HEI

STATEMENT

Synopsis of Research Report 174

HEALTH EFFECTS INSTITUTE

Health Impact of Changes in Air Pollution Levels and PM Composition Brought by the 2008 Olympic Games in Beijing

INTRODUCTION

HEI's Outcomes Research Program has been designed to evaluate the effects of regulatory and other actions taken to improve air quality. The overall goal has been to provide evidence about the extent to which air quality regulations may or may not have improved air quality and health. Some funded studies have looked at the effects of interventions lasting only a limited period of time. These studies took advantage of a unique event such as the 1996 Atlanta Olympics, for which traffic and other changes were to be made in the local area with the goal of improving air quality for the duration of the event. The current study capitalized on a similar unique event.

In 2006 Dr. Junfeng (Jim) Zhang, then of the University of Medicine and Dentistry of New Jersey–School of Public Health and the Environmental and Occupational Health Sciences Institute at Rutgers University, submitted a preliminary application to HEI, "Health Impact of Changes in Air Pollution Levels and PM Composition Brought by the 2008 Olympic Games in Beijing," in response to a request for preliminary applications issued by HEI. The investigator indicated that the Chinese government was launching a series of aggressive policies to reduce local and regional emissions that affected air quality in the greater Beijing metropolitan area in the period leading up to and during the 2008 Beijing Olympic Games. These controls aimed to limit both vehicular traffic on Beijing roads and emissions from industrial, power generation, and commercial facilities in Beijing, as well as construction activities. The goals of the study were to measure levels of air pollutants in the city and evaluate prospectively the impact on human cardiovascular responses of the likely changes in air pollution levels that would be associated with the control measures to be implemented. Zhang and colleagues hypothesized that levels of multiple cardiovascular biomarkers would change significantly during the Olympic air pollution reduction period compared with the pre-Olympics period, and would revert to pre-Olympics levels following relaxation of the air pollution controls after the Olympics. The investigators also hypothesized that changes in specific pollutants would be associated with changes in specific biomarkers.

APPROACH

Zhang and colleagues divided the study into three periods: the *pre-Olympics period* (June 2–July 20, 2008), the *during-Olympics period* (July 21–September 19), and the *post-Olympics period* (September 20–October 30). They made daily measurements of multiple air pollutants on the roof of a seven-story building located in the center of the Peking University First Hospital campus: mass concentration of particles less than or equal to 2.5 µm in aerodynamic diameter ($PM_{2.5}$), elemental carbon (EC) and organic carbon (OC), inorganic ions (including sulfate and nitrate), polycyclic aromatic hydrocarbons, and trace elements (including multiple transition metals such as nickel and vanadium). The investigators also measured levels of multiple gaseous pollutants — ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitric oxide (NO), nitrogen dioxide (NO_2), nitrous oxides (NO_x) — as well as ambient temperature and relative humidity at the central site. As a result of technical problems with the instrument at the central site, the investigators had to rely on a site 7 km from where the other pollutant measurements were

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Jim Zhang at the University of Medicine and Dentistry of New Jersey–School of Public Health, Piscataway, N.J., and colleagues. The complete report, *Cardiorespiratory Biomarker Responses in Healthy Young Adults to Drastic Air Quality Changes Surrounding the 2008 Beijing Olympics* (© 2013 Health Effects Institute), can be obtained from HEI or our Web site (see last page).

made for most measurements of the number of ultrafine particles (<100 nm in aerodynamic diameter) — that is, particle number concentration and total particle number (TPN).

The investigators reported results from 125 healthy young (ages 19–33) subjects — primarily medical residents who worked at Peking First University Hospital in Central Beijing and who lived within 5 km of the Hospital. At each of six clinical visits — two within each period (and separated by at least 1 week) — vital signs and a set of biomarkers were measured in each study subject. The endpoints measured included electrocardiography (ECG), heart rate (HR) and heart rate variability (HRV), systolic (SBP) and diastolic (DBP) blood pressure; biomarkers of systemic inflammation and oxidative stress, including white blood cell (WBC) counts and differential cell counts in plasma, as well as levels of fibrinogen, C-reactive protein (CRP), and urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG); biomarkers of pulmonary inflammation and oxidative stress: fractional exhaled nitric oxide (FeNO), and exhaled breath condensate (EBC) — specifically, pH (from which they calculated hydrogen ion concentration), nitrate, nitrite, nitrite+nitrate, and 8-isoprostane; and biomarkers of plasma clotting pathways: platelet activation (soluble P-selectin [sCD62P] and soluble CD40 ligand [sCD40L]), platelet aggregation, and von Willebrand factor [vWF]).

The investigators used two approaches to analyze associations between pollutant levels and most biomarkers — mixed models to examine the effects of period (pre-, during-, and post-Olympics), and a time-series analysis to examine pollutant effects, focusing on changes within the few days prior to a clinical visit (lag days 0–6, where lag day 0 is the day of a visit). Zhang and colleagues also conducted multiple sensitivity analyses for the associations between biomarkers and pollutant levels.

RESULTS

Compared with the pre-Olympics period, the mean during-Olympics concentrations of all measured pollutants, except O_3, decreased: large decreases (40–60%) were found for the pollutant gases SO_2, CO, and NO_2, and particulate pollutants ($PM_{2.5}$ and its components EC and TPN) also decreased substantially. Smaller changes were found in sulfate and OC concentrations. The decreases in concentration of SO_2, CO, and NO_2 were statistically significant, but the reductions in mean concentrations of $PM_{2.5}$, sulfate, EC, TPN, and OC were not. By contrast, O_3 concentrations increased during the Olympics. Compared with the during-Olympics period, post-Olympics concentrations of most pollutants increased, except for sulfate and O_3, which decreased.

During-Olympics levels of several cardiovascular markers decreased compared with pre-Olympics levels. The biggest percent decreases were observed in FeNO (60.3%), 8-OHdG (58.3%), EBC pH (which increased 3.5%, but corresponded to a decrease in hydrogen ion concentration of 46%), sCD62P (34%), EBC nitrite (30.0%), EBC nitrate (21.5%), EBC nitrite+nitrate (17.6%), and vWF (13.1%). Smaller decreases were also seen in HR (1.7%), SBP (1.8%), and levels of sCD40L (5.7%). Unexpected small increases in platelet aggregation (7.4%) and RBC numbers (0.9%) were also found. No significant changes were found in any HRV measurement or DBP. After the Olympics, concentrations of most biomarkers increased (after decreasing in the during-Olympics period).

INTERPRETATION AND CONCLUSIONS

In its independent review, the HEI Health Review Committee considered the study an important contribution to the literature regarding short-term interventions and their impacts on acute health responses — it is one of the first studies, and to date the most comprehensive, to evaluate changes in biologic endpoints associated with the control measures taken to reduce air pollution associated with specific, short-term events. The investigators capitalized on the large changes in air pollutants to conduct an analysis by period (pre-, during-, and post-Olympics) to assess whether biomarkers were associated with those changes. A more traditional time-series analysis, focusing on very proximate (within a few days) pollution–biomarker associations, gave a somewhat complementary perspective of the data. The exposure assessment for multiple pollutants was also relatively comprehensive. Apart from measurements of particle number, the measurements of all pollutants were made at a single central Beijing site, close to where the participants lived and worked. Furthermore, in this well-characterized group of healthy subjects, Zhang and colleagues evaluated a representative group of pulmonary, systemic, and urinary biomarkers in pathways considered relevant for understanding the pathophysiologic mechanisms of the effects of air pollutants. Zhang and colleagues also conducted appropriate sensitivity analyses — including adjusting for meteorology and (in the time-series analyses) for an effect of period independent of pollution — to provide further support for their interpretations. Thus, the study represents one of the most comprehensive to date to evaluate the effects of exposure to air pollution on a myriad of potential short-term cardiovascular biomarkers.

Reviewing Zhang and colleagues' comparisons of pollutant concentrations before and during the Olympics, the Committee agreed that the investigators found many during-Olympics changes in pollutant levels and that these were consistent with the effects of a successful intervention. However, the Committee noted that the investigators had not designed the study to identify the extent to which the control measures per se could be considered causal in producing the changes in ambient pollutant levels. Therefore, the changes in the biomarkers they had measured, which were consistent with the measured improvements of air quality, may not be directly attributed to the interventions.

The large during-Olympics decreases (40–60%) found for the pollutant gases SO_2, CO, and NO_2, and for particulate pollutants (EC and TPN, with smaller changes in $PM_{2.5}$, SO_4^{2-}, and OC concentrations) were generally consistent with other studies of pollutant concentrations in Beijing conducted in the time period around the Olympics. The major decrease in during-Olympics concentrations of SO_2 was most likely due to the restrictions imposed on construction and power plant activities in and around Beijing. Decreases in NO_2, CO, EC, and TPN (the last a marker of ultrafine particles, which dominate this measure) were most likely attributable to restrictions on traffic. After the controls were relaxed in the post-Olympics period, concentrations of most pollutants (except O_3) increased, and changes were seen in PM components that were generally consistent with increases in traffic and other emissions sources.

Changes in the levels of several cardiovascular biomarkers from the pre- to during-Olympics periods were observed, and the Committee agreed with Zhang and colleagues that these changes were generally consistent with the investigators' hypothesis that changes would be in a direction reflecting a decrease in adverse effects. Using both by-period and time-series analyses, the investigators found large changes in some biomarkers in several pathophysiologic pathways through which PM may exert its effects — coagulation in the circulation (sCD62P and vWF), inflammation in the airways (FeNO, EBC hydrogen ion, nitrite, and nitrate), and the activation of oxidative stress (urinary 8-OHdG). However, unexpectedly and without obvious explanation, levels of some biomarkers — in particular platelet aggregation in the coagulation pathway — changed in the opposite direction from other biomarkers in the same pathway. Given the number of observations made in the study, a few might have increased by chance.

The finding that the post-Olympics mean levels of several biomarkers increased compared with during-Olympics levels was largely consistent with the investigators' hypotheses that changes in air pollutant levels in the different periods would be reflected in changes in biomarker levels and that the pre- to during- and during- to post-Olympics changes would be inversely related. It is noteworthy that these observations were made in young healthy subjects and so may not reflect changes that might be seen in susceptible populations, such as those with pre-existing cardiorespiratory conditions (e.g., asthma or cardiovascular disease) or those with variations in genes whose protein products are involved in physiologic defenses. In addition, given the study's focus on acute reversible changes after exposure to air pollution, this study does not shed light on whether these changes would have any impact, positive or negative, on disease or adverse outcomes.

Although the investigators had hypothesized that individual pollutants would be associated with changes in individual biomarkers, multiple pollutants were associated with every biomarker. In hindsight, attributing changes to specific pollutants was likely to be challenging, given that the intervention was multifaceted and affected multiple sources and pollutants.

The multiple sensitivity analyses Zhang's team conducted bolstered the interpretation that the changes in biomarkers were related to changes in levels of air pollution. However, the Committee thought that some caution should be retained in attributing the between-period biomarker differences to pollution, given the possibility that other unmeasured risk factors — such as changes in virus infections, ambient noise levels, or subtle alterations in lifestyle patterns and stress levels in the participants in response to the atmosphere surrounding the Olympics — might have contributed to the differences observed. Because of the large influence of between-period contrasts in the time-series analyses of the association of specific pollutants with biomarkers, similar caution is needed for these results. The time-series analyses were generally consistent with the between-period analyses, but could not discriminate among the several pollutants, which changed in concert. Exposure misclassification may also have been an issue — that is, pollutant measurements made at the outdoor site may not have accurately reflected the actual level of exposure of the study participants. However, the Committee considered that it was unlikely there was a systematic pattern to this type of error, and so this possible error was considered unlikely to have an impact on the effect estimates reported in the current study.

The Committee suggested that future studies to evaluate the effects of an intervention in a city should include a nearby control area — as similar in characteristics to the area of the intervention as possible — in which exposure would be measured and a similar group of participants would be followed with the same instruments over the same time period. Although the cost of the study would increase substantially, the Committee thought inclusion of this control would enhance the investigators' ability to attribute the changes in pollutant levels and biomarkers to the intervention and greatly reduce the limitations of the interpretation of the results as noted above.

Overall, this study carried out by Zhang and colleagues provides important supporting evidence that air quality improvements such as those found during the Beijing Olympics can improve health biomarkers, with the potential for beneficial health effects in the affected population.

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