Title: Epidemiological studies of environmental chemicals and breast cancer (2006-2016): A review informed by biological mechanisms

Purpose of the study. To distill the human evidence about environmental chemicals and breast cancer, we evaluated epidemiologic studies published since our 2007 review in Cancer. Our aims were (a) to integrate new evidence and (b) to evaluate how well study designs captured hypotheses suggested by toxicological and biological evidence, for example considering timing of exposure.

Methods: We systematically searched the PubMed database for articles with breast cancer outcomes published in 2006-2016 using terms for 134 environmental chemicals, sources, or biomarkers of exposure. We critically reviewed the articles and mapped them against biological evidence of genotoxicity, endocrine disruption, and windows of susceptibility.

Results: We identified 158 articles; 52 studies used geographic location to estimate exposure, 39 used biological measures, and the rest used employment or self-reports. Consistent with experimental evidence, key studies suggested higher risk for exposures during breast development to dichlorodiphenyltrichloroethane (DDT), dioxins, perfluorooctane-sulfonamide (PFOSA), and air pollution (risk estimates 2.14-5.0), and for occupational exposure to solvents and other mammary carcinogens, such as gasoline components (risk estimates 1.42-3.31). Most studies did not assess exposure during a biologically relevant window. Few considered genetic variation, but the Long Island Breast Cancer Study Project reported higher breast cancer risk for polycyclic aromatic hydrocarbons (PAHs) in women with certain genetic variations, especially in DNA repair genes. Two studies reported mixed results for novel assessments of estrogenic activity.

Conclusions: New studies that targeted toxicologically relevant chemicals and captured biological hypotheses about genetic variants or windows of breast susceptibility added to evidence of links between environmental chemicals and breast cancer. However, many biologically relevant chemicals, including current-use consumer product chemicals, have not been adequately studied in humans. Studies are challenged to reconstruct exposures that occurred decades before diagnosis or access biological samples stored that long. Other problems include measuring rapidly metabolized chemicals and evaluating exposure to mixtures.