

# STATISTICAL SIGNIFICANCE

*Environmental exposures are present on continuous spectrum of exposure levels and throughout the lifespan and can affect population health. Individuals, however, may respond differently to the same exposure due to heterogeneous susceptibilities. Under such circumstances, it is crucial for statisticians to develop a systematic way of detecting and identifying a susceptible population under the continuous exposure setting, understand the subgroup characteristics, and provide suggestions in policy-making and public health policy assessments.*

## Susceptible Populations & Heterogeneous Effects

### ENVIRONMENTAL EXPOSURES

Negative environmental exposures are ubiquitous, including a wide range of natural and synthetic substances such as air pollutants, soil contaminants, and chemicals in drinking water, and have been shown as critical risk factors of chronic diseases and cancers. For instance, many studies have shown that people exposed to air pollutants (e.g., PM<sub>2.5</sub>, PM<sub>10</sub>, and SO<sub>2</sub>) had an increased risk of developing lung cancer and cardiovascular diseases (CVD). Indeed, the level of exposure is one of the key factors to the association of disease risk. To better understand the health risk of these environmental exposures, scientists aim to explore the exposure-response relationships for continuous exposures.

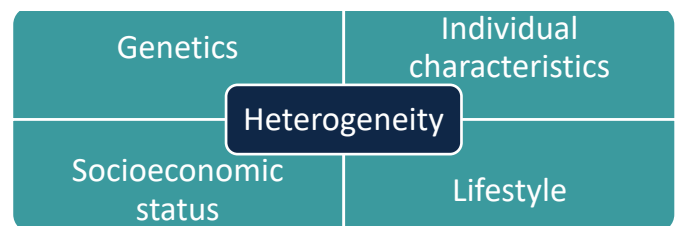


Urban air pollution includes activities from transportation, industrialization, and domestic use of fossil fuels. Source: TCTMD.

### POPULATION HETEROGENEITY AND SUSCEPTIBILITY

In fact, the impact of environmental hazards and occupational exposures on population health is never wholly uniform across the population. Health risks are different between individuals due to heterogeneity in genetics, individual characteristics, lifestyles, and socioeconomic status. For example, young and elderly are more vulnerable to air pollutants; BPA exposure is more strongly associated with the development of diabetes in premenopausal women than in postmenopausal women.

Therefore, identifying **susceptible populations** to environmental exposures becomes crucial steps for guiding development health policy and improving population health.



Some major components of population heterogeneity.

### SUBGROUP DETECTION AND IDENTIFICATION

One common strategy for subgroup identification is to evaluate the interaction between an exposure and a pre-defined group variable. To avoid the issues of false-positive findings and possible power loss due to post-hoc statistical tests are conducted over many potential subgroups, statisticians develop novel hypothesis testing procedures that systematically detect the existence of a meaningful subgroup with **heterogeneous effects** under the continuous exposure setting and depict the characteristics of the identified subgroup.

### OTHER APPLICATIONS AND SIGNIFICANCE

The proposed hypothesis testing procedures are applicable for subgroup detection in both observational studies with **continuous risk factors** and randomized trials with **continuous treatment**. A motivating example is a trial of convalescent plasma for COVID-19 hospitalized patients and interested in identifying a subgroup of patients who respond differently to a range of antibody titers. In the era of precision medicine, identifying **susceptible populations** or **subgroups with heterogeneous treatment effects** becomes a critical step in health risk assessment and treatment benefit evaluation, and ultimately improves population health.