HEI

HEALTH EFFECTS INSTITUTE

STATEMENT

Synopsis of Research Report 181

Personal Exposure to Mixtures of Volatile Organic Compounds: Further Analysis of RIOPA Data

INTRODUCTION

Exposure to various volatile organic compounds (VOCs) has been associated with a wide range of adverse health outcomes. Assessments of exposure and health effects are complicated because many indoor and outdoor sources contribute VOCs, and because certain personal activities and behaviors may influence exposure substantially. Dr. Stuart Batterman of the University of Michigan in Ann Arbor and his colleagues used data from the Relationships of Indoor, Outdoor, and Personal Air (RIOPA) study and, to a lesser extent, the 1999–2000 data from the National Health and Nutrition Examination Survey (NHANES) to identify factors that influence exposure and to characterize exposure distributions for individual VOCs and mixtures, with particular emphasis on extreme values (high exposures).

The original RIOPA study was conducted in Los Angeles, California; Houston, Texas; and Elizabeth, New Jersey; it included approximately 300 subjects who did not smoke and who lived at various distances from air pollution sources. In addition to personal, indoor, and outdoor exposure measurements, the investigators collected information on factors that might affect exposures (determinants), such as housing characteristics, personal activities, and geographic and meteorologic information.

The 1999–2000 NHANES obtained personal measurements of VOCs for approximately 650 adult subjects in a U.S. population-based sample.

Aims of the current study were to investigate determinants of exposure to individual VOCs and to characterize the distributions of both individual VOCs and VOC mixtures, with particular emphasis on high exposures.

APPROACH

Fifteen VOCs were analyzed, including benzene, methyl *tert*-butyl ether, 1,4-dichlorobenzene, toluene, tetrachloroethylene, and chloroform.

Exposure determinants for individual VOCs in the RIOPA data set were modeled using linear mixed-effects models adjusted for clustering within cities and among individuals. A different set of determinants was used for each VOC and for each sample type (personal, indoor, outdoor).

Various distribution models were fitted for each VOC using personal exposure data from RIOPA and NHANES. The primary focus in these analyses was characterizing extreme values using

What This Study Adds

- Batterman and colleagues used data from RIOPA and NHANES to identify factors that influence exposures and to characterize exposure distributions for VOCs and VOC mixtures, with particular emphasis on high exposures.
- Factors shown to influence personal exposure included city, wind speed, home air exchange rate, number of rooms in the home, attached garage, pumping gas, and other family members showering.
- Distributions other than lognormal models may perform somewhat better in estimating high personal exposures and cancer risks. Interpretation of results was problematic because of the treatment of values below the limit of detection, the deletion of outlier values, and the use of a convenience sample.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Stuart Batterman at the University of Michigan, Ann Arbor, and colleagues. The complete report, *Personal Exposure to Mixtures of Volatile Organic Compounds: Modeling and Further Analysis of the RIOPA Data* (© 2014 Health Effects Institute), can be obtained from HEI or our Web site (see next page).

generalized extreme value models. Consequently, extreme value analyses were based on small numbers of highly exposed subjects (12 or 24 from RIOPA and 32 or 64 from NHANES), defined as subjects in the top 5% or 10% of the exposure distribution. For three VOCs (chloroform, 1,4-dichlorobenzene, and styrene) Batterman and colleagues fit two types of mixture models: a finite mixture of normal distributions, and a Dirichlet process mixture (DPM) of normal distributions.

Mixtures of VOCs studied in RIOPA were identified using positive matrix factorization and toxicologic modes of action. Then copulas, a class of probability models, were used to characterize the distribution of and dependence among different VOCs in the mixtures.

The performance of the different exposure distribution models was evaluated using goodness-of-fit statistics and simulated data. The investigators also compared cancer risks using standard risk assessment approaches.

MAIN RESULTS AND INTERPRETATION

Significant determinants of mean personal VOC exposure included city, wind speed, home air exchange rate, number of rooms in the home, attached garage, pumping gas, and other family members showering. Similar determinants were identified for indoor exposure, largely because the RIOPA participants spent most of their time at home (average 90%). In contrast, only a few significant determinants were identified for outdoor VOC exposure — city and weather characteristics.

In its independent review of the study, the HEI Health Review Committee noted that the study was well conceived and conducted and that, in particular, the analyses of exposure determinants were a novel and useful contribution to the literature. The Committee thought that their practical applicability was hampered to some extent because the investigators used a different set of possible determinants for each VOC and for each sample type; the exact magnitude of the effect of an exposure determinant could not be readily estimated.

The Committee did not agree with the investigators' treatment of values below the limit of detection (LOD) in the determinant analyses. The method of replacing all values below the LOD for a particular VOC with one single value (1/2 of the LOD), though commonly used, can cause problems if the number of observations below the LOD is considerable, as in this study. Thus the Committee felt that caution should be exercised in interpreting the determinant analyses for VOCs with high proportions of such values.

The analyses focused on extreme values were considered interesting. The investigators demonstrated that distributions other than the commonly applied lognormal models may perform somewhat better in estimating high personal exposures and cancer risks. In further distribution fitting for individual VOCs, the Committee appreciated that the investigators applied mixture models, which allowed estimation of entire VOC distributions because concentrations below extreme values also affect total population risk. The investigators' interpretation of the analyses for characterizing extreme values was thought to be problematic for several reasons. First, the results were affected by the considerable number of observations below the LOD and the way they were handled. This approach did not affect the extreme value analyses directly, but it did affect the comparison of those distributions with conventional lognormal distributions; the latter were fitted using the full data set, rather than only the top 5% or 10%, as for extreme value analyses. Second, the investigators deleted what they considered to be outliers and other influential values. The Committee thought these deletions were not adequately justified scientifically. Finally, the Committee suggested caution in generalizing the interpretations of the distribution characterizations because the RIOPA data set — which underlies the majority of analyses — was a convenience sample, not a representative population-based sample, as was NHANES.

CONCLUSIONS

Batterman and colleagues used RIOPA and NHANES data to investigate determinants of exposure and to characterize exposure distributions for VOCs and VOC mixtures, with particular emphasis on high exposures. The Committee thought the study was well conceived and conducted and the analyses of determinants were a novel and useful contribution. In the distribution fitting for individual VOCs, the Committee appreciated that the investigators applied mixture models, allowing estimation of entire VOC distributions. The statistical analyses focusing on extreme values were considered interesting, but the interpretation of results was problematic. The applicability in air pollution research of the methods for extreme value analyses developed in this study may be limited and further research is needed.

HEALTH
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INSTITUTE

101 Federal Street, Suite 500
Boston, MA 02110, USA
+1-617-488-2300 phone
+1-617-488-2335 fax

pubs@healtheffects.org
www.healtheffects.org

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