INTRODUCTION

There is ample epidemiological and toxicological evidence that short- and long-term exposures to ambient air pollutants are associated with CVD events such as heart attacks and stroke. At the same time, evidence also indicates that the likelihood of CVD events is associated with social and economic disadvantage factors.

In the United States, population subgroups with lower socioeconomic status, which are primarily non-White, and which encounter other adverse social and community-based stressors, experience disproportionately higher levels of air pollution compared with other population subgroups. Because of the interplay between air pollution exposures, social stressors, and CVD outcomes, disentangling the role of social stressors as modifiers or confounders of the associations between air pollution and CVD is imperative to identify potentially vulnerable populations and to provide the additional scientific evidence needed to support mitigation measures.

In the current study, Dr. Jane Clougherty and colleagues sought to quantify the combined effects of exposures to multiple pollutants and stressors (e.g., violence and chronic stress) on CVD events and to identify which social stressors influence susceptibility to the health effects of air pollution, using data for 1.1 million people living in New York City (NYC).

APPROACH

Clougherty and colleagues pursued three specific aims. The first aim was to assess whether social stressors confound or modify the relationships between CVD events and air pollutant exposures. It also assessed the separate and combined associations of stressors and air pollutants with CVD events, all estimated at the same spatial (census-tract) resolution and annual timescale. The second aim was to examine the association between daily

What This Study Adds

- This study examined whether the associations between community- and individual-level cardiovascular disease (CVD) events and ambient air pollutant concentrations vary with social stress.
- Unique datasets included data on CVD events in all New York City hospitals, citywide levels of fine particulate matter, nitrogen dioxide, sulfur dioxide, and ozone, community-level social stressors, and noise disturbance.
- The study demonstrated that variations in the social stressors in NYC were associated with CVD events, reinforcing the importance of considering such stressors in air pollution health analyses.
- At the same time, the study found that associations between the pollutants and CVD were attenuated when adjusting for social stressors.
- Given the several limitations in the analysis, the HEI Review Committee disagreed with the investigators’ interpretation of Aim 3 results that associations between air pollution and CVD were stronger in communities with higher stressor levels.
- Future studies attempting to disentangle social stressor from air pollution effects on CVD events should build on the steps taken here by further investigating important social stressor confounders and modifiers.
average exposures to individual pollutants and copollutants and the short-term individual-level risk of CVD events, evaluating exposures during multiple days before the CVD event. The third aim was to examine effect modification by community-level social stressors on the relationship between the short-term air pollution exposures and CVD events assessed in Aim 2.

The investigators used existing datasets for the health outcome analyses to construct air pollution exposure estimates and to characterize multiple social stressors. They obtained data on in- and outpatient CVD events between 2005 and 2011 from all NYC hospitals (1,113,185 events). Data on concentrations of fine particulate matter less than 2.5 µm in aerodynamic diameter (PM$_{2.5}$), nitrogen dioxide (NO$_2$), sulfur dioxide (SO$_2$), and ozone were obtained from the NYC Community Air Survey (NYCCAS). The data were collected between 2008 and 2010 over a 2-week period during each season from 155 sites across NYC, and provided information about spatial variability. To obtain information on temporal variability in air pollutant concentrations, the investigators used daily air pollution data from the U.S. Environmental Protection Agency (EPA)'s Air Quality System (AQS).

A unique aspect of this study was the use of many different datasets to obtain data on community-level social stressors (e.g., poverty metrics, violent crime rates, a socioeconomic deprivation index [SDI], and racial and economic segregation) and noise. The investigators then used statistical techniques to create social stressor indices that combined the many stressor variables into groups. These included the SDI, which represented material hardship; a variable representing racial and economic segregation; and three indices representing (1) violence and physical disorder, (2) crowding and poor resource access, and (3) noise and air pollution complaints collected from several datasets (U.S. Census, NYC Housing and Vacancy Survey, NYC Police Department, and NYC School Districts).

For Aim 1, Clougherty and colleagues applied 100 × 100–m concentration surfaces of each pollutant across the study area that NYCCAS had previously developed using a land use regression model combined with spatial smoothing. Associations of annual average pollutant concentrations and social-stressor exposures with annual CVD in- and out-patient hospitalizations at the census-tract level were analyzed using negative binomial regression models. The investigators conducted analyses using several mutually adjusted models (i.e., one pollutant and one stressor in the same model) and fully adjusted models (i.e., multiple pollutants and selected social stressors). They tested the sensitivity of their results to spatial autocorrelation and spatial scale and by running all main models with ischemic heart disease events (their most prevalent CVD subdiagnosis) as the health outcome.

For Aims 2 and 3, the investigators performed analyses at the individual level, including daily data for in-patient CVD events only (837,523) occurring over the study period (2005–2011). To adjust for nontime-varying covariates (e.g., age, race, and sex), the investigators implemented a case-crossover approach in which individuals with a CVD event served as their own control during a time when they did not have an event. Control days were selected using time-stratified sampling. The investigators assigned annual average NYCCAS pollutant concentrations to each geocoded residence, which they combined with daily citywide average AQS data to estimate exposures at each residence for up to 6 days preceding the event and referent dates.

For Aim 2, they used conditional logistical regression to examine associations between multiple pollutants on the day of the event and up to 6 days before and all CVD events and CVD subdiagnoses. They performed copollutant (i.e., multiple pollutants in one model) adjustments using penalized splines.

For Aim 3, the investigators evaluated effect modification in their same-day copollutant exposure models from Aim 2 by including interaction terms between each pollutant and the social stressor data subdivided into quintiles or into two groups divided by the median. The investigators also ran several sensitivity analyses.

**KEY RESULTS**

In Aim 1 models testing each pollutant independently against census-tract-level CVD events, the investigators reported positive associations with NO$_2$ and SO$_2$ concentrations and inverse associations with O$_3$ exposure. In the investigators’ assessment of confounding, results were attenuated in models including one pollutant and one stressor in the same model and in fully adjusted models. When they evaluated effect modification, the investigators reported stronger associations between SO$_2$ and CVD across quintiles of increasing poverty. They also reported that associations between NO$_2$, PM$_{2.5}$, or SO$_2$ and CVD were higher across quintiles of increasing felony assault and violent crime rates, based on using the P value for trend and P values for associations between air pollutants and CVD within strata of the stressors. There were no differences in the magnitude of associations between pollutants...
and CVD by quintiles of SDI, income, or ICE I&R.

When the investigators ran case-crossover models at the individual level to examine associations between copollutant exposures and CVD event (Aim 2), they reported an increase in CVD event risk per 10-unit increase in NO$_2$ (ppb) and PM$_{2.5}$ ($\mu$g/m$^3$) exposure and a decreased risk with O$_3$ (ppb) exposure on the day of the event (lag day 0). Associations reported between CVD events and NO$_2$ or PM$_{2.5}$ exposures across all other lag days (1 to 6 days before the event), and for any associations between CVD and wintertime SO$_2$ levels, were generally consistent with the null.

In their evaluation of social stressor effect modification at the individual level (Aim 3), the investigators did not report consistent increases in CVD risk with any of the pollutants across social stressor quintiles (e.g., a consistent increase in CVD events across communities with higher violent crime rates). They reported that NO$_2$ was positively associated with CVD in the highest quintile of community violence and SDI, which they supported with the $P$ values for associations between air pollutants and CVD within individual stressor strata. Tests of interaction were consistent with the null for the UHF-level factor scores and noise.

**REVIEW COMMITTEE EVALUATION**

In its independent review of the study, the HEI Review Committee found that Clougherty and colleagues used several rich and well-validated data sources to address important questions about the role of social stressors as possible confounders or effect modifiers in investigations of the relationships between air pollutants and CVD events. The Committee appreciated the use of a case-crossover design to control for non-time-varying confounders in Aims 2 and 3. They also commended the investigators for their inclusion of noise as a potential stressor as well as their extensive sensitivity analyses to test and assess alternative approaches to the exposure assessments, stressor categorizations, and inclusion of copollutants in the models.

The Committee thought that a limitation of the study was the potential for temporal mismatch among the CVD data, exposure data, and stressor data because it was not always clear when temporal mismatches occurred or the potential implications for the results. They thought that exposure assessment could have been improved with a dataset incorporating day-to-day variations in spatial patterns of pollutant concentrations to fully capture the spatial and temporal variability.

The Committee also thought that the investigators could have improved their interpretation and presentation of social stressor confounding results in Aim 1 by comparing results from their three types of models: (1) single-pollutant models, (2) mutually adjusted models, and (3) fully adjusted models. This would have allowed them to identify and discuss the presence and magnitude of confounding for specific stressors more fully. The Statement Figure, for example, illustrates confounding by violent crime and the SDI for PM$_{2.5}$ using the results presented in the report.

![Statement Figure](image)

*Statement Figure. Attenuation of the association between PM$_{2.5}$ and CVD event rates (Aim 1) when social stressors (violent crime or the SDI) were added to the models. Data are shown as the incidence rate ratio (IRR) with 95% confidence intervals per interquartile range (IQR) for PM$_{2.5}$ (1.37 $\mu$g/m$^3$).*
but displayed in a manner that allows for the reader to draw conclusions about the presence and magnitude of confounding. In this example, the investigators reported a positive association between PM$_{2.5}$ and CVD event rates. However, the results were attenuated when these stressors were added to the models.

In addition, the investigators’ main conclusion for Aim 1 was that the associations between the social stressors and CVD events were stronger than those between the air pollutants and CVD events. There is an important caveat to this interpretation, which the investigators discussed in their report: the social stressors had large variability in this study and relatively large magnitudes of association with CVD, while the pollutants had relatively small variability across the study population and thus small magnitudes of association. Overall, the Committee thought that the investigators missed an opportunity to specify which stressors were important modifiers or confounders of the associations in Aim 1.

The Committee also disagreed with investigators’ approach to interpreting and conclusions about effect modification results. To support the conclusion that there was evidence of stronger associations in communities with worse stressor characteristics, the investigators used $P$ values for associations within individual strata of the census-level stressors and tests for trend. The Committee thought that the more appropriate evidence to support conclusions about effect modification would have involved statistical tests of interaction, as discussed above, as well as discussion of differences among the IRRs between strata. The Committee’s interpretation of the results in Aim 3 is that magnitude and direction of the associations varied greatly among the stressor categories.

CONCLUSIONS

The study helps highlight the importance of considering the role of distinct social stressors as risk factors for health outcomes such as CVD events. At the same time, the study added to the existing epidemiology literature on associations between air pollutant exposures and CVD events, while also examining the role of those social stressors on the relationships. It also added to the limited body of evidence exploring copollutant exposures and CVD.

There is a need for future studies to continue disentangling social stressor effects and build on the steps taken in this study. In particular, future studies should ensure systematic assessment of confounding and effect modification. They should also identify specific social stressors that act as confounders, identify the degree of potential confounding, and identify social stressor modifiers to help understand disproportionate susceptibility to pollution.