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California Breast Cancer Prevention Initiatives: Setting a research agenda for prevention

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ABSTRACT

The environment is an underutilized pathway to breast cancer prevention. Current research approaches and funding streams related to breast cancer and the environment are unequal to the task at hand. We undertook the California Breast Cancer Prevention Initiatives, a four-year comprehensive effort to set a research agenda related to breast cancer, the environment, disparities and prevention. We identified 20 topics for Concept Proposals reflecting a life-course approach and the complex etiology of breast cancer; considering the environment as chemical, physical and socially constructed exposures that are experienced concurrently: at home, in the community and at work; and addressing how we should be modifying the world around us to promote a less carcinogenic environment. Redirecting breast cancer research toward prevention-oriented discovery could significantly reduce the incidence and associated disparities of the disease among future generations.

1. Introduction

As Alice Stewart, epidemiologist and discoverer of the link between *in utero* exposure to ionizing radiation and childhood cancer observed, "the best way not to see something is not to look for it" [1]. We know too little about breast cancer and the environment because historically scientific challenges and non-scientific economic, social and political forces have put the environment out of sight and out of mind [2].

Prevailing models of scientific inquiry are ill-suited to uncovering the complex web of circumstances leading to clinically apparent breast cancer [3–5]. While breast cancer arises from a convergence of the environment and genes, [6] most research has explored one or the other factor. Environmental influences on health encompass neighborhood and social factors such as racism and the physical and chemical exposures where people live, work, and play [5]. Yet most epidemiologic studies of breast cancer have focused on a narrow range of discrete behaviors or exposures, rather than the confluence of these interconnected factors [4,7–9]. Such a convergence may in part explain the fact that African American women are three times more likely to be diagnosed with triple negative cancer than White or Latina women [10] and at younger ages [11]; that African American women diagnosed at the same stage as Non-Latina White women have poorer survival outcomes [12]; and that in general, breast cancer in racial/ethnic minority populations appears to have a poorer prognosis [13].

Moreover, despite increasing human exposure, the role of toxic chemicals, pollutants and other similar agents has been only marginally explored. Since 1945, chemical production has increased more than 15-fold [14]. In the United States, approximately 700 new chemicals are introduced into commerce each year and more than 84,000 chemical substances are listed by the US Environmental Protection Agency for manufacturing, processing or importation [15,16]; 3000 of these chemicals are used or imported in high volumes (greater than 1 million pounds) [15]. Every day everyone is exposed to environmental chemicals in air, water, food and consumer products. Yet the overwhelming majority of chemicals, including those identified as animal mammary carcinogens or endocrine disrupting compounds, have never been examined in an epidemiologic study of breast cancer, nor been included in an animal cancer bioassay [17,18].

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Breast cancer research exploring exposure to chemical mixtures, critical windows of susceptibility, and environmental agents with the capacity to modify known risk factors are largely lacking [19]. And yet, history has provided us with experiments that document that early life exposure to environmental agents can have a profound impact on breast cancer, i.e., diethylstilbestrol (DES), ionizing radiation from the atomic bomb, and DDT [20–22].

Globally, funding to investigate prevention in general and avoidable environmental exposures specifically represents a small fraction of the resources directed to cancer research [23] (Fig. 1). This trend is mirrored in the United States, where only 6.5% of the National Cancer Institute's (NCI's) $5.1 billion 2011 budget request was allocated to "cancer prevention and control" [24]. A federal interagency review of breast cancer and the environment found that at most, 10–11% of breast cancer research projects funded by the National Institutes of Health (NIH) and the US Department of Defense focus on environmental health and that no other federal agency supports substantial research on the environmental causes of breast cancer [6].

Thus, we have looked neither well nor hard for the role of the environment in breast cancer etiology. The gap produced by these limitations in the research has led many to believe that the environment plays little to no part in disease etiology. For example, the NCI's breast cancer prevention advice to patients downplays environmental etiology, stating "studies have not proven that being exposed to certain environmental exposures (such as chemicals, metals, dust, and pollution) increase the risk of breast cancer" [25].

Times are changing. Over the past few years, calls for shedding light on cancer and the environment have come from influential entities, including the Institute of Medicine, [3] the President's Cancer Panel [8], the federal Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC), [6] and the Agency for Toxic Substances Disease Registry with the US Centers for Disease Control and Prevention's National Center for Environmental Health [26]. A critical observation common to these diverse reports is that the environment represents a vastly underutilized pathway to prevention. As the IBCERCC stated, "By urgently pursuing research, research translation, and communication on the role of the environment in breast cancer, we have the potential to prevent a substantial number of new cases of this disease in the 21st century" [6]. The California Breast Cancer Research Program (CBCRP) is doing just that. Below we describe a four-year initiative to set a research agenda that will illuminate the links between the environment and breast cancer and uncover opportunities to prevent disease.

2. The California Breast Cancer Research Program

The CBCRP is the nation's largest state-funded breast cancer research effort and among the largest breast cancer research funders in the world. The CBCRP was founded in 1993 by the California legislature and through the efforts of breast cancer activists, scientists, clinicians, state legislators, and University of California officials [27]. The CBCRP is funded by a state tax on tobacco products, voluntary state personal income tax form contributions and individual contributions.

The CBCRP's program funding recommendations and strategic planning are the responsibility of the Breast Cancer Research Council (Council), a group of 15 people chosen to represent those affected by breast cancer and the institutions that can help find a solution. CBCRP supports new approaches that other agencies may be reluctant to fund. Since 1994, the CBCRP has awarded more than $235 million in 966 grants to 107 institutions across the state.

Subsequent to a comprehensive review of CBCRP's research portfolio, in March 2004, the Council dedicated 30% of funds between 2004 and 2009 to the coordinated, directive, collaborative Special Research Initiatives (SRI) to support research that addressed:

1. The identification and elimination of environmental causes of breast cancer; and
2. The identification and elimination of disparities/inequities in the burden of breast cancer in California.

The goal of the SRI was to fund research that not only increased knowledge about these questions, but also pointed to solutions that would reduce the suffering from breast cancer and move science closer to eliminating the disease. In total, 21 grants totaling $23 million were awarded to address the environmental causes of breast cancer and the unequal burden of the disease [28].

In March 2010, after another thorough programmatic review, the Council built on the existing SRI by expanding the scope and devoting 50% of its research funds during 2011–2015. This new effort was titled the *California Breast Cancer Prevention Initiatives* (CBCPI). They committed an anticipated $24 million to directed, coordinated, and collaborative research to pursue the most compelling and promising approaches to:

1. Identify and eliminate environmental causes of breast cancer.
2. Identify and eliminate disparities/inequities in the burden of breast cancer in California.
3. Population-level interventions (including policy research) on known or suspected breast cancer risk factors and protective measures.
4. Targeted interventions for high-risk individuals, including new methods for identifying or assessing risk.

Implementation of the CBCPI research agenda-setting began in 2010 and will be completed in 2015. This paper presents the CBCPI's methods and results of efforts to date to identify key research questions addressing the four topic areas, and proposes future directions in research to lead to the prevention of breast cancer.

3. Materials and methods

An overview of the process of developing the research agenda for the CBCPI is presented in Fig. 2. The full details of the dynamic process for determining specific research questions to fund within the four areas were articulated in a Strategy Development Plan [29].

3.1. Public and scientific engagement

We convened three expert groups to provide leadership and scientific expertise for the CBCPI, a Steering Committee and two sets of Strategy Advisors, one focused on Environment and Disparities and the other focused on Population-Level Interventions and Targeted Interventions for High-Risk Individuals. To recruit these individuals, we identified areas of expertise needed and generated a list of scientists with relevant expertise. Public engagement in the process included advocate participants in the CBCRP Research Council, community participants in the three expert groups, and community participation in Stakeholder events.

3.2. Identifying pivotal research questions

We used the following qualitative and quantitative methodologies to review, analyze and compile the relevant scientific findings and research recommendations to inform the development of pivotal questions for the CBCPI.