



Summary of *Environmental Pollutants, Diet, Physical Activity, Body Size, and Breast Cancer: Where Do We Stand in Research to Identify Opportunities for Prevention?*

An overview of the supplement by the research team

Julia Green Brody, PhD,¹ Ruthann A. Rudel, MS,¹ Karin B. Michels, ScD, PhD,^{2,3} Kirsten B. Moysich, PhD,⁴ Leslie Bernstein, PhD,⁵ Kathleen R. Attfield, BS,¹ Sharon Gray, MA, MLS¹

Background

Breast cancer is the leading cause of death in US women between their late thirties and early fifties. Screening and improved treatment have contributed to improved survival. Incidence appears to have stabilized after rising for decades, and mortality has declined in the U.S. But these trends are discouraging in contrast with progress against other major killers such as heart disease and lung cancer in men. In this context, the breast cancer advocacy community has called for greater attention to research into breast cancer prevention as a major public health priority alongside screening and treatment.

Patterns in the incidence of breast cancer indicate that it's not just hereditary and that some routine environmental exposures as well as lifestyle may play a major role. This makes prevention a realistic goal in many cases. Based on large studies of twins, researchers estimate that factors other than inherited genes are involved in the vast majority of breast cancers. Incidence is rising rapidly in developing nations and in US immigrant populations. Five-fold variation in breast cancer incidence rates across the globe tells us that living in developed areas increases risk.

At the invitation of Susan G. Komen for the Cure, a multi-disciplinary team led by Silent Spring Institute in collaboration with researchers at Harvard Medical School, Roswell Park Cancer Institute, and the University of Southern California, undertook a systematic analysis of peer reviewed scientific research in topic areas with promise for breast cancer risk reduction. The review to date includes these topics: human studies of physical activity, body size, diet, and environmental pollutants, as well as toxicologic studies conducted in animals to identify chemicals that may be human breast carcinogens. We limited the review of diet to studies that collected information about what women ate before they were diagnosed, rather than asking them to recall their diet from earlier years. Results of previous research have been consistent in establishing that ionizing radiation, certain hormonal pharmaceuticals, age at first period and

¹ Silent Spring Institute, Newton, MA

² Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

³ Department of Epidemiology, Harvard School of Public Health, Boston, MA

⁴ Department of Epidemiology, Roswell Park Cancer Institute, Buffalo, NY

⁵ Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA

menopause, childlessness, age at a first full-term pregnancy, and alcohol consumption contribute to breast cancer. Detailed summaries of the reviewed articles are available in new online databases at www.silentspring.org/sciencereview and www.komen.org/environment. The databases include information on 460 articles on human studies on the association between breast cancer and diet, environmental pollutants, physical activity, and body size. They also include information on 216 chemicals that increased breast tumors in animal studies. This is the most comprehensive resource on mammary carcinogens available. Summary articles that integrate what we do and don't know from human studies of diet and environmental pollutants, and animal assessments of mammary gland carcinogens are published in the *Environmental Factors in Breast Cancer* supplement of *Cancer* for which this commentary is an introduction. This information is valuable for regulators to consider in decisions about limiting human exposure, for manufacturers to evaluate in reformulating products and re-engineering processes to avoid suspect chemicals, and for epidemiologists to identify new strategies for breast cancer studies.

Results

Environmental pollutants

Relatively little research has addressed the possible effects of environmental pollutants on breast cancer, leaving large gaps in knowledge in this area. The overwhelming majority of chemicals identified in animals as mammary carcinogens or hormone disrupting compounds have never been included in a human study of breast cancer, and the overwhelming majority of chemicals to which we are exposed have never been included in an animal cancer study. Most research about environmental pollutants and breast cancer dates only from the 1990s.

Breast carcinogens. Exposure to chemicals identified as potential mammary carcinogens is widespread, given that 73 have been present in consumer products or as contaminants of food, 35 are air pollutants, 29 are produced at more than one million pounds per year in the US, and 25 have involved occupational exposures to more than 5,000 women. Nearly all of the chemicals caused mutations and most caused tumors in multiple organs and species, providing evidence of likely carcinogenicity in humans. Regulators have not made good use of this information to reduce exposure or even to require employers to offer mammograms for workers exposed to chemicals identified as mammary carcinogens.

While researchers continue to improve the methods in animal studies to make them more relevant to human health, this type of study remains the primary means of understanding and anticipating effects of chemicals in humans. All known human carcinogens that have been tested in animals are also carcinogenic in animals.

Human studies on environmental pollutants. Research in recent years shows evidence of increased risk of breast cancer associated with exposure to polychlorinated byphenols (PCBs -- banned chemicals previously used in electrical equipment and other products) in women genetically susceptible to the effects of these chemicals. Several recent studies also find that breast cancer risk increases with exposure to polycyclic aromatic hydrocarbons (PAHs), ubiquitous air pollutants from vehicle exhaust and combustion. Results of the studies of organic solvents and dioxin suggest a possible association and support the need for additional research in these areas. PAHs and some organic solvents are animal mammary carcinogens and PCBs and dioxins are hormone disruptors, providing evidence of biological mechanisms that may link these chemicals to breast cancer.

Prospective studies of diet

Studies that monitored diet before diagnosis do not provide consistent evidence of associations with breast cancer. We considered studies of fat intake, fruits and vegetables, antioxidant vitamins (vitamin A, C, E and beta-carotene), serum antioxidants, carbohydrate intake, glycemic index and glycemic load, dairy consumption (including vitamin D), soy products and isoflavones, green tea, heterocyclic amines, and adolescent diet.

Physical activity, weight gain, body size

The evidence is now substantial that lack of physical activity, adult weight gain, high waist-to-hip ratio and other body size factors are associated with higher breast cancer risk. Public health initiatives and research to identify the most effective prevention strategies should be breast cancer priorities.

Recommendations

Future research. The large number of widespread chemicals that cause breast cancer in animals and new emerging research in human studies tell us the time is right to substantially increase investments in studies of environmental pollutants and breast cancer. Improved exposure assessment, exploring early life exposures, and separating effects on different tumor types and on premenopausal women are key strategies for future research to reveal links to environmental pollutants and diet. Most importantly, suspect chemicals should be investigated much more aggressively in both laboratory and human studies.

Strength of evidence approach. While it does not yet yield clear health directives, research about environmental pollutants can support informed decision-making within a “strength of evidence” framework. Healthcare providers and other experts who are asked to comment on uncertain risks can help by formulating precise statements that clarify what we do know and what has not been meaningfully studied. Broad statements often quoted in the news media that “there is no evidence that X causes breast cancer” leave the wrong impression, particularly because “no evidence” often reflects research areas that have not been studied or where testing has proven to be very difficult because, for instance, many environmental pollutant exposures are simply unknown to the individual and can’t be measured over many years. As evidence of links begins to emerge, individual choices and public health policies to reduce suspect exposures should be based on what we know now, while additional scientific knowledge unfolds. In the same vein, breast cancer patients and their physicians routinely face uncertain decisions about treatment because much about the disease remains unknown.

In 2007, The American Cancer Society expects 178,480 women in the U.S. will have invasive breast cancer, another 58,490 will be diagnosed with a precancerous condition that could lead to breast cancer, and 40,460 will die from breast cancer. Because breast cancer is so common and the environmental chemical exposures suspected to affect risk are so widespread, the number of women spared by reducing exposures could be profound.