pollution and cardiovascular parameters. As discussed in the Study Design section, studying less healthy subjects, continuous monitoring of oxygen saturation and pulse rate, the use of personal exposure monitors, and alternative data analysis should be considered in future studies.

The finding that barometric pressure was associated with changes in oxygen saturation and pulse rate is intriguing and suggests a need for studies to determine whether barometric pressure may be relevant to the morbidity and mortality effects of pollutants. The investigators noted that barometric pressure is generally positively associated with particulate air pollution, so not including barometric pressure in models may result in underestimating the health effects of particle pollution.

CONCLUSIONS

Dockery and Pope conducted a preliminary study to explore mechanisms of PM-associated health effects in two populations of elderly subjects living at high altitudes (Utah Valley). The study was designed to examine the hypothesis that elevated levels of PM affect blood oxygen saturation.

The investigators found that elevations in ambient levels of PM were not significantly associated with oxygen saturation except for males 80 years of age or older. Also, PM levels did not affect clinical symptoms. In a post hoc analysis, the investigators reported a small increase in daily pulse rate associated with exposure to PM on the previous 1 to 5 days. These findings are intriguing and warrant further
investigation using continuous monitoring techniques with
careful control of medications and other potential con­
founding factors.

Although the investigators did not find support for their
primary hypothesis, they established the feasibility of
measuring oxygen saturation and pulse rate in a community
setting. The comparative good health of the study partici­
pants, the "snapshot" oximetry and pulse measurements,
and the generally low levels of pollution during the study
period limit the interpretation of the findings.

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