What the Epidemiology of Early-Onset Cancers Can Teach Us About Environmental Exposures, Susceptibility and Prevention

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Early-onset cancers (EOCs) continue to increase globally and within the U.S. (Annual Review of Public Health 2026); two-thirds of EOCs are diagnosed in women (Oncologist 2025). The increase is particularly revealing as younger birth cohorts have a much lower prevalence of smoking. Each of the 10 most common cancers seen in young adults have been associated with environmental exposures including UV radiation, air pollution, heavy metals, solvents and endocrine disrupting chemicals (EDCs). EDCs include PFAS, also known as forever chemicals, polycyclic aromatic hydrocarbons (PAH), certain pesticides, persistent organic pollutants, BPA and phthalates. Kidney cancer, although rarer, is one of the fastest increasing EOCs and the National Academies of Sciences, Engineering, and Medicine (NASEM) recommends screening for kidney and thyroid cancers in individuals with very high blood PFAS levels (JAMA 2024, Guidance on PFAS Testing and Health Outcomes). Colorectal cancer is now the leading cause of cancer-related death among adults under 50 in the U.S., and just last month prior pesticide exposure was linked to epigenetic fingerprints in early-onset colorectal cancer (Nature Medicine 2026).

It is important to recognize that there are many ways environmental chemicals can affect cancer risk including direct carcinogenic effects, epigenetic changes, disruption of hormonal signaling, alteration of the immune system and response, and by permanently mutating the genome through somatic mutations. Some impacts of chemical exposures can be intergenerational. Our understanding of family clustering of cancers has expanded beyond solely attributing EOCs to germline mutations to awareness that shared environment and intergenerational transmission of risk through exposures in utero can affect family clustering. Silent Spring Institute comprehensively synthesized database evidence from the International Agency for Research on Cancer (IARC), the U.S. Environmental Protection Agency (EPA), the National Toxicology Program and other registry sources that included experiments in cells and animals, and identified over 900 chemicals that we are commonly exposed to that are hormone increasing, DNA damaging mammary carcinogens, as well as well-known endocrine disruptors (Environmental Health

Perspectives 2024); half of which we found were also in every day plastic products (Environmental Science & Technology Letters 2024).

Recently, our group has modeled EOC kinetics by expanding the classic Multistage Clonal Expansion Model to include tumor size at diagnosis and demonstrated that the rise in breast, colorectal, and thyroid EOCs cannot be attributed to earlier detection alone. Through using national cancer registry data for three distinct birth cohorts for the three most common EOCs, we found that the aggressiveness of the first-stage mutated cells is higher in recent birth cohorts born in the 1980s compared to cohorts born earlier and that it is higher in women compared to men. This translates into the time from initiation to malignancy being shorter in recent birth cohorts (Cancer Research 2025).

The trend in EOCs cannot be explained by germline (inherited) mutations in genes relevant to cancer as germline mutations do not change that quickly. That means that the majority of EOCs are explained by changes in genes that are acquired (somatic) throughout life. There is remarkable overlap in genes that are mutated somatically versus in the germline (Nature Communications 2020). Somatic mutations can occur randomly and/or be driven by environmental exposures, but we would not expect random mutations to change substantially by birth cohorts. Thus, we need to investigate the environmental drivers that are causing these somatic mutations. The challenge of measuring somatic mutations in large-scale epidemiology studies, until recently, has had a large impact on our understanding of environmental exposures and cancer risk outside of an occupational setting (American Journal of Epidemiology 2024).

Breast cancer remains the most prevalent EOC and can be used to illustrate the importance of measuring susceptibility to estimate the impact of environmental carcinogens. For example, we have documented, using global cancer registry data from over 185 countries available for the last three decades as well as Connecticut's cancer registry data available for the last 90 years, that the increase in early-onset breast cancer cannot be solely explained by changes in fertility. In fact, examining data of women diagnosed under 40 years of age, early-onset breast cancer has been increasing ever since the 1930s and even before the baby boom was over (EclinicalMedcine 2021, JAMA Network 2020). The increase in early-onset breast cancer cannot be attributed to increases in childhood and adolescent body size, unlike some of the gastrointestinal cancers, as larger body size is inversely associated with premenopausal breast cancer. Recent birth cohorts have had other exposures that are different including the types and use of hormonal agents, changes in alcohol intake, and increases in the prevalence of environmental chemicals including EDCs. Importantly, environmental chemicals may affect EOCs

through accelerating aging, by altering the immune environment and, for breast cancer specifically, through earlier breast development (Annual Review of Public Health 2026).

Over the last two decades, we have observed remarkable consistency between environmental exposures including pesticides, heavy metals, air pollution and breast cancer risk when exposures are measured when the breast is changing in form and function during key windows of susceptibility (WOS) (Breast Cancer Research 2019). However, most of the studies that have been published (~90%) have not measured exposures during WOS. For example, studies of organochlorine exposures conducted outside of WOS have not been consistent, but when we examined DDT exposure during early infancy and pubertal windows through blood biomarkers, the associations with early-onset breast cancer were over five-fold (JNCI 2019). We also found that early life exposures to higher levels of DDT were related to epigenetic changes (Reproductive Toxicology 2020) and higher breast density, which is a strong risk factor for breast cancer (Reproductive Toxicology 2020).

We further examined the importance of estimating the effects of environmental exposures in more susceptible populations by conducting studies within the Breast Cancer Family Registry. For example, when we measured polycyclic aromatic hydrocarbons (PAH) protein adducts in blood we found that higher levels of PAHs were linked to breast cancer risk and this association was particularly strong in women who had higher absolute breast cancer risk (British Journal of Cancer 2017). We also conducted a systematic review across a number of environmental carcinogens and found remarkable consistency with higher breast cancer for these different chemical classes compared to the literature on later-onset breast cancer (Environmental Research 2020). However, just like with WOS, only a minority of studies (~10%) were conducted in younger women. Recently, we have replicated these findings with PAHs and breast cancer risk (manuscript under review) and found that while the association with PAHs and breast cancer was positive for both early- and later-onset breast cancers, it was much stronger in women under 50 years of age. Thus, as with gene identification, which used EOC studies for identification of genes that were still important for later-onset, studying EOCs for environmental causes of cancer is a rigorous way of identifying causes for later-onset cancers as well, but should have much greater consistency and strength of association.

To further examine the impact of PAHs on changes to the breast tissue, we conducted a follow-up study of a New York City birth cohort and measured through optical spectroscopy components of the breast tissue including water and collagen, which map to higher breast density, a strong risk factor for breast cancer and lipid levels, which map to lower breast density (Scientific Reports 2022). We found that higher PAH exposure

measured during the mother's pregnancy was linked to higher density in the mother 10-15 years later and to the daughter during her adolescence (Breast Cancer Research 2022). We are following up on these results through a comprehensive analysis of targeted and untargeted chemicals. Specifically, we conducted a state-of-the art metabolomic analysis which captures chemicals the way we are exposed to them – hundreds at a time – and found that we were able to explain a large portion of the breast tissue variability through a metabolomic analysis (if replicated in larger cohorts, this could translate into a non-invasive way to predict breast density much earlier in life and as young as adolescence, leading to better screening tools for early-onset breast cancer).

The last 35 years have seen an overall decrease in cancer incidence at a population level, this is because of the decline in cancers diagnosed in men over 70 years largely attributed to population-based tobacco regulations and interventions (JNCI Cancer Spectrum 2019). Like tobacco, regulations are the most effective at reaching the population, including regulations that can affect multiple chronic diseases (this is sometimes referred to as primordial prevention) as well as cancer specific regulations to control carcinogens. Regulations include the Clean Air Act, the Asbestos Hazard Response Act, the National Emissions Standards for Hazardous Air Pollutants, and EPA drinking water standards (e.g., PFAS); some of the existing regulations may be reversed and rigorous analyses of the community health impacts are critical.

Similar to tobacco control, however, interventions at the household-level can complement (but not as a substitute for) regulatory programs. For example, we are currently evaluating a household intervention to reduce indoor air pollution through the use of air filters. Silent Spring has also developed digital tools and personalized report-back to guide households in straight-forward ways to reduce exposures to environmental chemicals within their home through swapping out products used for cleaning, personal care, or pest control (Environmental Health Perspectives 2017, Environmental Health Perspectives 2021). Household interventions are an important aspect of prevention as they can reduce risk across multiple generations of people living in a household. As most people spend the majority of their time indoors, household interventions can also help reduce exposures immediately. There is a critical need to evaluate, implement, and scale household environmental exposure interventions for inclusion in the National Cancer Institute's evidence-based-interventions (EBIs) portfolio for primary prevention, which currently only includes interventions related to tobacco control, sun safety, physical activity and diet (Cancers 2022).

In summary, the increase in EOCs demands investment in research on the etiology as well as intervention research. We are at a pivotal point where the exposure science is at

a place where we can measure hundreds of chemicals at a time – the way we are exposed to them. We have learned from investment in research on treatments that many cancers share common mechanisms. Just like with pan-cancer treatment trials, we should consider pan-cancer etiological studies to examine commonalities as well as contrasts across sex-specific cancers. There is also a major research gap to address in examining whether environmental chemical exposures including EDCs affect treatment outcomes and subsequent cancers. Now that we have younger birth cohorts that are not smoking, it will also be important to estimate attributable fractions of other environmental exposures in non-smoking cohorts.

For cancer prevention it will be important to consider interventions that address diet in combination with reducing exposures to chemicals given the way we produce, prepare, and consume food. For example, several interventions have tested whether food packaging and reductions in the use of plastics specifically can reduce body burden of EDCs such as phthalates. For example, in 2011 Silent Spring conducted an intervention study that demonstrated a reduction in urinary levels of BPA and DEHP three days after participants adopted a "diet" without canned foods and plastic compared to their usual use of plastic and canned packaging (Environmental Health Perspectives 2011). Just last month, a randomized controlled trial conducted in Australia also observed lower urinary levels of and monobenzyl phthalate after seven days in an intervention group assigned a "low-plastic diet" compared to a group assigned a usual diet (Nature Medicine 2026). These short-term interventions highlight the potential for interventions to reduce the body burden of potential carcinogens.

Finally, in addition to primary prevention, rigorous evidence is needed to help us identify ways to identify susceptible populations earlier. Germline genetics will not be sufficient for screening for EOCs. As discussed, NASEM already recommends screening for early-onset thyroid and kidney cancers in individuals with high PFAS exposure. Here again, we may learn from breast cancer where early screening guidelines include prior radiation exposure alongside a family history and known genetic mutations in breast cancer genes. A change in guidelines requires robust epidemiology, and in the Breast Cancer Family Registry, the past thirty years of research shows that even in individuals with the highest risk based on germline genetics (e.g., pathogenic variants in BRCA1/2), risk can be modified by many factors earlier in life, including radiation exposure (Cancer Epidemiology, Biomarkers & Prevention 2013) and physical inactivity (Cancer Epidemiology, Biomarkers & Prevention 2025). These observations hold great promise for prevention.

The following resources were developed by Silent Spring Institute to help people take simple steps in their daily lives to limit their exposures to harmful chemicals.

- Top 10 Tips for Healthier Home: General guidance on reducing exposures to hazardous chemicals in and round the home.
- Breast Cancer and the Environment: Simple steps for avoiding endocrine disrupting chemicals relevant to breast cancer.
- PFAS Exchange: An online resource center about PFAS contaminants in drinking water—helping communities understand their exposures and take action to protect their health. Includes medical guidance for healthcare providers.
- Detox Me mobile app (and more): Our free mobile app walks you through simple, research-based tips on how to limit your exposures to toxic chemicals where you live, work, and play. Includes top tips.
- Past CME/CEU Environmental exposures and cancer: a CME course for healthcare providers | Silent Spring Institute