Breast Cancer Prevention Partners

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A first-ever, comprehensive agenda for preventing breast cancer

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Paths to Prevention

The California Breast Cancer Primary Prevention Plan

Breast cancer risk is not simply about the individual; it is about a society that has the potential to function in a way that not only protects people's health but also builds resilience.

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Foreword

The California Breast Cancer Research Program (CBCRP) has made the prevention of breast cancer a primary goal.

Great strides have been made in breast cancer therapies and standards of care, leading to decreased mortality in California and elsewhere. However, breast cancer incidence has remained essentially unchanged for the last half century, indicating that a fresh approach to preventing breast cancer is needed.

History tells us that the most impactful public health interventions are those that create system-level changes, influencing a whole population and providing the context for individuals to lead healthier lives. We know this is true for breast cancer because there is a wide variation in breast cancer rates across the world and because when individuals migrate from countries with low breast cancer rates to countries with high breast cancer rates, they develop rates closer the their new country, as do their children and their children's children. Thus, population-level primary prevention is an area of great potential.

To turn the tide of breast cancer in California, CBCRP issued a request for a team to develop a comprehensive, primary prevention plan for breast cancer in the state. Breast Cancer Prevention Partners (BCPP) won the competition and was awarded the project.

We thought we knew what we would be getting. But BCPP did more than simply fulfill the requirements for this project. They brought this project into their circle, their mission, and everything they do, garnering additional funds and developing a community reach and a plan that surpasses expectations.

Paths to Prevention: The California Breast Cancer Primary Prevention Plan provides a blueprint for the state and areas of focus in which any state or local agency, non-governmental organization, voluntary organization, or community can participate. Gaps in our knowledge identified in the Plan can point to priority areas for further research and technology development. Where the evidence is lacking on the effectiveness of intervention strategies, innovative approaches informed by the science and community input can be developed and evaluated.

Many of the cancer risk factors addressed in *Paths to Prevention* contribute to other cancers and other chronic diseases, and communities that lower the rate of breast cancer will also experience other health benefits. Breast cancer prevention can serve as a bellwether for community health.

"As goes California, so goes the nation." Now is the time, and here is the plan, to make California the state with the lowest breast cancer rate in the country.

Marion (Mhel) H. E. Kavanaugh-Lynch, M.D., M.P.H.
Director
California Breast Cancer Research Program

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Introduction

Breast cancer is a complex and devastating disease. In the United States in 2020, it is estimated that breast cancer will cause more deaths of women under the age of 45 than any other cancer.[1] In 2020, an estimated 30,650 women in California will be diagnosed and more than 4,000 will die.[2]

Breast cancer affects women of all ages, ethnicities, and races. Yet according to the American Cancer Society, eight out of 10 women who are diagnosed with breast cancer do not have a family history of the disease.[3] And the incidence of breast cancer is on the rise, up 40% over the last four decades. After skin cancer, cancer of the female breast is the most common type of cancer in the United States. Every year, nearly a quarter of a million women (and 2,000 men) are told they have breast cancer. This begs many questions: Why? What is causing this disease? Why is it on the rise? And what can be done to prevent breast cancer before it starts?

There has been noteworthy progress in scientific research in the past 20 years that has helped identify a wide range of complex, interconnected, and potentially preventable risk factors for breast cancer. Some are well established, such as exposure to radiation or tobacco smoke. Others are less established but are emerging as causes for concern. These risk factors often overlap and interconnect, especially for people of color and marginalized communities who often experience multiple stressors simultaneously.

We also know that breast cancer is not a single disease—there are multiple types of breast cancer that may have a range of risk factors, affect diverse groups of people differently, respond differently to treatment, and which may require different potential interventions for prevention. It is unlikely that we will ever be able to tell people exactly what caused them or their loved one to develop breast cancer, nor can women completely eliminate their risk even when they "do everything right" in terms of living a healthy lifestyle. But we can approach prevention from a population perspective: What are the trends in our community or society that appear to be increasing breast cancer risk for certain populations? What are the factors that are contributing to risk? Why isn't incidence decreasing? What can be done about it?

As *Paths to Prevention: The California Breast Cancer Primary Prevention Plan* will explore, we do not know everything about the causes of breast cancer, but we do know enough to act. We have intentionally prioritized

investigating the needs of under-represented and politically marginalized populations who so frequently are not adequately considered in major public policy efforts. Many of the recommendations in this Plan also apply to health, equity and justice issues beyond just breast cancer. Breast cancer risk is not simply about the individual; it is about a society that has the potential to function in a way that not only protects people's health but also builds resilience.

Paths to Prevention describes some of the key actions that could be taken in California to reduce breast cancer. By combining a comprehensive review of the science documenting breast cancer risk with an extensive and inclusive process for input into what actions could be taken to reduce that risk, Breast Cancer Prevention Partners (BCPP), with funding from the California Breast Cancer Research Program and other foundations, has developed *Paths to Prevention: The California Breast Cancer Primary Prevention Plan*—an action plan of local, regional and statewide measures that can reduce breast cancer risk and protect women's health while also addressing a wide range of societal issues. What is presented here reflects the synthesis of what we learned over a multi-year process of researching the science; engaging an Advisory Committee comprised of academics, community representatives, health professionals, labor advocates, and government officials; and learning from community advocates from across the state.

The complexity of reducing breast cancer risk rivals the complexity of the disease itself. Yet as one of the biggest, most populous and most diverse states in the country, California has a rich history of community leadership and advocacy, a world-class research community and an innovative legislative body. With that we have some of the greatest potential to develop interventions and policy solutions at the local, county and state level to reduce breast cancer risk. There is no better body of people—and no more important moment than now—to take this on.

How *Paths to Prevention* is Different from Other Cancer Plans

Since 1998, the Centers for Disease Control and Prevention (CDC) has helped all 50 states, the District of Columbia, six U.S. Associated Pacific Islands and Puerto Rico, and eight tribes or tribal organizations create and implement cancer control plans.[4] In regard to breast cancer, these state plans emphasize early detection, treatment, and access to services. Where they do address primary prevention, the plans tend to be focused on recommended ways for individuals to change their behavior without significant consideration of social, environmental, and/or situational factors or obstacles that enhance or limit individual efforts.

Paths to Prevention is distinct and unique from other cancer plans in several important ways that include its:

- Focus on Primary Prevention
- Focus on Systemic Interventions
- Social Justice Lens
- Weaving Together of Both Science and Community Wisdom

Definitions

Primary Prevention—Preventing the onset of disease by eliminating or reducing exposures to risk factors. This is distinct from early detection, which is sometimes referred to as "secondary prevention."

Systemic Change—Addressing society-level issues, rather than focusing on individual behaviors, to reduce breast cancer risk at a population level.

The Plan focuses exclusively on preventing the disease before it starts, reducing risk, rather than early detection. While mammograms are vitally important in early detection of existing cases of breast cancer, it is a common misnomer that mammograms are a way to "prevent" the disease. Preventing breast cancer requires reducing or eliminating its risk factors.

Paths to Prevention shifts the focus of decreasing and eliminating risk from the individual to changes we can make as a society. The recommended interventions address systemic, society-level issues that increase risks for breast cancer. For example, recommendations to eat more fruits and vegetables lack meaning if we don't also encourage zoning and planning practices that ensure easier access to fresh foods than to fast food. Telling people to get more exercise does not mean much in the absence of safe and accessible green spaces and community gathering spaces for children and adults to play and move. While it is important for individuals to strive for a healthier lifestyle, we should not shame or blame individuals who do not/cannot make those changes. Rather, we should work collectively to support healthy communities for everyone in California.

The authors of this Plan were committed to incorporating a social justice lens to its development and recommendations, seeking to represent the needs and realities of California's diverse communities and population. We actively sought what little science was available that provided information on how marginalized communities are impacted by breast cancer risk factors. In developing recommendations, we considered those actions that will benefit all Californians and attempted to be cognizant of potential unintended consequences. The first two chapters in this Plan — "Race, Power and Inequities" and "Social and Built Environment"—both influence and provide a context and lens for our discussion of all the other risk factors presented.

For each of the risk factors, we started with an evaluation and discussion of the relevant peer-reviewed science. However, we know that far too many communities are not represented adequately, or at all, in that science. Throughout the course of this project, we expended significant effort and resources to ensure that community wisdom was represented in the Plan's recommended interventions (our process for accomplishing that is described below). The weaving together of the science and community wisdom has given *Paths to Prevention* a richness and relevance to those most impacted that would have been lost without those community voices, and we are deeply grateful to those community members that shared their time and knowledge.

To keep the authors true to this vision, we developed, in consultation with our Advisory Committee, the following Guiding Principles, which are explained more fully in the following section.

Guiding Principles of *Paths to Prevention*

1. Breast cancer is a societal issue. Reducing risk requires systemic change.
2. To create a healthy society, we must address discrimination, racism, and inequities in power and access.
3. Community wisdom is a valuable source of information and often highlights areas that scientific research has not yet investigated.
4. Breast cancer risk is multi-factorial. Interventions to reduce risk should be multi-factorial.
5. We do not need 100% certainty to act.

Breast Cancer's Impact

In the U.S., women's lifetime risk of breast cancer increased steadily and dramatically from the 1930s, when the first reliable cancer incidence data was established, through the end of the 20th century.[5] Between 1973 and 1998, breast cancer incidence rates in the U.S. increased by more than 40%.[6] Today a U.S. woman's lifetime risk of breast cancer is 1 in 8.[7]

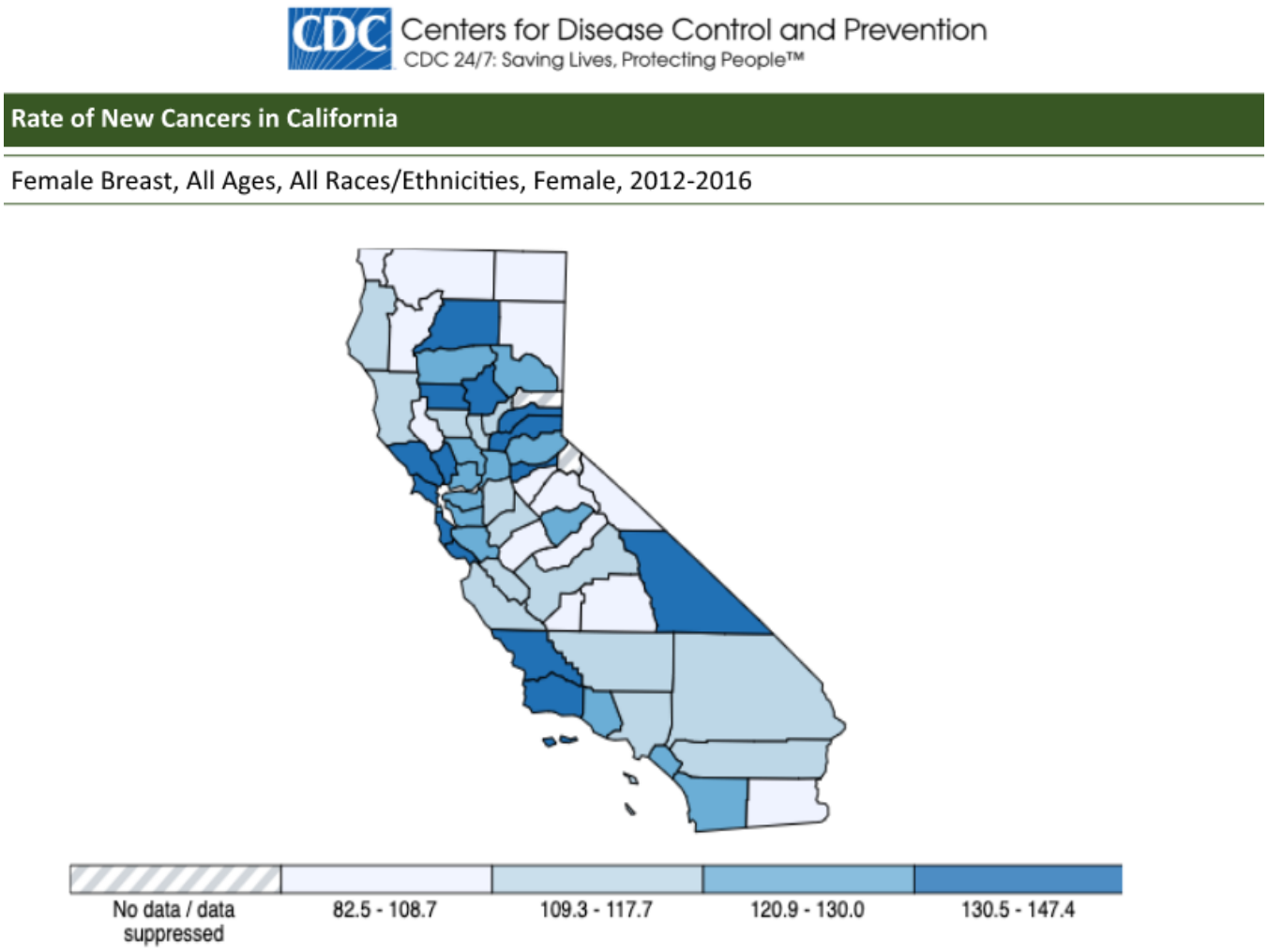
According to the CDC, in 2016 (the most recent year data is presented), California had a female incidence breast cancer rate of 118 per 100,000 people.[8] As seen in Figures 1 and 2 below, each county is affected differently by the disease, with incidence and mortality rates varying widely and without intuitive patterns.

Breast Cancer Affects Men Too

Men can also develop breast cancer. This Plan focuses on breast cancer affecting women due to considerably higher risk for women than men: a woman's risk is 1 in 8,[9] a man's risk is 1 in 833.[10] Additionally, the biology of the disease is different for women,[11] and significantly less research has been done on male breast cancer than female breast cancer. More research on men's breast cancer is needed.

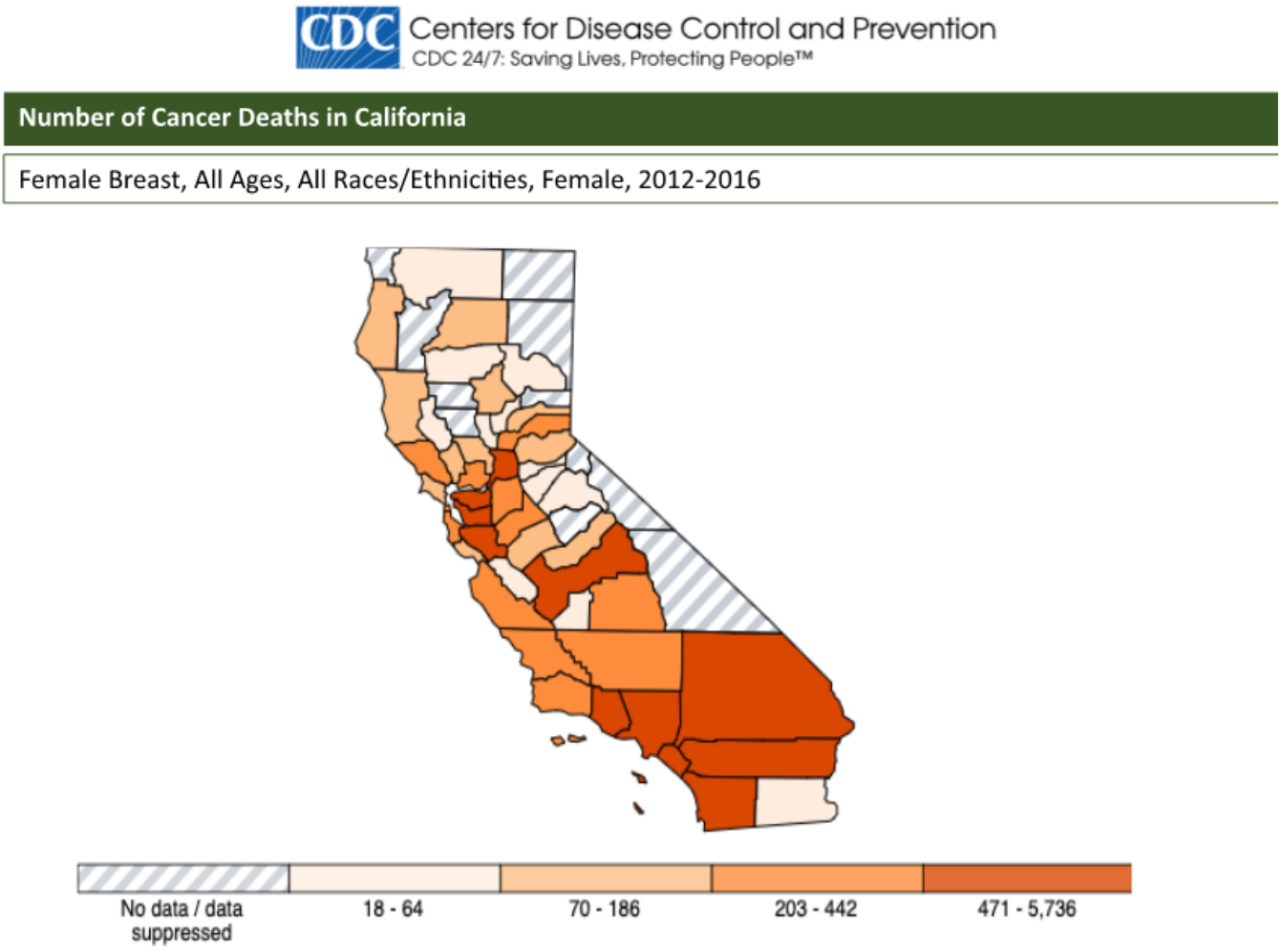
As cancer incidence data have become more nuanced over the past decade, it is clear that the incidence of breast cancer varies considerably by a number of factors, including age and ethnicity. Historically in the U.S., breast cancer incidence has been higher in White women than in Black women. However, in 2016, incidence in Black women caught up with that of White women. Further, among women younger than 45, breast cancer incidence is higher among Black women than White women.[12] Younger women in general, and younger Black women in particular, are more likely to present with the triple-negative subtype of the disease, a diagnosis that is both more aggressive and associated with higher mortality.[13,14]

Figure 1.



Data source- U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on November 2018 submission data (1999-2016): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, June 2019.

Figure 2.



Data source- U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on November 2018 submission data (1999-2016): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, June 2019.

Across racial and ethnic groups in the U.S., Black women have the highest breast cancer mortality rate of any racial/ethnic group (28.4 deaths per 100,000 women, age-adjusted and normalized to the 2000 standardized U.S. population). Asian, Native-Hawaiian, and Pacific Islander women have the lowest mortality rates (11.4), with White (20.3), Latina (14) and Native-American (14.6) women having intermediate mortality rates based on cancer registry data.[15]

Definitions Racial / Ethnic Categories

Throughout the ***Paths to Prevention*** the following categories are used to describe race and ethnicity – unless a study specifically disaggregates them into more granular descriptions (e.g. Mexican Americans, Vietnamese, Afro-Caribbean).

We acknowledge that these categories are highly imperfect. Each category covers a wide range of backgrounds, cultures, and other complexities; and do not account for overlap in individuals' and communities' racial identification. They also do not account for individuals of mixed race, including "bi-racial." While imperfect, these terms provide us with a way to talk about the science showing how breast cancer risk impacts specific races and ethnicities differently as well as the serious inequities that exist in our society due to racism.

Asian, Native Hawaiian and Pacific Islander (ANHPI) – people of Asian and Pacific Island descent unless disaggregated in specific studies (e.g. Japanese, Vietnamese, Native Hawaiian, etc.).

Black – people of African descent including African Americans, Afro-Caribbean, and Afro-Latina.

Latina – women of Mexican, South and Central American descent unless disaggregated in studies (e.g. Mexican, Brazilian, Guatemalan etc.). We include research referring to "Hispanic women" under this term as well.

Native American – U.S. indigenous people including Alaska Natives (Note: Hawaiian Natives are included in ANHPI).

White –people of European, Middle Eastern or North African descent (as designated by the Equal Employment and Opportunities Commission for the EEO-1*) unless disaggregated by studies (e.g. Irish Americans, Moroccans, Iranians, Danish).

* EEOC Employer Information EEO-1 report instruction booklet. Available at www.eeoc.gov/employers/eeo1survey/2007instructions.cfm Accessed October 2019.

Despite the universal drop in mortality rates across the past two decades and the similarity in incidence rates, over the same time period the disparities between mortality rates for White and Black women have grown significantly. The mortality rate for Black women diagnosed with breast cancer is 42% higher than the comparable rate for White women.[16]

Developing prevention recommendations in the context of numerous types of breast cancer, combined with differences in the way specific groups of women are impacted by breast cancer, is complex. There is no simple way to predict where interventions can have the greatest impact. But given the deep, systemic barriers to health and wellbeing that many women of color—especially Black women—face, the recommendations in this Plan have prioritized opportunities to disrupt and counter the myriad ways that legacy and existing racist policies have disadvantaged women of color.

Breast Cancer's Long-Term Effects

Aside from the physical and emotional suffering women and their families experience when facing a breast cancer diagnosis, additional challenges often include long-term economic impacts from medical debt, absence from work or long periods of under-employment while going through and recovering from treatment, insecurity about needing to explain extended unemployment to potential employers, and fear of employment discrimination due to their health history. Women may also face enduring side effects from treatment, such as pain, cognitive impairments, and physical limitations. The toll of this disease can be devastating in many ways, and often hits the people with fewer economic resources the hardest.

Breast Cancer Risk Factors

Breast cancer risk is a complex web of inter-related factors. Some are better established, such as radiation exposure, tobacco smoke (first- and secondhand), alcohol consumption, and lack of physical activity. Other risk factors are still emerging but no less compelling—for example, environmental exposures, the stress of poverty and racism, immigrating to the U.S. from countries with lower breast cancer rates, and others. All communities often face multiple risk factors simultaneously, but marginalized communities often have increased exposures to risk factors with fewer resources or opportunities to mitigate those factors. It is not uncommon to see the same communities facing higher exposure to industrial pollution, poor air quality, lack of access to healthy food, limited opportunities for physical activity, and likely other concerns. As will be described throughout this Plan, because of historically racist policies these problems are often concentrated in communities where people of color live.

Adding to the complexity, while breast cancer is often considered as a single disease, there are multiple subtypes of breast cancer that occur at different rates in different groups, respond to different kinds of treatment, grow and spread at different rates, and have varied long-term survival rates. In addition, risk factors may vary for each different subtype of breast cancer. Table 1 explains the different subtypes of breast cancer and proportion of diagnosis.

Table 1.
Subtypes of Breast Cancer and Proportion of Diagnosis

Subtype	Characteristics ER is Estrogen Receptor (positive or negative) HER-2 is Human Epidermal growth factor Receptor 2 PR is Progesterone Receptor	Range of Proportion of diagnoses[17,18]
Luminal A	ER+, HER-2-, often good prognosis	50-60%
Luminal B	ER+, HER-2-, faster growth than Luminal A	15-20%
HER-2 overexpression	Aggressive (grows quickly), but responds to targeted therapy	15-20%
Triple-negative	ER-, PR- and HER-2-; aggressive and more difficult to treat	15-20%
5-NP	ER-, PR-, HER-2- and also negative for epidermal growth factor receptor 2 (EGFR) and cytokeratin-5 (CK5)	~4%

Despite progress, there is still much to be discovered about what causes breast cancer. Yet the existing body of evidence on modifiable risk factors is sufficient to warrant action now. Looking to minimize these risk factors at a societal level can not only reduce the breast cancer burden across the state, it can also serve to promote a healthier society overall.

It is helpful to get a sense of the overall complexity of the many risk factors combined. Included in Figure 3: The New Paradigm of Breast Cancer Causation and Prevention is a visual snapshot of the biological, physical, social, and behavioral risk factors and their interconnection. This model represents only post-menopausal risk factors, which may differ from pre-menopausal risk factors. It also only considered data from human studies and lacks a significant body of literature that investigates breast cancer risk using animal and in vitro studies.[19] However, it provides a preliminary sense of the complexity of the disease and its potential causes.

For the purposes of developing the Plan, these risk factors have been synthesized and summarized as shown in Figure 4. The process of how this summary of breast cancer risk factors was derived and how it will be used as a central organizing tool for developing action proposals is explained in the following section.

Figure 3. The New Paradigm of Breast Cancer Causation and Prevention

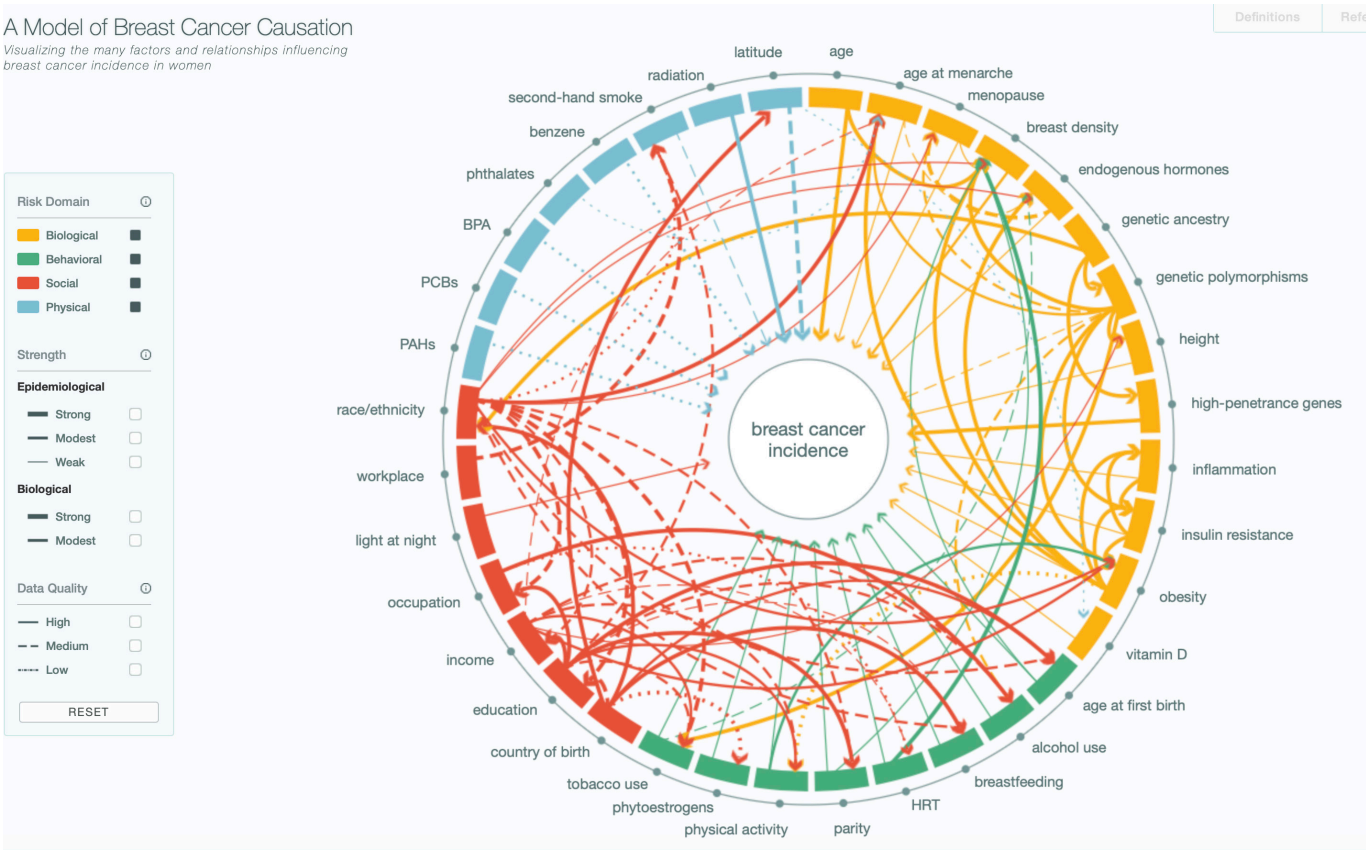
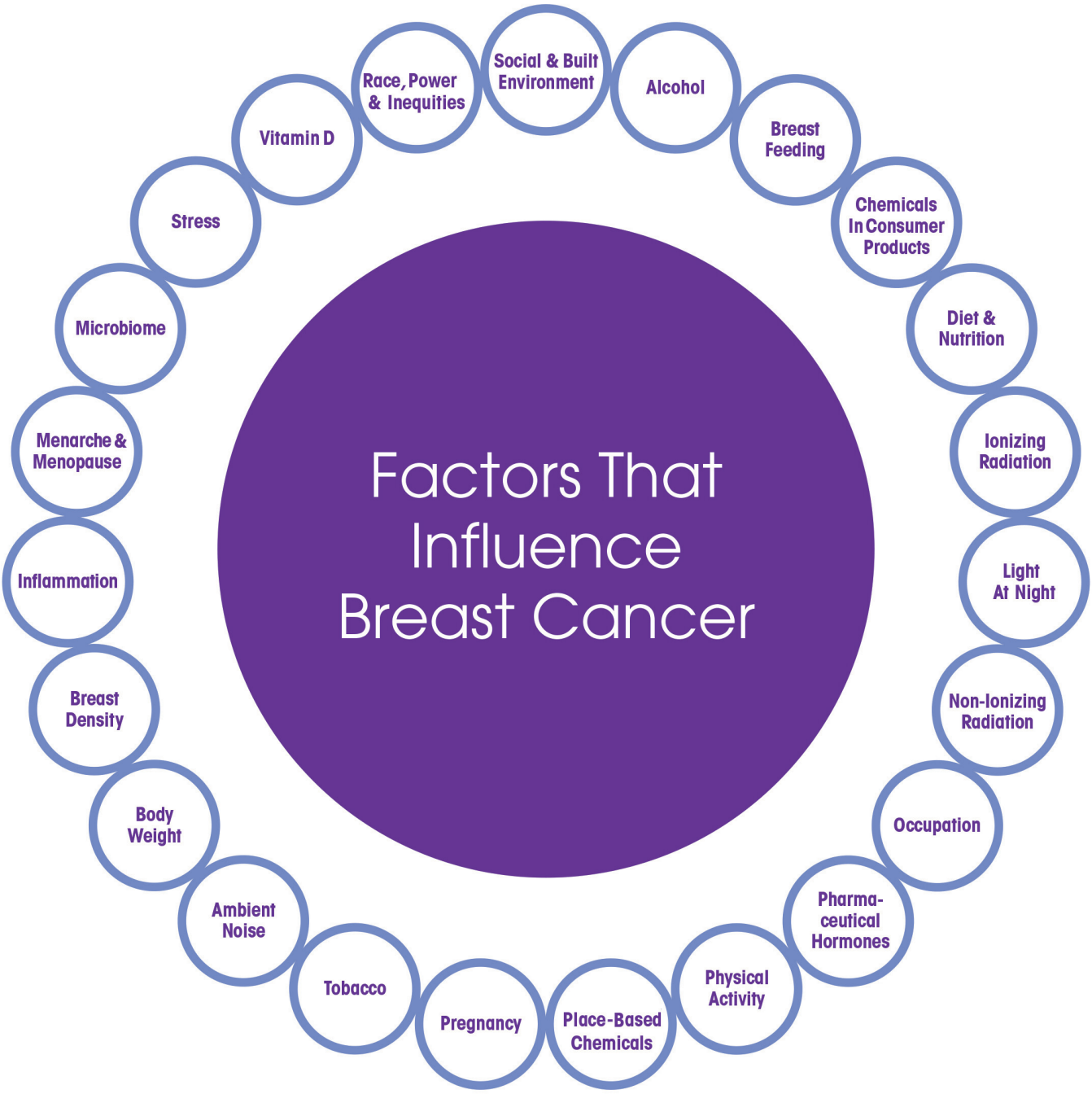


Figure 4. Simplified Visual Representation of Breast Cancer Risk



Breast Cancer Risk Over the Life Course

Experiencing or being exposed to breast cancer risks can have different impacts depending on the timing, as the breast goes through many stages of development over the course of a lifetime.

The basic structures of the breast develop early in prenatal development. By the beginning of the second trimester, breast tissue has a rudimentary system of buds and a primitive nipple, and by the end of the second trimester is sending growth factors into the tissues.[20] Early in the third trimester, breast tissues have the ability to respond to estrogen.[21] By birth, the nipple is well developed and the breast responds to maternal hormones. A few months later, breast tissues become responsive to progesterone. This period of prenatal development and early life is critical for later healthy development of the mammary tissue.

In puberty, breast cells begin to grow and divide rapidly, in response to specific patterns and doses of the natural estrogen, estradiol. Deep in the breast, the ducts grow into terminal end buds, much like the branches of a tree. These buds further divide and develop into the structures, called lobules, that may eventually produce milk. The branching of the ductal system is impacted by progesterone. Throughout these processes, androgens (including testosterone, which is secreted by the adrenals in females) help to regulate and balance the development of breast tissue.

In adult women, the breast extends from the collarbone to the lower ribs. Each breast has six to eight milk ducts that travel from lobules within the fatty tissues of the breast to the nipples. During pregnancy and lactation, the lobules mature. Milk-producing cells, called acini, increase in number and size. By the end of a pregnancy, the acini are fully mature and ready to produce milk.

A large body of research demonstrates that the timing of exposures across the lifespan can have an enormous influence on whether, how, and how much an environmental exposure might influence the risk for later development of breast cancer. Mammary gland cells are more susceptible to the carcinogenic effects of hormones, chemicals and radiation during early stages of development, from the prenatal period through puberty and adolescence, and on until the first full-term pregnancy. Particular concerns have been demonstrated for exposure during prenatal and early childhood periods. Much of this data comes from the use of animal models, but there also are several sources of data that support this claim from the human clinical literature.

Specific timing and duration of exposures, especially when they happen early in development, may cause more detrimental effects than later exposures. When we consider breast cancer prevention, we need to consider interventions that span prenatal development throughout a woman's lifespan.

Linking Science to Prevention Recommendations

With increasing recognition and understanding of the complexity of breast cancer risks, the time is ripe to develop state-wide recommendations to reduce those risks. Many experts agree that at least 50% of all breast cancer cases are preventable using risk-reduction strategies.[22] However, simply informing people of their potential risk is rarely sufficient to change behavior.[23] A family history of cancer may lead to a higher chance of pursuing screening, but not to lifestyle changes.[24] Many of the risk factors that individuals may be able to affect have systemic barriers to people making those changes. Interventions that address the systemic root of the problem hold the greatest potential for effective impact.

Paths to Prevention covers 23 different categories of breast cancer risk as well as protective factors and potential interventions to counter many of these factors. All risk factors included in this Plan were chosen because scientific literature indicates enough evidence to warrant either taking action or further research, though not all risk factors are equally well-established. Each risk factor is presented with a transparent description of the extent of the scientific evidence. Based on these risk factors, proposals for community-based interventions, public policies, and systems-level changes were developed by consulting a wide range of sources and individuals. The full methodology is described in the next section.

Preventing breast cancer requires investing in women's health at every stage of life. California is uniquely positioned to address breast cancer risk through local, school, community, business, regional and state-wide measures. The Plan that follows contains a blueprint for action to improve people's lives by building healthy, thriving communities, while also reducing breast cancer risk.

Research and Representation

The authors of ***Paths to Prevention*** committed to incorporating a social justice lens to the process and recommendations, taking an inclusive approach by representing the needs and realities of California's diverse population. However, this Plan is being written within the historical context of inadequate research focused on specific groups of people who deserve greater representation, including young women, lesbians, transgender people, incarcerated women, Native Americans, Blacks, Asian, Native Hawaiian, Pacific Islanders, Latinas, immigrants from different countries across generations, women with disabilities, and others. More funds should be directed toward ensuring these and other groups are fully represented in breast cancer research. Throughout this Plan, recommendations have been made to highlight where research is particularly lacking.

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How *Paths to Prevention* was Developed

Paths to Prevention: The California Breast Cancer Primary Prevention Plan was developed with a strong foundation of science and input from many stakeholders. The process was designed to meet three main goals:

1. **Be Guided by a Moral and Ethical Compass:** This Plan was designed using Guiding Principles that meet high standards of inclusivity, respect, and pro-active protection of people's health.
2. **Use the Full Breadth of Up-to-Date Science:** We ensured that the science behind the breast cancer risk factors considered in this Plan is up-to-date and drawn from foundational scientific documents, peer-reviewed literature, and consultation with leading experts in the field; and
3. **Make Recommendations Based on Meaningful Stakeholder Engagement:** Recommendations for interventions and public policies in this Plan can be pursued at the local, regional, and state-level across California. In order to develop these recommendations, the Plan was informed by a range of sources including an Advisory Committee (AC) and community advocates from across California.

Details of these three goals are described in detail below.

Guiding Principles

Central to our approach was a commitment to actively seek out the perspective and input of people who are often under-represented in research and policy arenas related to breast cancer and many other health issues. To help ensure that we stayed true to this pursuit, we developed (with considerable input from the Advisory Committee) a set of Guiding Principles for our work. At each stage of developing and refining the Plan we reflected back on these principles and asked the AC and community allies to help ensure we stayed true to these intentions.

The Guiding Principles are as follows:

1. Breast cancer is a societal issue. Reducing risk requires systemic change.

Disease prevention is often presented as something individuals are responsible for by improving their everyday habits. For breast cancer, this often includes recommendations such as eating healthy food, exercising, and not smoking.

BCPP encourages healthy individual habits whenever possible. However, **placing sole responsibility on the individual for engaging in these habits ignores systemic barriers that create obstacles to adopting healthy behaviors.** For example, if people are told to eat healthy food but live in an area where they only have access to fast food and corner stores, it will be difficult for them to follow this recommendation. People who need to work long hours, perhaps in more than one job, may lack time to exercise. In most instances, **people are exposed to air or water pollution or chemicals through no choice of their own.** These are not character flaws; they are **systemic barriers to health**. See Table 1 for more examples of the difference between individual action and systemic change.

In order to promote health, **we need to create conditions that support people's health at the societal level**. It is time to stop ignoring society's shortcomings while blaming individuals for not being able to create or maintain a healthy lifestyle. **We should live in a society where the healthy choice is the easy choice.**

2. To create a healthy society, we must address discrimination, racism, and inequities in power and access.

California is a land of great inequities. The state has one of the highest levels of income inequality in the country.[1] We have people with great influence over state, national, and even international decision-making, and we have some of the most marginalized, underrepresented communities in the U.S. **Breast cancer prevention should address the needs of all Californians.**

Since 2000, people of color have made up the majority of California's population,[2] **yet racism and racial inequities are not abating.** Racial inequality can be witnessed in higher unemployment rates for Blacks and Latinx;[3] less access to clean drinking water, especially for Latinx in unincorporated areas;[4] and people of color being disproportionately exposed to industrial pollution.[5,6] While these and other impacts disproportionately affect people of color, approximately 13.5% of White Californians are living in poverty[7] and may also lack access to the resources that support health and well-being. Many disenfranchised groups, from Lesbian, Gay, Bisexual, Transgender, Queer, Asexual, and Intersexed (LGBTQAI) to incarcerated women, face their own unique challenges.

These inequities, often intensified by multi-generational trauma, impact all levels of people's lives, including the way individuals make decisions about their health. Such **inequities may even affect the ability to make choices about health,** due to economic, social, and structural barriers. The impact of not being able to access healthy food, living in neighborhoods that are unsafe, not knowing if you or a family member could be deported at any moment, racial profiling or economic insecurity, compounded by a person feeling like they have little say in these matters, all hold the potential to increase risk for breast cancer and many other health problems.

More scientific research is needed to understand the link between stressors like these and breast cancer risk, but early signs point to the need to proactively address these concerns.

Actions to prevent breast cancer must support the well-being of the most marginalized among us. This starts by increasing the depth of scientific knowledge available to distinguish the impacts on different marginalized groups, but also extends to developing appropriate interventions that prioritize improving the lives of people who have most often been under-represented in public policy. These interventions should be developed and implemented with leadership from disproportionally impacted communities.

Table 2.
Examples of Individual vs. Systemic Change

Individual Change	Systemic Change
Exercise more	Create safe, affordable and accessible space and organized activities that promote physical activity. Fund community centers where physical activity is accessible and affordable. Develop workplace policies to support work/life balance so people have time to exercise. Address discrimination and racial and economic inequities that are barriers to exercise. Reduce air pollution so outdoor exercise isn't harmful.
Eat better food	Ensure that fresh, affordable, culturally relevant, and preferably organic food is available to all people by supporting affordable and culturally appropriate farmers markets, nutrition support programs, and universal school breakfasts that are easily available and do not promote shame. Offer community food preparation instruction for healthy, culturally appropriate recipes. Change agricultural policies and subsidies to support chemical and pesticide-free farming techniques. Address discrimination and racial and economic inequities that are barriers to healthy eating.
Don't smoke	Support aggressive efforts to discourage smoking—and vaping—before it starts through public education and advertising efforts, especially for middle school and high school age individuals. Reduce or eliminate stressors that drive people to smoke.
Breastfeed your babies	Provide universal paid maternity leave. Allow adequate pumping time and provide a secure environment to pump and store breast milk in all workplaces. Eliminate structural, legal, and cultural barriers to breastfeeding.

3. Community wisdom is a valuable source of information and often highlights areas that scientific research has not yet investigated.

We used rigorous standards to ensure that this Plan was informed by up-to-date peer reviewed scientific literature on factors affecting breast cancer risk as well as potential interventions (where available). We also know that **the lived experience of people provides invaluable wisdom**—both in terms of breast cancer's impact as well as the problems that need to be solved in their communities to reduce breast cancer and other health risks. Local communities also have a deep understanding of how a potential intervention will or will not be effective given the specific circumstances in their area. We recognize that **community perspectives are often under-represented and under-valued in science and public policy.** This is especially true of vulnerable and disenfranchised communities such as communities of color, immigrant communities, LGBTQAI communities, non-English-speakers, incarcerated women, and others.

We hosted community listening sessions (described below) around the state to hear communities' concerns about breast cancer, access to resources, and environmental exposures. We also learned about inspiring efforts and successes to create community spaces, address local needs, and create opportunities. Where it was relevant, we provided translation for participants. These meetings deeply informed the development of this Plan.

4. Breast cancer risk is multi-factorial. Interventions to reduce risk should also be multi-factorial.

Many breast cancer risk factors are complex and can interact with each other, often in ways we do not yet fully understand. For example, an investigation of xenoestrogens (chemicals that mimic natural estrogen in the body) showed that exposure to several of these chemicals at the same time had an additive or synergistic effect compared to exposure to one chemical at a time.[8] Additionally, consuming food or liquids contaminated with persistent organic pollutants (POPs), such as polychlorinated biphenyls (PCBs), can increase risk for obesity, and obesity, in turn, may increase risk for breast cancer.[9]

Furthermore, the effects of inequities in social and built environments mean that the **communities affected by one risk factor are often more likely to face other risk factors.** In many of the communities we visited, we consistently met people who were simultaneously struggling with lack of healthy food access, safe recreation space, and economic opportunity, and were also impacted by living or working in areas with high industrial pollution, heavy traffic, pesticide exposure, and other stressors. This was true in both urban and rural areas. Generally, **we lack data on how these risk factors interact or cumulatively impact overall risk.**

The best solutions will address multiple risk factors simultaneously. For example, we know that good nutrition is protective against breast cancer in general, but it may also reduce the impact of some chemical exposures by reducing how much is absorbed into the body.[10] **This Plan sought to identify opportunities to make changes that can be readily implemented, such as nutrition programs, to complement recommendations for some of the more difficult changes that need to be made, such as long-term planning and infrastructure changes.** Adding the breast cancer lens to something as fundamental to health as good nutrition across the lifespan holds potential for greater impact.

5. We do not need 100% certainty to act.

Public policy should protect our health and be guided by the principle that credible evidence of risk, rather than absolute proof of harm, is sufficient to mandate policy change in the public's best interest. **Public policy must take precautionary steps to support health even if we do not have certainty about its impact on reducing breast cancer risk, as long as it does no harm and safeguards against unintended consequences.**

These five guiding principles served as the compass for developing *Paths to Prevention*. Some of the recommendations made in this Plan will be new and unique, and others will reinforce existing recommendations from the large and varied network of advocates working across California to build a healthier society. Our recommendations have been made in solidarity with and in support of the many existing movements for environmental, health, economic, racial, gender, and climate justice. Breast cancer provides another lens to support these efforts. Many people are working to solve California's pressing problems from different vantage points, but with the same end goal: to build a stronger, safer, healthier, more equitable state for all Californians.

Ensuring a Broad and Inclusive Lens in Building *Paths to Prevention*

Any Plan such as this one will be influenced by the people leading the effort, as well as the political and cultural context of the time it is written. The principal investigators and the project coordinator are White, cis-gendered, able-bodied, college educated, professional women originating from various economic backgrounds and different parts of the U.S. who now live in the San Francisco Bay Area. The broader team at BCPP working on this project included women of color. None of us are breast cancer survivors, but many of us have had people close to us experience the disease.

To ensure a broad and inclusive lens in developing ***Paths to Prevention***, we consulted extensively with a wide range of people. The Advisory Committee consists of racially diverse women and men who are scientists, public health professionals, health care professionals, government employees, labor advocates, and community organizers. Our community outreach efforts (described in more detail below) allowed us to meet more than 125 people from across California who represent differing socio-economic levels, races, cultures, education levels, access to resources that support their health and well-being, potentially differing immigration status (we did not ask explicitly), language fluencies, and other characteristics. Our study groups included both academics and community organizers, and whenever possible, we tried to engage speakers who have perspectives distinct from the core staff of the project.

Sources of Input and Information and Methods

BCPP sought input from a wide range of sources in the development of *Paths to Prevention*. This includes an Advisory Committee, foundational documents, literature searches, community members, study groups, and outside experts as needed. The process of collecting information from these various sources was done simultaneously, with the results of each stream of information woven together at the end. Below is a description of the sources of information and the process used to identify the most useful way to extract and synthesize what was learned.

1. Advisory Committee

Given the complexity of creating this comprehensive Plan, a diverse Advisory Committee (AC) was engaged to guide the process. BCPP identified individuals with deep knowledge of specific risk factors, representing numerous specialties, occupying different personal and professional perspectives from across California. We recruited academics, community and nonprofit leaders, health care professionals, labor advocates, and government agency staff who collectively could represent the depth and breadth needed to consider the range of breast cancer risk factors and potential interventions and policy responses. We also included participants from the California Breast Cancer Research Program and Centers for Disease Control and Prevention as *ex officio* members of the committee.

The AC participated throughout the process, from study design to giving substantial feedback on Plan drafts. This included attending four in-person meetings and attending and often presenting in the study groups (described below). Every effort was made to incorporate the AC's input into the Plan, though ultimately BCPP staff made final decisions about what to include in this document. A full list of Advisory Committee members can be found in the Acknowledgements.

2. Foundational Documents

Paths to Prevention is not the first effort to summarize the complexity of breast cancer risk. To build our breast cancer primary prevention framework, BCPP first identified risk and protective factors articulated in seven foundational documents for our review.[11,12,13,14,15,16,17] These foundational documents were chosen because they used peer-reviewed literature to consider breast cancer risk and prevention and were developed by committees and task forces that were able to vet and explore their findings using the views of people with a range of expertise. The foundational documents used in this report are:

- World Cancer Research Fund/American Institute of Cancer Research/World Cancer Research (WCRF/AICR) 2018 report on the Prevention of Breast Cancer: Food, Nutrition, and Physical Activity.
- Interagency Breast Cancer and the Environment Research Coordinating Committee. Breast cancer and the environment: Prioritizing prevention; 2013.

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3. Scoping Reviews and Conceptual Reviews of the Literature

From the foundational documents, a preliminary list of breast cancer risk factors, as well as preventive and protective factors, were identified for inclusion in this Plan. This list was presented to the AC for further consideration. The AC's discussion confirmed this list and proposed areas for expansion. Participants in community listening sessions (described below) also suggested topics for review. Through these various refinements, a total of 23 risk and preventive factors were established for review and consideration. The full, complied list can be seen in Figure 4 above.

Once the list of factors was established, scoping reviews of the scientific literature were conducted to ensure that the Plan incorporated the most up-to-date science available. Scoping reviews are a method of synthesizing evidence to provide a wide perspective on a body of research.[18] They are especially relevant for complex areas of research where different research methods may apply and offer a rigorous, transparent, and comprehensive approach to reviewing the literature. Unlike systematic reviews, researchers may not rate the quality of the literature, because scoping reviews are a means to get a broad overview of the body of research.

Where reviews and compilations of literature already existed for a risk or protective factor, the date range for the scoping reviews was limited by identifying the most recent meta-analysis or systematic review cited in the Interagency Breast Cancer and the Environment Research Coordinating Committee Report (one of the foundational documents). This report was chosen because it was published relatively recently (2013) and takes the most comprehensive view of primary prevention of breast cancer among all the foundational documents. Additionally, the sections were vetted by a robust group including the Advisory Committee and expert science reviewers (see full list in the Acknowledgements). For each of the 23 factors, the literature from 2012 to 2019 was searched in PubMed with a comprehensive list of relevant keywords (full list available on request from BCPP). Titles were screened for relevance and then abstracts were screened for inclusion by two independent researchers. A third researcher acted as a tiebreaker for inclusion. In total, over 68,000 titles, and 3,700 abstracts were screened, and ultimately 2,206 articles were included in the review over the 23 factors.

It is important to note that the level of available scientific evidence varies considerably by topic. This Plan does not weigh factors against one another but assesses if adequate evidence exists to suggest concern. When appropriate, the authors have noted topics that fall under the "emerging concern" category, meaning we are at the early stage of scientific understanding of the role it plays in breast cancer, but there is enough evidence to suggest the need for a proactive public health approach to addressing the concern.

4. Study Groups

Over the course of developing *Paths to Prevention*, nine on-line study group sessions were held. Study groups provided an opportunity to integrate additional perspectives, knowledge and needs on each topic. Topics were chosen from the list of scoping reviews mentioned above (see Fig. 4).

Study groups were 1.5 hour-long webinars open to the public and broadly marketed to scientists, environmental health and justice advocates, labor advocates, and other stakeholders. They each followed a similar pattern:

- Explore the scope of the science behind known and suspected risk factors for breast cancer;
- Discuss new and emerging science and identify strengths, weaknesses, and gaps in the research; and
- Explore potential interventions to address these risk factors.

Not all scoping review topics were covered in the study groups. Topics were selected by the AC based on the need to more deeply explore complexities in the science and potential interventions. For example, study groups related to tobacco or alcohol were not held because a well-established body of science and interventions already exist in these areas.

All study groups were recorded and made available to the public. Recordings can be found here: http://bit.ly/2fmF6cA. A full list of study group topics and the presenters is available on request.

5. Community Engagement

California is a large, diverse state that is home to a wide range of communities that have been affected by breast cancer. Communities hold valuable information about the issues relevant to their local context and often have experience developing interventions to address local needs and an intimate understanding of the community's strengths, challenges, and barriers to effective change. Community knowledge is not often included in published literature, but it is essential to the process of creating a Breast Cancer Prevention Plan that has relevance and currency in the most impacted communities.

In order to incorporate these important perspectives into *Paths to Prevention*, Breast Cancer Prevention Partners undertook a multiple-step process of community engagement and relationship building:

a. **Engaging Community Advisors:** BCPP contracted with three AC members: Janette Robinson Flint, executive director of Black Women for Wellness; Caroline Farrell, executive director of Center on Race, Poverty & the Environment; and Sarah de Guia, executive director of California Pan Ethnic Health Network, to take on expanded advisory roles to ensure BCPP had an inclusive and informed perspective on community engagement for this project. They advised the BCPP team throughout the process, helped host community listening sessions, and identified community leaders to engage.

b. **Listening Sessions:** Over the course of the project, the BCPP team met with community members and groups across the state to introduce them to the CA Breast Cancer Primary Prevention Plan and to hear their perspectives on breast cancer risk and potential actions that could be taken to reduce risk. Each session was 2.5-4 hours long (depending on local need and availability) and was organized with the help of a local community leader. We chose locations across the state with geographic variety and rural and urban representation. We also sought to work with local hosts our team had existing relationships with or people who our Advisory Committee members recommended.

   Over the course of this project we visited 11 communities and met with more than 125 people. Cities we visited include Delano, Fresno, Los Angeles, Nevada City, Oakland, Pacoima, Richmond, Sacramento, San Francisco, Seville, and Tracy. When relevant, we provided Spanish translation for participants.

   At these events we collected extensive notes on the local perspective of what needs to be addressed in order to reduce breast cancer risk. This provided an opportunity to expand the staff's understanding of barriers to be overcome as well as some examples of local or regional organizing efforts that could be considered in the development of this Plan.

c. **Report Back:** In November 2018, at the completion of the community listening sessions tour, the team synthesized what we had learned from our sessions and distributed these notes to all participants in the listening sessions. We invited participants to provide feedback on any additions or misinterpretations in the information presented. After listening session participants had a chance to review the materials, BCPP staff compiled key themes and highlights from each community and presented them in a webinar to which anyone interested in the project was invited. These themes are highlighted in the text box below.

d. **Draft Report Review:** In April 2019, BCPP convened a small, core group of community representatives for two days to provide in-depth feedback on a draft of key sections of the Plan. We intentionally asked people we felt would be willing to provide an honest critique of any of our recommendations and help us think through potential unintended consequences.

10 Themes Emerging from *Paths to Prevention* Listening Sessions

After conducting community listening sessions across California, the following 10 themes emerged as particularly relevant to shaping the Plan:

1. **Prevention efforts must benefit everyone** regardless of race, economic status, immigration status, and other characteristics that generally marginalize and oppress people.

2. **Stop blaming individuals for structural inequities**. Address structural barriers such as lack of access to healthy food and safe spaces for physical activity.

3. **Work with existing communities and structures to address needs.** Look to churches, spiritual groups, schools, and community groups for education, outreach, and organizing opportunities.

4. **Support and develop community centers.** Central community centers can be a critical resource in underserved areas.

5. **Improve air quality.** Air quality is a critical concern throughout California, in both rural and urban areas.

6. **Improve both water quality and access to water** across the state, with a special focus on unincorporated areas that are especially underserved.

7. **Address food deprived areas, food access, and food cost.** Lack of access to healthy foods, both in terms of location and expense; ready availability and affordability of unhealthy fast foods; and lack of time to prepare, knowledge of or cultural familiarity with healthy foods all add to the challenge of maintaining a healthy diet.

8. **Explore significant updates in the way planning and zoning is done.** Reduce multiple stressors and unhealthy exposures and provide additional support to rural and unincorporated areas which have been intentionally marginalized in the past.

9. **Create more equitable cities (and towns).** In almost every community visited, we saw stark contrasts in services and resources available in different parts of the same city.

10. **Reduce Pesticide Exposure.** Both urban and rural areas are exposed to pesticides, but effects may be most profound in rural areas, especially agricultural areas.

6. Intervention Literature Research

Literature reviews on the effectiveness of existing risk reduction efforts were conducted to identify potential interventions for consideration in the Plan. Where appropriate, interventions were considered that were not designed specifically to address breast cancer. For example, efforts to reduce smoking were largely initiated to address lung cancer risk, but lessons from those interventions are relevant to inform efforts to reduce breast cancer since smoking is also a breast cancer risk factor. This is similarly true for nutrition and physical activity interventions.

The intervention research was done in three phases:

a. First, we searched databases and agencies that evaluate multiple sources of evidence and make recommendations, including:

   - The Cochrane Library
   - The U.S. Preventative Task Force
   - UK National Institute for Health and Care Excellence (NICE)
   - Research-Tested Intervention Programs, U.S. National Cancer Institute
   - Community Preventive Services Task Force, U.S. Dept. of Health and Human Services

b. Second, we conducted a substantial search for interventions related to all scoping review topics in PubMed.

c. Third, BCPP reviewed the interventions gleaned from these sources to get a sense of the breadth and depth of preventive interventions with relevance for breast cancer. If an intervention appeared successful and had some demonstrated potential to reduce breast cancer risk, we included it in the list of interventions to review for possible inclusion in the Plan.

7. Additional Intervention Research

BCPP conducted extensive internet searches to identify and assess potential intervention ideas highlighted by nonprofit organizations; community groups; school districts; and local, regional, and state governments. This area of research was applied especially to risk factors that had been identified, but where inadequate intervention ideas were offered over the course of all other inputs described above.

All the data and information gathered from the above steps was then synthesized and woven together to form the recommendations in *Paths to Prevention*.

How Recommendations Were Made

Interventions presented in this Plan were chosen to address the breast cancer risks and protective factors investigated in the scoping review process. The results of the scoping reviews were summarized to identify key scientific themes about the connection to breast cancer risk. These themes were then translated to overarching goals for interventions. Once these goals were established, all the interventions identified throughout the process were considered for how they would meet those goals. Our sources for potential interventions are described above.

After the goals were identified, interventions were reviewed to identify key objectives, or general areas of activity, that should be addressed. In order to arrive at more specific action recommendations, referred to in this Plan as strategies, we evaluated the 450 intervention ideas using the following criteria:

- Does the intervention support the science-based intervention goals?
- Is the intervention in alignment with the Guiding Principles of *Paths to Prevention*?
- Is there evidence that the intervention has been successful in the past (if the intervention has been studied) or does it show potential for success (especially if communities indicated that it was helpful)?
- Does the intervention address cross-cutting, systemic problems?
- Was there general agreement that the intervention would do no harm, i.e. not create unintended consequences?

Where possible, we tried to include recommendations that could be implemented in a wide range of realms, including not just state-level legislation, but also ideas for adoption by cities, school districts, counties, companies, and other institutions.

Additionally, some recommendations we presented broadly but may not have a precise formula to address. For example, we know that physical activity is protective, but to date there are not specific science-based recommendations of how much or what kind of physical activity is needed at different life stages. In cases such as these, we made recommendations that encouraged physical activity generally, recognizing that only in extreme cases would there be risk associated with this recommendation.

The process of finalizing the recommendations involved numerous people over numerous rounds of review. BCPP staff sought input and revisions from the AC at no fewer than three points throughout the development of the plan. Additionally, community representatives who had been involved in study groups or listening sessions were also invited to provide feedback into drafts of the Plan (see above for description). Figure 5 shows an overview of the process.

The interventions presented in this Plan are not exhaustive, but in our view, highlight some of the best examples we encountered through our research across the many sources we reviewed. Our hope is that a wide range of other organizations across the state, including BCPP, will collaboratively lead efforts to implement the pieces of this plan that speak most to the needs of the people they are connected to. We also fully expect that some of these recommendations will serve as a diving-off point for people to develop their own proposals that address the specific needs of their community.

Figure 5. Weaving the Pieces Together

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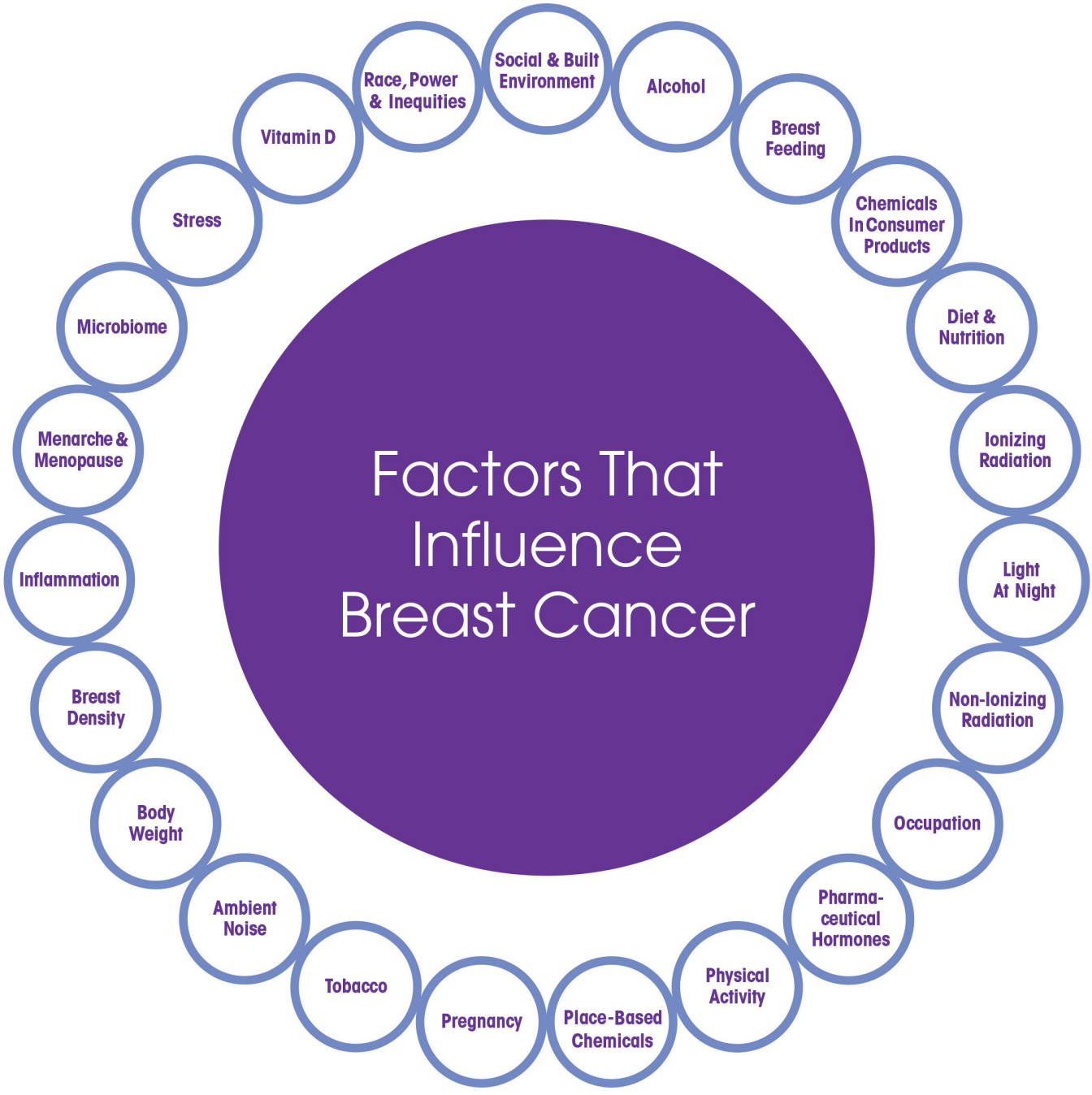
Paths to Prevention: A Living Document

Paths to Prevention seeks to spark ideas, discussion, new partnerships, and new approaches to breast cancer prevention. Some of the recommendations will be spot-on, ready for implementation from the start. Others require more inquiry before people dive headfirst into putting them into action. Which recommendations fall into either category may depend on the context in which they are considered. A perfect solution for Los Angeles might not be relevant for the Central Valley or the Sierra foothills. The needs of one place may change in an instant—perhaps because of wildfire, earthquakes, or floods. Plans must evolve in response to people's lived realities.

Paths to Prevention serves as a diving-off point, but it is in working with the Plan—in having vigorous debate about the merits and shortcomings of any ideas, in experimenting and then learning from what happens, in responding to the unexpected, in allowing ourselves to be inspired and transformed by the full range of ideas, approaches, and personalities of all the people involved—that emergent, relevant, and needed solutions are created. This emergence allows for spontaneity, creativity, and greater inclusiveness in how society's challenges are addressed. *Paths to Prevention* will be at its strongest when there is fluidity between the proposals in the Plan and the needs and desires of the communities working to make change happen.

Risk Factors Chart



SECTION 1

RISK FACTORS FOR BREAST CANCER THAT INFLUENCE AND PROVIDE A CONTEXT FOR ALL OTHERS

1

Race, Power, and Inequities

Science Summary

Breast cancer incidence is not distributed equally among different ethnic or racial communities or groups, due to a number of complex, often interrelated factors. For example, Black women are twice as likely as White women to be diagnosed with triple-negative breast cancer, a more aggressive subtype of the disease. In addition, elevated risk among some groups may be misrepresented, such as when rates are reported as lower for all women of Asian and Pacific Islander descent, ignoring potentially elevated breast cancer risk among young Japanese and Filipina women.

What the Foundational Documents Say

Multiple reports have highlighted the need to report cancer disparities based on ethnicity or country of origin, rather than on major categories of race or ethnicity.[1,2] The 2012 Institute of Medicine report noted that there are 60 distinct ethnicities in the Asian and Pacific Islander population.[2] Similarly, Latinas include women from Mexico, Central America, and South America with heritage from multiple indigenous populations, as well as from European colonizers and West Africans as a result of slavery.

Furthermore, race and ethnicity have complex relationships with socio-economic status in the U.S., and both factors are related to breast cancer risk.

An ongoing concern is the disparity in breast cancer incidence among Black women, who, until 2012, had lower overall incidence of breast cancer than White women but higher incidence among women below age 45.[2,3] Breast cancer incidence among Black women of all ages is now equal to incidence among White women (the group with the highest risk historically).[4]

The complex reasons for disparities in risk along with historical lack of data, particularly for women of color, underscores the need to engage the affected community in conducting research and communicating and disseminating research findings.[3]

The Current State of the Evidence

Health disparities can be defined as "differences in health, which are not only unnecessary and avoidable but, in addition, are considered unfair and unjust."[5] Many discussions of disparities acknowledge social inequities and stress throughout the lifespan[6] as contributors to disease, including breast cancer risk. More specifically, social determinants of health are presented as multi-faceted and complex, particularly as they relate to elevated risk of triple-negative breast cancer among Black women.

Race is a cultural construct that refers to a shared heredity as well as shared dietary, environmental, lifestyle, and socio-economic conditions that may affect cancer incidence. Teasing apart these different contributions to health can be nearly impossible, since they overlap in systematic ways.[7] The disparities in power, access, experiences of racism, and lifetime stress are captured by the concept of weathering.[8,9] Weathering characterizes a lifetime of cumulative adversity experiences by U.S. Blacks due to "historically structured differences by race in lived experience, exposure to stressors, and access to coping resources over the life-course."[10] Another concept, allostatic load, describes the adverse effects of cumulative stressors on multiple physiological systems, and may explain some of the ways that social disparities lead to health disparities.[8] More information on stress, including the impact of adverse childhood experiences (ACEs), is detailed in the "Stress" section of this Plan. Williams and colleagues underscore the need for primary prevention, beginning early in life, to reduce racial disparities in breast cancer risk, citing physical activity, reduced alcohol consumption, and breastfeeding as strategies that could be especially important for Black communities.[8]

Relationships among residential segregation and neighborhood-level SES with breast cancer are complex, with some adverse effects due to lack of resources counterbalanced by shared culture, social ties, and informal networks of support. Some of these protective factors can be disrupted by gentrification, which can result in disruption of these social networks.[9]

Scientific protocols can either hide social factors or highlight them. For instance, when factors such as race or SES are statistically "controlled for," the impact of those factors is flattened.[11] As the study showed, when those factors are intentionally included by oversampling underserved populations and listening to community stories, research can advance the understanding of disparities and health.

Risk Disparities and Social Inequity

One study examined risk of different breast cancer subtypes stratified by both race and ethnicity. Regardless of socioeconomic status, Black women had elevated risk of triple-negative breast cancers compared to risk of HR+ breast cancers. However, for Latina women, risk of triple-negative (and HR+/Her2+) breast cancer was only elevated compared to HR+ breast cancer among those with lower SES.[12]

In the Black Women's Health Study, however, higher SES (top 4th and 5th quintiles) was associated with ER+ breast cancer but not ER- breast cancer,[13] a pattern that was replicated in a study of women with breast cancer

that found associations of higher SES with increased risk of HR+/HER2- breast cancers and HR+/HER2+ among White, Black, Latina, and API women.[14]

Social inequity in the form of institutionalized racism may affect risk of ER- breast cancer. One study found that among Black women, being born in one of the 21 states and the District of Columbia that practiced legalized racism in the form of Jim Crow laws (from about 1870-1964) was associated with a 9% increased risk of ER- breast cancer compared to Black women born in other states. Furthermore, the risk of ER- breast cancer was 41% higher for Black women born in Jim Crow states than for White women born in those states, but 27% higher for Black women born in non-Jim Crow states compared to White women born in those states.[15] Another study found that women under the age of 50 who experienced major discrimination in the workplace had 32% higher risk of breast cancer compared to women who did not experience discrimination.[16]

Specific Disparities by Race, Ethnicity, and Country of Origin

Breast cancer incidence is not distributed equally among different communities or groups. Race/ethnicity, country of origin, age, and ancestry all shape patterns of overall breast cancer risk, and, importantly, risk of different subtypes of breast cancer, which vary in aggressiveness and treatment options.

Defining Racial / Ethnic Categories

Throughout ***Paths to Prevention***, the following categories are used to describe race and ethnicity—unless a study specifically disaggregates them into more granular descriptions (e.g. Mexican Americans, Vietnamese, Afro-Caribbean).

We acknowledge that these categories are highly imperfect. Each covers a wide range of backgrounds, cultures, and other complexities and the categories do not account for overlap in individuals' and communities' racial identification. They also do not account for individuals of mixed race, including "bi-racial." While imperfect, these terms provide us with a way to talk about the science showing how breast cancer risk impacts specific races and ethnicities differently, as well as the serious inequities that exist in our society due to racism.

Asian, Native Hawaiian and Pacific Islander (ANHPI)—People of Asian and Pacific Island descent unless disaggregated in specific studies (e.g. Japanese, Vietnamese, Native Hawaiian, etc.).

Black—People of African descent including African Americans, Afro-Caribbean, and Afro-Latina.

Latina—Women of Mexican, South American, and Central American descent, unless disaggregated in studies (e.g. Mexican, Brazilian, Guatemalan etc.). We include research referring to "Hispanic women" under this term as well.

Native American—U.S. indigenous people including Alaska Natives (Note: Hawaiian Natives are included in ANHPI).

White—People of European, Middle Eastern, or North African descent (as designated by the Equal Employment and Opportunities Commission for the EEO-1 *), unless disaggregated by studies (e.g. Irish Americans, Moroccans, Iranians, Danish).

* EEOC Employer Information EEO-1 report instruction booklet. Available at www.eeoc.gov/employers/eeo-1survey/2007instructions.cfm Accessed October 2019

Black Women

As noted for other racial and ethnic groups, Black and African-American women include women from many different ethnicities, cultures, and regions, including African, Caribbean, Afro-Latinas, and others who may have distinct risks of breast cancer that are not captured by current research and whose unique experiences may not be addressed through current interventions.

Overall incidence rates among Black women have increased steadily over the past decade, and in 2012 attained levels on par with that of White women (the group with the historically highest rates).[4] Some estimates suggest Black men have elevated risk of breast cancer compared to White men.[17]

Younger Black women (under age 44) have higher risk than White women in the same age range, with estimates varying by study between 2% and 59% higher.[18,19,20] This risk may be most elevated among women aged 20-34; a 2018 study found 32% higher risk among Black women in this age range compared to White women aged 20-34. The same study found a 14% higher risk among Black women aged 35-39 years compared to White women in the same age range.[20] Numerous studies have found elevated risk of triple-negative breast cancer among Black women with breast cancer compared to White women, with estimates ranging from 1.75 to 3 times the risk;[21] a recent study found nearly double the risk of triple-negative breast cancer.[22] This elevated risk of triple-negative appears to sustain across all ages.[23]

Black women with breast cancer are almost twice as likely to have triple-negative breast cancer as the ER+/PR+/HER2 subtype.[24]

Latinas

Breast cancer risk among Latinas depends upon age, Native-American ancestry, and subtype, although most studies report only on Latinas as a large single group. Overall risk may be lower for Latinas under age 44, compared to White women.[19] Among U.S. Latinas of all ages and Mexican women of all ages, those with the highest proportion of Native-American ancestry (>54% and >84%, respectively) had the lowest risk of breast cancer.[25] Latinas with breast cancer appear to have higher rates of both triple-negative and HER2+ breast cancers, compared to ER+/PR+/HER2- cancers.[24]

Among Latinas of Mexican descent, breast cancer risk factors may be shaped by country of residence (U.S. or Mexico) and acculturation. In a series of studies, researchers found that English-dominant Mexican Americans were twice as likely to experience menarche at an earlier age almost 1/8 as likely to breastfeed,[26] and twice as likely to have a BMI >30 and to consume more than one alcoholic beverage a week compared to women living in Mexico.[27] An interview study of Black and Latina women found that both groups experienced major life stressors, such as economic hardship, caretaking responsibilities, distrust of health-care professionals, and inflexible work policies that affected their ability to care for their own health. For Latinas in this study, difficulties around immigration (69% of the women in the study were born outside the U.S.) and a sense of social isolation added to their reports of life stress.[28] See the "Stress" section in this Plan for details on the links between life stress and breast cancer.

Native North Americans

Data on American Indian/Alaska Native (AI/AN) women are sparse, particularly data that disaggregate risk by region or tribe. As an aggregated group, the frequency of specific subtypes is similar to the general population.[24] One study found 15% elevated risk of breast cancer among AI/AN women in Oklahoma compared to White women.[29] Another study disaggregated Native North Americans into six regional groups: Northern Plains, Alaska, Southern Plains, Southwest, Pacific Coast, and East. They found that risk of breast cancer was elevated among native women in the southern plains compared to White women, and modestly, but non-significantly elevated, among Alaska Natives compared to White women.[30]

Asian, Native Hawaiian, and Pacific Islanders

Recent work has sought to disaggregate the overall statistics for Asian, Native Hawaiian, and Pacific Islanders based upon country of origin and specific ethnicity. As an overall group, Asian and Pacific Islanders have the lowest incidence of breast cancer,[31] but rates vary substantially by specific group, place of birth, generation of immigration, and age.

As a group, U.S.-born Chinese, Japanese, Filipina, Korean, South Asian, and Vietnamese women born in the U.S. have 58% higher risk than women born in those same countries.[32] A 2017 analysis found increasing incidence in all Asian-American ethnic groups in California except Japanese between 1988-2013.[33]

U.S. Chinese women. Overall, Chinese women have lower risk of breast cancer than White women. However, U.S.-born Chinese women have 84% higher risk than those born in China.[32] Chinese-American women in California have lower risk of triple-negative breast cancer than hormone receptor-positive cancer.[24] However, one study found risk among young Chinese women (under age 45), to be modestly but not statistically significantly elevated, indicating the need for more research on younger Chinese women.[18]

U.S. Filipina women. Overall, Filipina women have rates similar to that of White women; however, those born in the U.S. have slightly higher risk (about 32%) than foreign-born Filipinas.[32] Among young Filipina women, risk is 72% higher than for young White women.[18] Of women with breast cancer, risk of hormone receptor-negative breast cancers is about two-thirds that of ER+/PR+ positive breast cancers, but risk of HER2-positive cancers is about 23% higher than ER+/PR+ breast cancer risk.[24]

U.S. Japanese women. Japanese women may have slightly higher risk of breast cancer overall (about 2%) than White, with no difference among U.S.-born Japanese women and women born elsewhere.[32] When subtypes are examined, Japanese women overall have a 15% higher risk of ER+/PR+ positive cancers and Japanese women aged 20-44 have a 59% higher risk of breast cancer compared to White women in the same age range.

U.S. Korean women. Korean-born women have incidence rates that are approximately 1/3 of that of U.S. White women. There is no data on the risk for U.S.-born Korean women.[32] Korean women have 63% higher risk of HER2+ breast cancers, compared to ER+/PR+ breast cancers.[24]

U.S. Southeast Asian women. Data on breast cancer risk among Vietnamese women is fairly sparse. One study found reduced risk among Vietnamese women, with rates about 60% of White women.[32] Among the broader group of women from Southeast Asia, risk of hormone receptor-negative cancers appears to be similar to that of White women. Risk of HER2+ breast cancer may be modestly (about 17%) higher than ER+/PR+ breast cancer.[24] Incidence rates among women from Cambodia (35/100,000), Laos (41.7/100,000) and Vietnam (61.4/100,000) are considerably lower than for White women (around 139/100,000).[34]

Pacific Islander. Pacific Islander women have been defined differently across different studies. However, there are variations in breast cancer incidence within this group. Samoan women's overall breast cancer incidence rates are approximately 116 breast cancer cases per 100,000 women, while Native-Hawaiian women's incidence is 135.9/100,000.[34] One study looking at Pacific Islander women with breast cancer as a group found that risk of triple-negative breast cancer was 31% lower than HR+/PR+ breast cancers.[24]

South Asian & Indian. South Asian women (defined in this study as women from India, Sri Lanka, and Bangladesh) have 23% lower risk of breast cancer overall than White women.[32] However, in a study of California women from the Indian subcontinent, researchers reported 25% higher risk of triple-negative breast cancers than ER+/PR+/HER-2- breast cancers.[24]

Risk Perception /Awareness

Several studies examined communities' understanding of breast cancer risk. One study examined risk perceptions and found that women of average risk had fairly accurate understanding of their risk, but only 18% of women at higher risk perceived themselves to be at higher risk. Black women below age 50 had notably higher concern about breast cancer than women of any other ethnicity.[35]

Two studies have examined Black women's understanding of breast cancer risk. Lewis and colleagues conducted six focus groups with a total of 50 Black women in the U.S. Southeast. Women mentioned personal care products, plastic, medication, aluminum-coated items, pollution, and chemicals in food as potential causes of breast cancer. Many discussed food, including pesticides, plastic water bottles being left in cars, and local pollutants as potential risk factors. Women also shared a sense of mistrust of medicine, as a result of historical mistreatment by medical researchers. [36]

The second study by Kaiser and colleagues conducted four focus groups with 35 Black women in Chicago. Women in these focus groups generally saw breast cancer as equally likely among all women, regardless of race. However, stories shared in the focus groups that focused on the effects of breast cancer on Black women were more personal and more detailed than accounts about breast cancer's effect on all women.[37]

Both sets of focus groups expressed a desire for more information, and in the Lewis, et al. study, participants specifically expressed a need for accurate and reliable information, presented visually and in clear language.[36]

Nuances and Emerging Considerations

Several researchers have examined whether the racial/ethnic differences in risk of breast cancer subtypes can be explained by reproductive history. In one study, about 10% of the elevated risk of ER+ breast cancer among White women compared to Black women could be explained by age at first birth, parity, and lactation/breast-feeding.[38] In another study, socio-economic position and reproductive factors mitigated risk for hormone receptor-negative breast cancers, suggesting a social influence on risk by subtype.[39] Another study found that late menarche and multiparity were protective for ER+ tumors among White women, but not Black women, while late age of first live birth increased risk of ER+ breast cancer for both Black and White women. White women who were nulliparous (women who have not given birth) also had increased risk of ER+ breast cancer, while nulliparous Black women did not.[40]

Research Gaps

As several studies have indicated, it is important to estimate risk for specific populations because of the tremendous variability within large categories of race, based upon country of origin, ancestry, and acculturation. Studies have noted these disparities among women of Asian descent from different countries and regions, highlighting the need for more research to understand these patterns. However, we found no studies that offered a similar disaggregation of women from Mexico, Central America, and South America, who are often described by the broad category of

Hispanic or Latinx. Similarly, very little research examines risk among indigenous women from different regions. Among Alaska Natives, breast cancer rates tripled between 1969 and 2008,[41] and a study of native women in Oklahoma found elevated risk.[29] Poverty, historical trauma, subpar housing, and gaps in chemicals regulation on tribal lands suggest several exposures of concern among AI/AN women. As discussed in the Introduction to this Plan, established science reflects similar racial and ethnic biases as the rest of our society. In seeking to overcome those biases, research must incorporate community wisdom and experience in order to fully understand the impact of breast cancer on the diversity of women in California.

Sexual minority (lesbian, bisexual, transgender) women may have an elevated risk of breast cancer of 6-10%.[42] Future research should examine changing reproductive patterns among these communities to determine if these findings can be explained by reproductive patterns, other group differences, and social strains associated with heterosexism (societal privileges based upon heterosexuality).

Overall, it is difficult to isolate the varied contributions to differential risk among individuals from different ethnic backgrounds and cultures, because residential segregation, socio-economic status, heredity, and exposures to racism co-occur in systematic ways.

Take-Home Message

- Health inequities are differences that are unfair and inequitable but potentially preventable with systemic interventions that address the root cause of the inequities.
- Black women have increased risk of more aggressive subtypes of breast cancer, which may be partially explained by historical and institutionalized racism.
- There is a need to disaggregate breast cancer risk from large static categories of race/ethnicity (e.g. "Asian and Pacific Islander" and "Latina"), and consider country of origin, place of birth, acculturation, and the features of the neighborhood or community where people live, which can impact other risk factors.
- People want accurate, reliable information about breast cancer risk factors, presented in a clear manner.

Race, Power, and Inequities: Context for Interventions

California is home to a large and diverse population. Nearly 40 million people live here,[43] yet no race or ethnic group constitutes a majority of the state's population.[44] In 2014, Latinos surpassed Whites to become the state's largest ethnic group.[44] There are 109 federally recognized Native-American tribes and 78 more seeking recognition.[45] More than a quarter of the people surveyed in the 2010 Census who live here were not born in this country,[43] with immigrants from more than 60 different countries[44] speaking at least 220 languages.[46]

In 2018, 144 billionaires lived in the state,[47] yet 19% of the population lived in poverty.[48] Nearly 1.5 million lesbian, gay, bisexual, or transgender people live here.[49] Approximately 22% of the population has a disability.[50] More than 110,000 people are refugees.[51]

Despite our diversity, political underrepresentation persists. In 2019, more than half of the people in the California Legislature were White, 70% were male, none were transgender, and none made under $100,000 per year. Only 10 out of 126 were African American and one was Native American.[52] This leaves a significant portion of the population lacking legislative power and representation.

The problem goes beyond formal decision-making structures. Racism is a fundamental cause of adverse health outcomes, leading to significant racial and ethnic inequities in health.[53] Even reaching greater levels of economic security does not reverse this reality. In fact, racial inequities in health tend to be more pronounced for people of color, especially Black people, who are at the upper end of the socio-economic spectrum, likely linked to the consistency of acute (specific events) and chronic (ongoing, "everyday") discrimination.[54]

Much more research is needed to understand the differential rates of breast cancer subtypes in women of various races and backgrounds, and how that relates to differences in risk factors. However, at community listening sessions across the state, women were confident that multi-generational trauma—for example, the living legacy of enslaving people from Africa or the genocide of Native Americans—plays a role in their increased risk.

Participants described living intersectional lives—experiencing multiple forms of oppression simultaneously. Where economic opportunities were lacking, there was also often high exposure to air and water pollution, lack of access to healthy food, and other concerns. This is no accident; it is a result of intentional policies to oppress communities of color and other marginalized groups by creating barriers to financial, material, and social opportunities, as well as emotional and community safety.

Addressing racism while also addressing economic instability and other forms of marginalization and oppression is critical to reducing inequities. Failure to address social problems from an intersectional lens can lead to unintended consequences and perpetuate systems of oppression that created many of the problems in the first place. There are cultural, social, economic, and biological factors that together give shape to breast cancer risk.[8]

There are no simple solutions to heal the depth of harm that many Californians have and continue to experience. However, there are models of healing justice[55] that are taking root, inviting communities to develop healing pathways out of oppression through building resilience and reimagining how to live beyond the trauma. Many movements[56] use this framework in storytelling, healing rituals, and other approaches, and it has the power to transform the way social change work is done. Any interventions to address inequities must ensure that affected communities lead the way and have the opportunity for collective healing.

A true vision of preventing breast cancer in California must take a radically inclusive approach to addressing the needs of our highly diverse population. Community organizing, especially in communities of color, has demonstrated success in developing effective policy solutions that address structural inequalities.[57] Central to all interventions must be a commitment to having the affected communities lead in identifying both the problems and the solutions.

Power inequities run so deep in our society that it is beyond the scope of this project to identify all aspects of what could be done to address this. Additionally, reducing breast cancer risk is only one aspect of the overall goal of ending racism and other oppressions, yet breast cancer prevention provides an additional lens in support of these societal struggles. Here we focus on some of the ways California could build capacity to tackle these problems and heal the trauma of oppression. The connection between oppression and breast cancer risk crosses a number of other topics covered in this Plan and are explored in further detail in other sections.

Community Input on Race and Inequity

Community listening session participants described living intersectional lives—experiencing multiple forms of oppression simultaneously. Where there was lack of economic opportunities there was also often high exposure to air and water pollution, lack of access to healthy food, and other concerns. Participants largely understood this to be a result of intentional policies to oppress communities of color and other marginalized groups by creating barriers to financial, material, and social opportunities as well as emotional and community safety.

Women also expressed deep concern about the need to address and heal multi-generational trauma, for example, the living legacy of enslaving people from Africa or the genocide of Native Americans, as an important commitment to reducing a wide range of breast cancer risk factors they experience.

Throughout the community listening sessions, we heard many Black women discuss how they often do not get full and appropriate treatment even when they have access to quality clinics and doctors. One of the specific issues raised was that Black women are often not believed when they display symptoms, causing them to be diagnosed with later-stage cancer and die more frequently. While access to and quality of care is outside the scope of this Plan, this issue was raised multiple times and is of high concern for general health, and can therefore undermine prevention efforts.

Reducing breast cancer risk is only one aspect of the overall goal of ending racism and other oppressions, yet breast cancer prevention provides an additional lens in support of these societal struggles.

INTERVENTIONS

Overarching Goal: Build power and create accountability to address the historical roots and ongoing trauma of discrimination and systemic oppression based on race, ethnicity, income status, gender identity and orientation, sexual orientation, immigration status, disability, or other factors that may increase breast cancer risk.

Intervention Goal 1

Create accountability to address historical harm and trauma, which have lasting effects on the opportunities and structures that shape many aspects of breast cancer risk today.

Objective 1: Explicitly name historical harm as it relates to government agencies and programs.

- **Strategy 1:** Declare racism a public health crisis. Milwaukee County in Wisconsin was the first in the country to do so and can serve as a model for cities, counties, and the state of California.[58]

Objective 2: Take action to right the wrongs of the past that affect people's well-being today.

- **Strategy 1:** Support the recognition of tribal identity and tribal lands for Native-American people in California.[59]
- **Strategy 2:** Support California's voting rights efforts and encourage—and safeguard to the extent possible—full participation in the 2020 U.S. Census to ensure representation of the state's diverse populations.
- **Strategy 3:** Support and protect California's sanctuary state status at the city, county, and state level.
- **Strategy 4:** Call on Congressional leaders, through state legislative action, to support federal efforts to address historical wrongs; for example, offer reparations to Blacks or return land to Native-American tribes.
- **Strategy 5:** Shift investments from policing, criminalizing communities of color, and incarceration to investment in community resources and restorative justice models.[60]
- **Strategy 6:** Adequately fund mental health services, especially those services that support people who experience historical trauma from cumulative emotional and psychological wounding across generations, such as is prevalent in Native-American communities.[61]
- **Strategy 7:** Expand anti-discrimination and civil rights legislation to strengthen fairness in housing, employment, education, policing, planning, and distribution of state funds, as well as protect the religious, spiritual, and cultural traditions of marginalized communities.
- **Strategy 8:** Expand school curricula to ensure a more complete, accurate, and representational history of all people. Curricula should include the atrocities (slavery, genocide, etc.) and challenges different groups have experienced as well as the culture, political movements, and victories of different groups.[62]

Intervention Goal 2

Build power and capacity for women in California to drive societal change that reduces breast cancer risk.

Objective 1: Grow women's leadership in community organizing, advocacy, and election to public office.

- **Strategy 1:** Expand foundations' investment in non-profit organizations specializing in educating, training, and capacity building for women—particularly women of color, low-income women, disabled women, and

Intervention Goal 2 (continued)

Build power and capacity for women in California to drive societal change that reduces breast cancer risk.

LGBTQAI people—to be involved in the political process, including training to prepare women to seek and serve in decision-making positions.

- **Strategy 2:** Support policies that improve women's capacity to support themselves and engage in the public process. Examples include laws that establish a living wage, so that women working in lower-wage jobs (where they are over-represented) do not need multiple jobs to make ends meet; and policies that provide free, high-quality childcare to anyone who needs it, including young mothers in high school and college so they are free to continue their education.
- **Strategy 3:** Educate and train women, particularly girls and young women, to understand breast cancer risk and how to advocate on their own behalf to reduce those risk factors.
- **Strategy 4:** Expand representation of people of color, low-income people, and other under-represented people on local, county, and state boards and commissions.

Objective 2: Build capacity in California's rural communities, especially in unincorporated areas, for women to advocate on their own behalf to ensure basic public-health needs are met.

- **Strategy 1:** Develop educational tools and training programs for people in rural and unincorporated areas to learn best practices to influence decision makers.
- **Strategy 2:** Conduct comprehensive needs assessments at the county level to ensure that the needs of under-represented people are understood and addressed, especially in planning and infrastructure investment (See the "Social and Built Environment" section for more details on why and how this relates to breast cancer risk).
- **Strategy 3:** Build a greater awareness in state legislatures of the need to include the concerns of unincorporated areas in their efforts, specifically to address the tendency for local and county decision-makers to exclude the interests of people living there.

Intervention Goal 3

Expand culturally appropriate education and awareness efforts related to breast cancer prevention.

Objective 1: Require medical providers and health care systems[63] to be adequately prepared to serve the language and cultural needs of their patients, including offering adequate translational services, providing culturally appropriate education and support services; and receiving ongoing training on how to ensure implicit bias against specific groups of women does not interfere with ensuring fair and equitable medical care for everyone.

Objective 2: Develop breast cancer prevention messages in partnership with the communities they are intended to inform to ensure cultural appropriateness.

Objective 3: Offer culturally relevant education, including public service announcements and ads, on breast cancer risk factors, targeted to various under-served populations and provided in a wide range of languages.

Objective 4: Develop or support existing campaigns to reform the media's representation of women, and women of color in particular, to offer positive examples of women's relationship to their bodies, their beauty, their sexuality, their self-worth and, if relevant, their roles as breastfeeding mothers, in order to encourage and support women's advocacy and engagement in activities to reduce breast cancer risk.

Intervention Goal 4

Endorse and support movements that address discrimination, marginalization, and oppression that can underlie and exacerbate breast cancer risk factors.

Objective 1: Organizations working for social change in California should adopt frameworks and principles that support justice, including the Jemez Principles,[64] Environmental Justice Principles,[65] and the Louisville Charter for Safer Chemicals.[66]

Objective 2: Community organizers and social change advocates should work in multi-cultural, multi-racial solidarity to ensure that policy and intervention proposals aimed to prevent breast cancer and other illnesses do not lead to unintended consequences.

- **Strategy 1:** Support the principles and efforts of movements that advocate for oppressed and marginalized communities, including racial justice (for example, Black Lives Matter), Native-American rights, and immigrant rights; Lesbian, Gay, Bisexual, Transgender, and Queer rights; disability rights; and others.
- **Strategy 2:** Build organizations and institutions that work within a racial justice framework. In particular, predominantly White-led organizations (including breast cancer and public-health organizations) must invest time and energy in building a workplace that is diverse and inclusive, and in developing strategies that promote racial justice and address White privilege and unconscious bias within their organizations and their social-change strategies.
- **Strategy 3:** Strengthen connection and collaboration between health and justice advocates in California to promote cross-movement work, address the full spectrum of social concerns in the state, serve as strategic advisers to each other's efforts and vet each other's work for unintended consequences. As an example, share knowledge and promote cross-cultural collaboration between Black and Native-American women who share similar experiences and outcomes on metastatic breast cancer.

Intervention Goal 5

Expand research to better understand how various social determinants of health (SDOH) impact breast cancer incidence and risk.

Objective 1: Support research on breast cancer risk factors as they relate to specific groups of women; for example, women from different races (especially for women of mixed-races),[67] immigration status, socio-economic status, gender identity, sexual identity, abilities, etc.

Objective 2: Support research on the connection between racial and ethnic background and breast cancer subtype, as well as the role of racial discrimination and violence in elevating breast cancer risk.

Objective 3: Promote the systematic collection of data on Social Determinants of Health (SDOH) to facilitate surveillance and research on how these determinants impact breast cancer risk.[68]

Objective 4: Support research regarding breast cancer and incarcerated women, including surveillance of incarcerated women during and after incarceration and risk factors unique to this population.

Objective 5: Support research on the link between breast cancer risk and multigenerational trauma and the chronic stress of racism.

Objective 6: Support research on the effectiveness of policies and interventions to reduce breast cancer risk, particularly among marginalized groups.

Objective 7: Expand funding for community-based participatory research to better understand breast cancer risk and how to prevent the disease by increasing the California Breast Cancer Research Program's funding through expansion of the current Breast Cancer Fund cigarette tax to all tobacco products.

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The Social and Built Environment

Science Summary

Aspects of the social and built environment have far reaching impacts on a wide range of health and societal issues. Addressing these negative features of the social and built environment may reduce breast cancer risk and other negative health concerns in two major ways: (1) by reducing pollution, improving transportation, increasing access to clean water and healthy food, and expanding opportunity for physical activity, and (2) by improving health by allowing those living in problematical conditions to move safely through their neighborhoods and communities and interact with others to increase social affiliation and decrease isolation.

What the Foundational Documents Say

The 2013 report by the Interagency Breast Cancer and the Environment Research Coordinating Committee considered the impact of the built environment (described as human-made or modified surroundings) on breast cancer incidence. The report considered the socio-cultural experience as part of the environment and recognized that low-income communities often face greater exposure to urban air pollution and to chemicals and pesticides that have been implicated in both pre-and post-menopausal breast cancer. The report also highlighted that characteristics of the built environment such as buildings, parks, roads, or energy sources may influence pubertal onset and breast cancer risk through effects on behavioral factors and environmental exposures. For instance, features of the built environment in low-SES neighborhoods may limit access to physical activity and fresh produce which may impede healthy diet choices and lead to increased body weight. Unsafe environments also impede social interactions and thus increase social isolation, which is associated with depression and anxiety.

The Current State of the Evidence

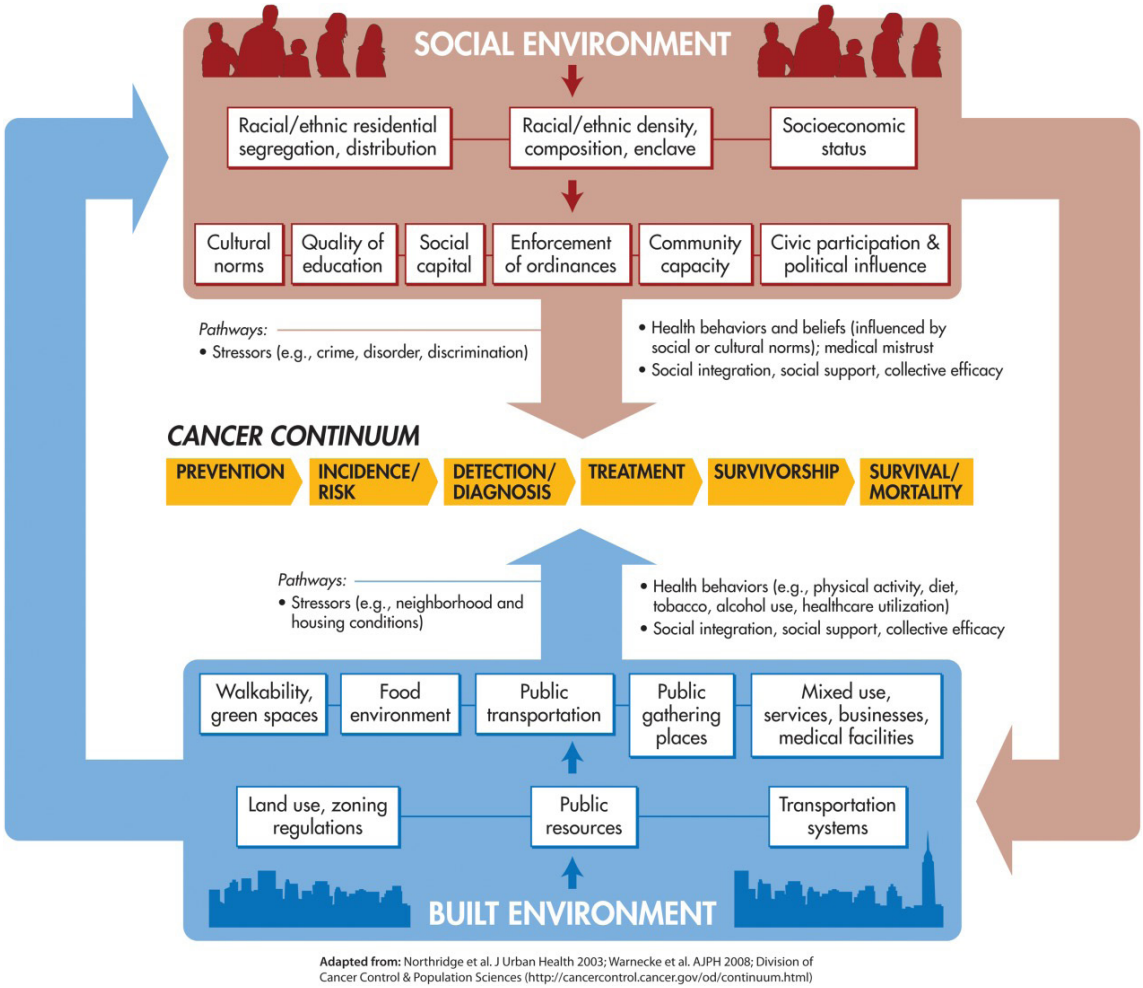
Social and built environments are intersecting aspects of the places where people live, work, and engage in recreational, educational, and other activities. The built environment generally refers to physical aspects, including homes, buildings, schools, streets, open spaces, and other infrastructure.[1] The social environment more broadly includes the social structures that shape human interaction, culture, and social relationships. Since many aspects of the built environment are shaped by social forces, these two concepts are deeply intertwined.[2] Many aspects of the

social and built environment—such as workplace locations; industry and waste facilities that expose people to toxic chemicals and noise; the configuration of parks, streets, sidewalks, bike lanes, and public transit that can enhance or limit physical activity; and the location of schools, food infrastructure, and neighborhood safety—can have far-reaching effects on health. Environments that are poorly maintained can foster illegal activities such as crime, thus leading residents to become hypervigilant and less likely to venture out to engage in social activities.

Characteristics of the social and built environment are profoundly shaped by social inequality, income inequities, educational opportunities, systemic racism, and opportunities for meaningful and well-paid work. We examine these characteristics, which deeply shape people's lived experiences, in two separate sections of this chapter to allow a deeper analysis of each topic.

Figure 5: Factors in the social and built environment which impact cancer— From Gomez, et al, 2015[3]

Research since 2012 highlights four aspects of the social and built environment that may play a role in breast cancer risk.



Adapted from: Northridge et al. J Urban Health 2003; Warnecke et al. AJPH 2008; Division of Cancer Control & Population Sciences (http://cancercontrol.cancer.gov/od/continuum.html)

Affluence and Socioeconomic Status (SES): Affluence is generally linked to increased breast cancer risk, a trend that persists globally. Research has previously focused on White women and has consistently shown higher risk of breast cancer associated with higher individual and neighborhood SES and other measures of affluence.[4,5] Data on other ethnicities has been more mixed.[6,7,8,9] Recent research has shown that this association may be driven by increased risk of luminal (ER+/PR+/HER-2-) breast cancers, which are the most commonly diagnosed breast cancer subtypes especially among White women. A study of Black women also found higher SES (both neighborhood and individual) associated with ER+ breast cancers though no association for SES and ER- cancers.[10] Findings from a number of studies have suggested that observed associations with SES may be largely but not completely accounted for by reproductive factors associated with both ER+ breast cancer and SES, including later childbirth and lower parity.[10,11,12]

Few studies have examined the influence of early life SES on women's later life breast cancer risk, however two looked at the effect of parental education, parental occupation and childhood neighborhood SES. These found that family income and maternal education levels are positively associated with breast cancer risk, but not neighborhood SES. When they looked more closely, they found that the direct effect of maternal education was on the daughters' own education, occupation, age at first birth and parity in adulthood, which then affected the risk of breast cancer. However, family income's effect was not fully accounted for by these factors, indicating the need for further research to understand the relationship.[13,14]

Local Exposures: In a nationwide study based on county-level data, women living in counties with poorer built environment, characterized by poor road safety, transit behavior, business environment, and subsidized housing, had a five-fold increased risk of breast cancer.[15] The same study also found a 5-fold increased risk in those living in adverse social environments, defined by poverty, median housing value, educational attainment of residents, unemployment, and housing patterns. These factors interact with other factors like place-based chemical exposures. This analysis also found a 3-fold increased risk for poor air quality. It is difficult to impossible to tease apart the various types of unhealthy aspects of the built environment; however, this also means that addressing one aspect of the social and built environment can ripple into other factors of everyday life.

Urbanization: Urbanization has been linked to increased breast cancer risk around the globe. Women in urban areas of Wisconsin had a 17% higher risk than women in rural areas of Wisconsin after individual risk factors were considered.[16] In France, being born in an urban area was linked to a 7% increase in breast cancer risk;[17] and two studies in China found associations between living in urban areas and breast cancer.[18,19] These relationships may be affected by SES. An analysis of U.S. Cancer Registry data (Surveillance, Epidemiology and End Results; SEER) found that the positive relationship between more urban areas and breast cancer incidence was fully accounted for by SES quintile and the density of primary care physicians.[20]

Nuances and Emerging Considerations

Important nuances regarding breast cancer incidence exist especially regarding race, including the impact of neighborhood characteristics. Most research to date has examined White women. Data on women of Asian descent and Native Americans are particularly sparse or non-existent. Recent studies have begun to address this gap, but more research is needed. While in general studies show higher breast cancer incidence in urban areas, one study looking at women in the Multi Ethnic Cohort (MEC) in Southern California found a 50% lower breast cancer risk among Japanese Americans residing in the most versus least urban areas in Los Angeles.[7] A study of women in the San Francisco Bay Area found increasing risk with higher neighborhood SES for Whites, Blacks and both U.S.-born and foreign-born Latinas, but an additional protective effect for Latinas living in an ethnic enclave (a community with a greater proportion of the ethnicity, strong cultural identity, and adherence to the ethnicity's cultural mores).[6]

Additional research is needed to determine the effect of neighborhood factors on subtypes of breast cancer. In contrast to studies looking at breast cancer as a whole, one looking at inflammatory breast cancer (a rare and aggressive type where cancer cells block lymph vessels in the skin of the breast) found that clusters of inflammatory breast cancer were more likely to be in counties with high unemployment, rural areas, areas with a greater percent of the people living in poverty, and poor-Black-rural, poor-Black-urban or poor-White-urban areas.[21] The section on Race, Power, and Inequities examines the literature on race, ethnicity, and risk of more aggressive subtypes of breast cancer.

These broad socioeconomic effects may mask other factors. One study found that more unhealthy food sources in a neighborhood were associated with a 10% increase in breast cancer.[7] Others have found lower physical activity, higher obesity, and more prevalent smoking behavior (risk factors related to breast cancer—see other sections) in Black people living in segregated areas than in those residing in less segregated areas.[22] Other sections in this document explore aspects of the social and built environment that affect access to healthier foods and the potential for physical activity, which are necessary to address these disparities.

Take-Home Message

- Aspects of the social and built environment have far reaching impacts on a wide range of health and societal issues.
- Addressing these negative features of the social and built environment conditions may reduce breast cancer risk and other negative health concerns in two major ways: (1) by reducing pollution, improving transportation, increasing access to clean water and healthy food, and expanding opportunity for physical activity, and (2) by improving health by allowing those living in problematical conditions to move safely through their neighborhoods and communities and interact with others to increase social affiliation and decrease isolation.
- The emerging data on breast cancer risks show a need for more research on the multiple factors affecting breast cancer subtypes as well as the effectiveness of current interventions that address the inequities identified in this report.

Social and Built Environment: Context for Interventions

California is wildly diverse in the resources it does—or does not—offer to the people who live here. These resources can have a profound influence over people's health and well-being. Children of color in California are estimated to be three times more likely to live in high-traffic areas compared to White children.[23] Nearly a quarter of California residents live further than a half mile from a park.[24] Only 5.3% of Californians commute to work by public transportation,[25] yet California has one of the longest average commute times in the country.[26]

People living in unincorporated areas are particularly underserved. One analysis estimates that 2.8 million Californians live in unincorporated areas not recognized by the 2000 census (because their communities were not characterized as Census Designated Places).[27] These areas often lack basic infrastructure such as safe and effective water delivery systems and have been systematically underrepresented in the political process across the state.

These and other inequities in the social and built environment are not accidental. They are a result of many decades of policies, such as zoning decisions, redlining (explicitly enforced by Federal Housing Administration policies adopted in the 1930s),[28] and other forms of disinvestment in communities of color, that resulted in segregations and gave disproportionate advantages to White people to accumulate and leverage wealth.[29,30,31] Aside from individual hardships, these policies ripple out to all aspects of people's lives. For example, with nearly 33% of funds for California's public schools coming from property taxes and other local sources,[31] lower-income neighborhoods have few resources to invest in children's education and wellbeing. This lack of equitable, local funding can have a profound impact on people over the course of their lives.

Some inequities come from secondary policies that address how infrastructure is used. For example, Oakland is home to one of the largest ports in the country. Once goods are offloaded from ships, much of it is transported by truck to destinations across the country. In 1963 Caltrans banned trucks weighing more than 4.5 tons from driving on Highway 580, a major potential route from the port to other key destinations. This ban shifted trucks to driving on nearby Highway 880, which has a higher concentration of people of color and low-income people living nearby. The end result is residents near Highway 880 are exposed to 50-80% more key pollutants than people living near Highway 580.[32]

California is also facing a housing crisis: we are home to the ten least-affordable major markets in the country and rank near the top in cost-burdened households.[33] There simply is not enough housing available: a disproportionate 22% of the nation's homeless population live here, with significant gaps in new housing units expected for the foreseeable future.[34] This kind of competition for housing increases the cost of living and makes it harder for low-income people to stay in their established neighborhoods.[35] The social and emotional pressure of being pushed to the margins where they may not know their neighbors and have less access to jobs[36] creates significant stress for families and communities as a whole.[37]

Access to a healthy built environment—one that has safe and adequate infrastructure; well-functioning public transportation systems; available outdoor green spaces that are safe to play in as well as indoor community centers with recreation activities;[38] and access to food, water, and clean air all support people's health. Conversely, not

having these resources can harm people. Estimates indicate that in some areas, the difference of living one mile apart can mean a difference of 15 years in a person's lifespan.[39] Yet improving the built environment often leads to gentrification and displacement, thus tearing apart the social fabric of established communities.[40,41] Addressing the built environment with meaningful community involvement, specifically the community that has lived in an area long-term, is critical to improving people's health and ensuring that the integrity of communities is maintained.

Improving California's social and built environment would help reduce breast cancer risk and other health concerns impact by creating healthier environments and reducing stress at many levels. Significant potential exists to increase physical activity and possibly reduce obesity by improving the built environment,[42,43,44,45] particularly when coupled with programs that promote the use of parks, sidewalks, bike paths, and other resources. [46,47,48] One study that looked at U.S. adult women at higher risk for breast cancer found that just living near outdoor green space can reduce sedentary behavior, and by extension breast cancer risk.[49]

The built environment can greatly influence young people's health and the development of life-long habits. The walkability within a half-mile of an adolescent's home was found to increase the minutes of moderate to vigorous physical activity they get.[50] Equally important was the finding that students living within a five-minute walk to a fast food outlet had higher body mass indexes.[51] In other words, California must increase the presence of health-supportive environments, as well as reduce environments and establishments that do not support health. (Note: Interventions related to food and diet will be described in the "Diet" section).

The benefits of living in areas with options for active transportation, such as biking and walking, extend to being more likely to know your neighbors, participating politically, trusting others, being socially involved[52] and, in the case of children going to school using active transportation, being happier and having a general increased sense of well-being.[53]

One challenge with improving the social and built environment is that many aspects involve significant investment and long-term planning. Deep, systemic change is likely to be slow, but there is reason for optimism. In 2017, California's Office of Planning and Research issued new guidelines for cities and counties in developing their general plans.[54] These plans are the local government's long-term blueprint for the community's vision for growth. For the first time, California's guidelines include specific recommendations for how city and county general plans could address health and equity moving forward. These guidelines not only set the compass for future development, they also give community members access to best practices, model language, and case studies on community health.[55] Some of the greatest potential to address making the built environment a healthier place to live seems to lie in the ability of planners and public health specialists to develop effective working relationships,[56,57] and these relationships should be built in conjunction with equitable community engagement.

While long-term planning and investment in improving the built environment is necessary, there is also potential to make better use of existing resources. In many communities, schools lock up their outdoor playground and indoor meeting rooms during weeknights and weekends. Creative use of these existing spaces could provide opportunities for community exercise, dance, nutrition classes, or other health-supportive activities. It can be difficult to get permission to use these spaces, but exploring ways to simplify the process, such as joint use agreements (formal agreements between two separate government entities, often a school district and a city or county, setting forth the terms and conditions for the shared use of public property[58]) and demonstrating the benefit to the larger community holds promise for the more immediate future.[59]

In order to look forward to improvements in the social and built environment, it's important understand the past. This is critical to ensure that the inequities established from old policies are not repeated, leading to codifying disproportionate burdens and/or displacement and the subsequent community disintegration. To build a healthier future for all people, all interventions should be developed, approved, and implemented with leadership from the communities who live there. See the text box on "Community Engagement in Planning and Decision-making" for ideas on how to do this well.

Community Input on Social and Built Environment

Community listening session participants expressed significant concerns about their built environment and how it relates to many other breast cancer risk factors: concentrated exposures to pollution from industrial operations, living close to major transportation lines, lack of green space for physical activity, lack of healthy food sources, and concentrations of low-quality and fast food establishments. Participants living in rural areas also expressed concerns about how extensively underserved unincorporated areas are, especially around access to adequate and clean water. Updating city and county plans to be more inclusive of the needs and concerns of all residents, regardless of income and race, was an important theme across the state.

Tribal Housing: Innovation and Tribal Wisdom

Research has indicated that a convergence of housing-related factors may be partly to blame for increased disease risks among Native Americans, including poorly designed and constructed homes, poverty, overcrowding, insufficient indoor ventilation, and the use of wood-burning stoves.

These factors can contribute to increased concentrations of an array of toxic indoor air pollutants. The Native American Housing and Self-Determination Act of 1996 (NAHASDA) granted tribes authority over the use of Department of Housing and Urban Development (HUD) funds.

Since then, tribes across the country have been working to improve housing on tribal lands by combining modern green design elements and indigenous knowledge passed down through generations. These healthier homes employ sustainable, locally-sourced and often natural materials, and promote cultural customs for holistic health.

In Ukiah, CA, members of the Pinoleville Pomo Nation have helped build modern, wood-framed homes with breathable wall systems of straw bales and adobe-like cob covered with a finish layer of clay-based plaster. They use the rounded walls of traditional Pomo architecture. These innovations and traditional techniques help prevent the buildup of moisture and the development of mold and improve ventilation and energy use for heating and cooling in the home.[60]

Community Engagement in Planning and Decision-Making

One of the most important aspects of addressing problems in the social and built environment is ensuring that people who live in the community where changes are being considered are given meaningful leadership, representation, and decision-making power in the process. Without this, there is a high risk of improving areas in ways that lead to displacing long-term residents and/or policing practices that do not reflect the needs of long-term residents. Other risks include a range of secondary and unintended consequences,[61] for example, bringing in a high-end grocery store does not solve lack of food access, it just provides healthy food that is often too expensive for many people and may act as a barrier to developing community-scale food solutions.

One approach to addressing these concerns is to develop a Community Benefit Agreement (CBA), which is a contract signed by community groups and a real estate developer that requires the developer to provide specific amenities and/or mitigations to the local community or neighborhood. There is a wide range of examples of existing CBAs.[62,63] Many of these have had meaningful impact, but developing the CBA and implementing it involves complex negotiations between communities, unions, planners, elected officials, and others.[63] Two resources that can help in the process include:

- **U.S. Office of Economic Impact and Diversity Community Benefit Agreement Toolkit**[64]
- **Partnership for Working Families Community Benefits Toolkit**[65]

With or without the development of a CBA, local and regional planning should allow and encourage active participation of community leaders that truly represent the long-term residents. Planning processes should provide increased accountability and transparency, respond to community needs, provide adequate notice of meetings, hold meetings at accessible times and locations, conduct meetings in the languages spoken by the community, ensure that presentations and materials regarding the process are accessible and understandable by community members, and provide authentic opportunities for feedback that will be seriously considered in the plans moving forward.

Resources to Support Livable Communities for All

Improving the social and built environment is a complex process, both in terms of determining what should be done as well as motivating the political will and funding to make it happen. Numerous organizations have developed helpful tools and frameworks to support this process. Below is only a partial list of what is available:

1. **The Guide to Community Preventive Services:**[66] A project of the Centers for Disease Control and Prevention, The Community Guide is a collection of evidence-based findings of the Community Preventive Services Task Force (CPSTF). This resource helps with selection of interventions to improve health and prevent disease in your state, community, community organization, business, healthcare organization, or school.

2. **Livability Calculator**[67] by the Transit Cooperative Research Program[68] provides tools for planning transit corridor improvements. Livability Principles include high quality transit, walking and bicycling accessibility, affordable housing near transit, transit accessible economic opportunities, cultural and recreational opportunities, access to government and social services, and healthy and safe neighborhoods.

3. **California Regional Transportation Guidelines**[69] added a new section in the 2017 Guidelines to discuss the role of transportation in public health and equity. These recommendations include policy considerations that foster accessible, livable, and healthy communities such as safe routes to school, equity considerations, and policies to promote transit, walking, and bicycling. The guidelines recommend that transportation agencies collaborate with local health departments and public health stakeholders. Transportation can provide access to healthy food, jobs, education, recreation, worship, community activities, and health care.[69]

4. **Creating Healthy Regional Transportation Plans (RTP):**[70] In 2008, California Senate Bill 375 (SB 375) magnified the importance of the RTP by adding a new component. This law requires California's 18 largest regions to create a Sustainable Communities Strategy (SCS) as part of their RTP. The SCS is an integrated plan for transportation, land use, and housing that must meet, if feasible, greenhouse gas emissions reduction targets for cars and light trucks set by the California Air Resources Board. SB 375 dramatically shifted the context and framework for RTP development, putting a new emphasis on performance and outcomes, and significant opportunities to create healthier, more equitable communities and regions. The report was released by TransForm[70] in Collaboration with California Department of Public Health.[71]

5. **CalEnviroScreen**[72] is a mapping tool that helps identify California communities that are most affected by many sources of pollution and uses other social determinates to identify communities especially vulnerable to pollution's effects.[73]

6. **Urban Habitat Board and Commissions Leadership Institute**[74] is a six-month fellowship program for people from low-income communities and people of color that teaches advocates how to understand complex and intersecting policy arenas, navigate the culture and language of commissions, and build effective relationships in and outside the commission.

California: How a Global Leader in Addressing Climate Change Can Leverage Efforts to Improve the Social and Built Environment

In 2005, Governor Arnold Schwarzenegger signed an executive order that required an 80% reduction in greenhouse gas emissions by 2050. Since then, California has adopted a range of legislative and regulatory standards for reaching those goals. The Global Warming Solutions Act of 2006 (AB 32)[75] required California to develop a scoping plan that would lead to reducing its greenhouse gas emissions to 1990 levels by 2020. In 2016, AB 32 was updated with SB 32, which expanded California's requirements to reduce greenhouse gas emissions to 40% below 1990 levels by 2030.[76] The success of this legislation led to the development of other requirements and funding streams that can be used to guide improvements in the social and built environment. Some of the interventions in this report, particularly in cleaner transportation options, can support these efforts.

Communities of color have been leading many of the efforts to address climate change. These communities are often hardest hit by polluting industries such as nearby fossil fuel extraction and power plants, and they often lack the resources to adapt to the coming changes. Over time, some of the concerns have been addressed by additional legislation and funding streams, though the process of having truly representative solutions is far from over. ClimatePlan[77] is a network of organizations in California focused on connecting California's climate efforts with land-use planning and transportation.

Some examples of legislation, guidelines, and funding sources related to California's climate efforts that may be helpful in improving the social and built environment include:

- **The Planning for Healthy Communities Act (SB 1000):**[78] Under SB 1000, cities and counties are required to adopt an Environmental Justice element, or integrate EJ-related policies, objectives, and goals throughout other elements of their General Plan. The bill also includes a process for communities to become meaningfully involved in the decision-making processes that govern land use planning in their neighborhoods.

- **California Climate Investments/Greenhouse Gas Reduction Fund (GGRF):**[79] To date more than $8 billion from California's Cap and Trade Program has been distributed to state agencies to support three priority areas: Transportation and Sustainable Communities, Clean Energy and Energy Efficiency, and Natural Resource and Waste Diversion.[81] The state's website also has a database of funding sources[80] available to individuals, governments, and institutions interested in reducing greenhouse gas emissions, as well as a map[81] showing where the three programs are being implemented.

- **The Transformative Climate Communities (TCC) Program (AB 2722):**[82] funds development and infrastructure projects that achieve major environmental, health, and economic benefits in California's most disadvantaged communities. TCC is one of many California Climate Investments programs80 and its funds can be used to build bike paths, community health programs, and walkable/greener communities.

- **Transportation Infrastructure Funding (SB 1):**[83] The state's gasoline tax is used for a range of transportation-related expenses, including $350 million funds in public transit support.

- **The Affordable Housing and Sustainable Communities Act:**[84] The State of California created the Affordable Housing and Sustainable Communities program in 2014 to invest in location-efficient affordable homes and transportation infrastructure to improve economic well-being and physical health for underserved Californians while also reducing greenhouse gas emissions (GHGs).

This is only a partial list of California's climate initiatives. For more information on the wide range of California's climate-related policies, see the UC Berkeley Law's California Climate Policy Dashboard.[85]

INTERVENTIONS

Overarching Goal: Design, redesign, and build communities to maximize health, minimize inequities, prevent displacement of existing communities, and offer the best opportunities to reduce breast cancer risk and risk for other health problems.

Intervention Goal 1

Update state, city, and county zoning and permitting laws, as well as city and county General Plans, to prevent polluting industries from being located near schools or concentrated in communities of color or low-income communities.

Objective 1: Rezone residential areas to prevent high concentrations of polluting industries.

Objective 2: Create buffer zones around schools, day care centers, playgrounds, and other locations used by vulnerable populations to prevent polluting industries or other establishments that can contribute to a higher risk of breast cancer from being sited nearby, including fast food restaurants, liquor stores, and smoke shops (or other retailers selling tobacco or vaping products).

Objective 3: Develop incentives such as tax breaks and micro-credit to establish locally owned, non-polluting business and industry, particularly in areas in need of economic development.

Objective 4: Move trucking routes away from residential areas.

Intervention Goal 2

Develop safe walk, bike, and public transit friendly cities to enhance physical activity opportunities and reduce pollution, both of which impact breast cancer risk and health in general.

Objective 1: Make cities and regions safer for using bicycles for transportation and recreation.

- **Strategy 1:** Expand the network of bike lanes and paths to accommodate and encourage recreational bike riding as well as commuting to work and businesses.
- **Strategy 2:** Work with public transportation authorities to expand access for bicycles on public transportation, including bike racks on buses, adequate space on subway/metro systems, eliminating barriers to the hours that bicycles are allowed on public transit, and providing adequate bike storage at key commute hubs.
- **Strategy 3:** Expand bike share networks in medium and high-density areas with a commitment to locating adequate bike stations in low-income areas and ensuring that membership and rental rates are affordable and/or available on a sliding scale.[86]

Objective 2: Improve the walkability in areas where people live, work, and play, to support physical activity and ease of access to services, community connection, and healthy food options.

- **Strategy 1:** Conduct a Walkability Assessment to determine some of the key areas of concern and barriers in the community. A wide range of strategies and resources are available,[87] including California Walks,[88] which offers technical assistance in conducting an assessment in an area.[89]

Intervention Goal 2 (continued)

Develop safe walk, bike, and public transit friendly cities to enhance physical activity opportunities and reduce pollution, both of which impact breast cancer risk and health in general.

- **Strategy 2:** Organize communities to advocate for sidewalks, safe intersections, well-connected walking routes, and adequate streetlights for safety while also minimizing proximity to sources of pollution (i.e. major transit routes and industries) and residential exposure to night at light.
- **Strategy 3:** Launch Safe Routes to School campaigns with a focus on low-income communities. Safe Routes to School[46,90] is a federally funded organization that offers funds to construct new bicycle lanes, pathways, and sidewalks.

Objective 3: Address safety concerns which may interfere with people's ability or willingness to use walking or biking routes and public transit, parks, and other public amenities.

- **Strategy 1:** Develop community safety plans[91] with leadership from affected community members. Plans should emphasize restorative approaches[92] to safety rather than investing in increased policing, which make many people, especially people of color, feel less safe.
- **Strategy 2:** Pass a state Vulnerable Road User law to provide legal protections to bicyclists and pedestrians by increasing penalties for certain road behaviors that result in serious injury or death.[93]

Objective 4: Create clean public transit options that effectively serve people's needs and reduce pollution that can increase risk for breast cancer.

- **Strategy 1:** Expand and coordinate regional transit plans and ensure they are developed with leadership from, and serve the needs of, disadvantaged communities. For example, local bus lines and regional subway systems should be coordinated to ensure adequate, efficient, and affordable transit coverage.[70]
- **Strategy 2:** Develop transit fleets that run on 100% renewable energy.
- **Strategy 3:** Create accessible public transit options for rural communities, with special emphasis on developing efficient routes to areas that offer access to employment opportunities and services such as health clinics, hospitals, grocery stores, and other amenities.
- **Strategy 4:** Develop livable transit corridors that integrate public transit such as light rail, streetcars, and bus rapid transit with safety-conscious walking and biking routes that connect with local business clusters and neighborhoods.[94]
- **Strategy 5:** Develop transit routes and schedules that support children using public transportation and provide affordable rates for kids.

Objective 5: Develop approaches to protect the health of the most vulnerable.

- **Strategy 1:** Provide clear, easy to use information in real time on local air quality so people, especially those with health concerns, can determine whether it is safe for them to walk or bike to their destinations.
- **Strategy 2:** Create zones that reduce heavy traffic use near the most vulnerable populations, for example, create healthy kids' zones that do not allow trucks or buses to idle nearby.

Intervention Goal 3

Ensure adequate housing, especially focusing on expanding access to affordable housing options, and ensuring that housing is free from pollutants linked to breast cancer and other diseases.

Objective 1: Increase affordable housing options especially in disadvantaged communities while ensuring the use of anti-displacement strategies. For example, seek to increase funding to affordable housing through the Working with the California Housing and Sustainable Communities Program.[85]

Objective 2: Reduce chemicals hazards in low-income housing, including ending the use of harmful pesticides, cleaning products, carpeting, paint, building materials, and any other products with cancer-causing and endocrine-disrupting compounds. Maintain current buffer zones to ensure affordable housing is not sited near highways and other sources of pollution

Objective 3: Increase Section 8 housing availability to meet the needs and demands of California's diverse regions.

Objective 4: Protect and expand rent control measures at the city and/or county level, for example by repealing the Costa Hawkins Rental Housing Act that limits the ability of local communities to protect residents from steep rent increases.[95]

Objective 5: California should become the second state to pass a statewide rent control law (Oregon was the first in February 2019). [96]

Objective 6: Restrict predatory lending policies that lure people into taking out home loans that they cannot afford.[97]

Intervention Goal 4

Build accessible, safe, affordable, and beautiful indoor and outdoor spaces where people can participate in physical activity and healthy activities.

Objective 1: Create accessible indoor multi-purpose spaces (especially in areas with poor air quality) for physical activity, including exercise and dance classes; recreational opportunities; food swaps; community building; and other activities that are accessible to everyone.

- **Strategy 1:** Seek funding to support construction, maintenance and programing for community facilities. Potential funding sources include the Community Facilities Direct Loan & Grant Program,[98] community foundations and corporate community giving programs.[99]
- **Strategy 2:** Develop additional governmental funding streams at the state, county, and municipal level to support critical healthy community services.

Objective 2: Create/expand access to outdoor spaces to use for physical activity.

- **Strategy 1:** Work with local government and planning departments to build more parks and parklets.
- **Strategy 2:** Open schoolyards on the weekend for public use and provide incentives for schools to include community programing, such as through joint use agreements. See the San Francisco Shared Schoolyards[100] project as an example.
- **Strategy 3:** Invest in beautification of public spaces, including efforts to revitalize existing resources and create new ones. Examples include planting more trees, installing benches, and funding public art projects.

Intervention Goal 5

Update and expand building codes to maximize healthy building requirements, reduce exposures to chemicals linked to breast cancer, encourage exposure to natural light, and improve options for physical activity.

Objective 1: Ensure all cities are in compliance[101] with and where possible exceed CALGreen standards,[102] the first-in-the-nation mandatory green building standards code (also known as the California Green Building Standards Code).

- **Strategy 1:** Cities and counties should strive to meet the more inclusive, energy and health protective CALGreen Tier 2 standards (CALGreen Tier 1 and 2 levels provide guidelines that exceed the minimum requirements).
- **Strategy 2:** Encourage cities and counties to exceed CALGreen Tier 2 standards by adopting "Beyond Code"[103] standards. Some examples of these upgraded standards include maximizing access to indoor sunlight, providing easy access to outdoor areas, expanding the restrictions on toxic products used in construction, and designing facilitates to increase physical activity options in the workplace such as using the stairs.

Intervention Goal 6

Invest in research to better understand the role of the social and built environment on breast cancer risk.

Objective 1: Enhance research to understand the breast cancer effects of urbanization and create interventions that reduce negative impacts.

Objective 2: Enhance research to understand which interventions are effective at improving the social and built environment to reduce breast cancer risk.

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SECTION 2

RISK FACTORS FOR BREAST CANCER FOR WHICH WE PROVIDE INTERVENTIONS TO REDUCE RISK

2

Alcohol

Science Summary

Alcohol consumption increases risk for breast cancer, as demonstrated by a large body of research. The more you drink, the higher your risk, and even light drinking increases risk. Very little research has specifically examined whether this finding is consistent across all racial and ethnic groups, although one study found that the risk associated with drinking was higher for Black women than for White women.

What the Foundational Documents Say

Overall, the foundational documents, authoritative reviews, and meta-analytic studies support the assertion that alcohol consumption is causally related to breast cancer, and many studies support a dose-response based upon 10 grams/alcohol per day. A standard drink (12 ounces of beer, 5 ounces of wine, or one shot of liquor) has approximately 14 grams of alcohol.[1]

The AICR continuous update project reported that consuming alcoholic drinks probably increases risk of pre-menopausal breast cancer and that the evidence is convincing that alcohol consumption increases risk of post-menopausal breast cancer. In both pre- and post-menopausal breast cancer, the relationship between alcohol consumption was dose dependent. For each 10 grams of ethanol consumption per day, pre-menopausal risk increases by 5% and for post-menopausal breast cancer, risk of both ER+/PR+ and ER+/PR- breast cancer increases by 9%.[2]

Both the IBCERCC report[3] and IOM report[4] listed alcohol as a known risk factor for breast cancer, and the IOM indicated that alcohol has one of the clearest relationships to the disease. The CBCRP gaps document discussed alcohol as a recognized risk factor.

Several meta-analytic studies between 2002 and 2008 show that the overall data across studies confirms a link between breast cancer and alcohol consumption. These analyses found increased risk of 22% comparing drinkers and non-drinkers,[5] and a 27% higher risk of ER+ breast cancer and 14% higher risk of ER- breast cancer when comparing those with the highest levels of consumption with those with lowest consumption.[6]

Furthermore, these earlier meta-analyses suggested a dose-response with 7-10% increased risk per 10 grams per day of alcohol consumption,[5,7] with evidence of increased risk of both ER+ breast cancer (approximately 12% higher risk) and ER- breast cancer (approximately 7% higher risk) per 10 grams alcohol/day.[6] A 2003 review estimated that 8% of breast cancer cases could be attributed to alcohol consumption.[8]

A 2017 updated review by the same authors noted that the International Agency for Research on Cancer (IARC) found sufficient animal and epidemiological evidence to conclude that alcohol is causally related to breast cancer.[9] The IARC Monographs in both 2010 and 2012 offer detailed reviews of the literature to date regarding alcohol and breast cancer. They conclude that alcohol is causally related to female breast cancer and that the data on male breast cancer is inconclusive.[10,11]

The Current State of the Evidence

Several meta-analyses and reviews since 2012 confirm the conclusions of the foundational documents. A 2015 meta-analysis of 16 studies found 28% higher risk among those with the highest consumption, when compared to the lowest consumption.[12]

A 2015 meta-analysis included 38 studies that specifically separated out people who never drank (abstainers) from occasional drinkers (which some other studies classified as abstainers), low-level, and high-level drinkers. They found 3% higher risk among occasional drinkers (<10g/week), 8% higher risk among low-level drinkers (<21g/day), 37% increased risk among hazardous-level drinkers (21-40g/day), and 34% higher risk among harmful-level drinkers (>40g/day), compared to abstainers.[13]

Several studies have included alcohol consumption as part of a healthy lifestyle index that includes other indicators, such as diet, smoking, physical activity, and body weight/BMI. In these studies, lower consumption of alcohol is considered healthier. These studies generally find that adherence to the index is protective and non-adherence increases breast cancer risk, regardless of the specific factors included in the index.[14,15,16,17] When these studies look specifically at alcohol consumption, controlling for the other factors, risk still appears to be increased. One study found 17% higher breast cancer rates among women who consumed more than 19.9 grams of alcohol/day.[15] Another study found alcohol intake in the range of 15-30 grams/day was associated with 79% higher breast cancer risk, compared to non-drinkers.[18]

A U.S. study of women under age 65 with private insurance or Medicaid, found that 12.3% of breast cancer cases among women aged 18-44 and 7.1% of breast cancer cases among women aged 45-64 could be attributed to alcohol consumption, and that $148.4 million in estimated medical costs are attributable to alcohol related breast cancers.[19] Another study estimated that 4.9% of breast cancers could be avoided if alcohol consumption were eliminated completely.[20]

Research globally is less consistent. This may be due to variations in study quality, although nearly all recent studies adjusted models are based upon similar risk factors. These variations may also be due to different common patterns of drinking globally, other cultural factors, and genetics that are not captured via the common covariates.

Among women in Brazil, risk was almost five times higher among women under 50 who had consumed alcohol and nearly four times higher among women over 50.[21] In Italy, a study of alcohol consumption of more than 10 grams/day was associated with 30% higher risk of breast cancer.[22] A study of South Korean women found that ever consuming alcohol was associated with 19% higher risk of invasive breast cancer.[23]

A study from Japan found no effect for any alcohol-related factors.[24] In Southern Australia, researchers found correlations between alcohol consumption and breast cancer in a population-based study, but odds ratios were not elevated in a case-control study at any age.[25]

Patterns of Drinking and Types of Alcoholic Beverages

Meta-analyses of light drinking also suggest increased risk. Pooled data from 110 studies of light drinking suggests 5% higher risk overall. Among studies from North America, estimates ranged from 2% to 9% higher risk.[26] A 2018 meta-analysis of 27 studies of very light (less than .5 drinks/day) and light (.5 to 1 drink/day), found 4% higher risk of breast cancer among very light drinkers, 9% higher risk among light drinkers, and 13% higher risk among moderate drinkers. This validates the idea that alcohol consumption is dose-dependent and suggests that any level of drinking may increase risk.[27]

In another meta-analysis of 26 studies specifically looking at wine consumption, overall risk was increased by 36% among those with the highest levels of consumption compared to the lowest. Among pre-menopausal women with the highest levels of wine consumption, risk was 79% higher, but there was no statistically higher risk among post-menopausal women. When the consumption of other alcoholic beverages was analyzed, there was no overall increased risk.[28]

A study from the United Kingdom found 27% increased risk per 10 units (standard drinks of any alcoholic beverage) of alcohol consumption per week and a linear association of nearly double risk per 10 units of consumption of spirits.[29]

In the Sister Study, a large cohort study of sisters of women diagnosed with breast cancer, binge drinking (defined as drinking four or more drinks at one time) was associated with 29% higher risk of breast cancer compared to low-level drinking. Among modest drinkers who binged, risk was 25% higher than low-level drinkers who never binged. Finally, blackout drinking was associated with 39% higher risk. All analyses controlled for other key risk factors.[30]

Alcohol dependency (defined as attendance at alcohol treatment centers) was associated with more than tripled breast cancer risk in a Danish study.[31]

Race/Ethnicity

One study found that drinking more than 14 drinks/week was associated with 78% higher risk overall. However, among Black women only, having 14 or more drinks nearly tripled the risk of breast cancer.[14]

Another study sought to understand whether alcohol consumption and dietary factors partially explained racial disparities in breast and other cancers. They found that, while nutrition and physical activity adherence both partly explained differences in breast cancer rates between Black and White women, alcohol did not explain the different incidence rates.[32]

A 2017 study looked at the association of alcohol and breast cancer risk in the AMBER Consortium, a cohort of Black women drawn from several different projects. They found 33% higher overall breast cancer risk among Black women who drank 14 or more drinks per week, compared to 0-4 drinks per week. When they looked at specific breast cancer subtypes, having more than 7 drinks/week was associated with increased risk of four subtypes: ER-, PR-, HER2- and triple-negative. Increased risk was in the range of 28-39% for all four subtypes.[33]

Subtypes

Several studies suggest an association between alcohol consumption and ER+ breast cancer. A study in the U.K. found 9% higher risk of ER+ breast cancer among drinkers, but no effect for ER- breast cancer.[34] Similarly, a Norwegian study found 14% higher risk of luminal A (ER+ and/or PR+) breast cancer among those who drank three or more glasses of wine per week. Another study found that those who drank at the time of their diagnosis were 35% more likely to be diagnosed with ER+ breast cancer than HER2+ breast cancer, and that there was no differential risk for triple-negative breast cancer.[35]

As noted above, in one study of Black women, alcohol consumption was associated with about 1/3 higher risk of ER-, PR-, HER2-, and triple-negative BC.[33] Due to the lack of additional studies examining disparities in subtypes of breast cancer stratified by race and ethnicity, it is not clear if different patterns would be found in different communities.

A large U.S. cohort study found trend effects for both invasive ductal and lobular breast cancer. Consuming more than 20 grams of alcohol per day was associated with 26% higher risk of invasive ductal cancer and 43% higher risk of invasive lobular cancer.[36]

Nuances and Emerging Considerations

Interactions with Hormone Replacement Therapy and B vitamins

There is some evidence that the effects of alcohol intake may interact with pharmaceutical hormones, and that B vitamins may ameliorate some of the risk of alcohol intake in some cases. In one study of Hormone Replacement Therapy (HRT) use and alcohol consumption, both increased risk independently (combined estrogen/progestin HRT nearly doubled risk, estrogen alone increased risk by 40%, and alcohol consumption increased risk by 25%). Among those on HRT who also consumed alcohol, risk was more than doubled.[37]

Intake of Vitamin B9 (folate) may be protective. Alcohol consumption as reported in 10g/day dose increments increased risk by 11% among those with low folate (Vitamin B9) intake.[38]

Family History and BRCA Status

Alcohol consumption may affect risk more notably among women with a family history of breast cancer. In one study, each 10 grams of alcohol consumed per day increased risk by 4% among those with no family history of breast cancer but increased risk by 16% among those with a family history.[39] A 2019 study of BRCA carriers found that alcohol consumption was not associated with risk among women with BRCA1 or BRCA2 mutations.[39]

Genes, Mechanisms, and Metabolomics

Studies and reviews have suggested multiple mechanisms for alcohol's effects on breast cancer risk. One experimental study randomly assigned 51 post-menopausal women to three different daily doses of alcohol consumption in a crossover study design. Each woman was randomly assigned to 0 grams/day, 15 grams/day or 30 grams/day for 8 weeks, and then switched to another dose, cycling through all three conditions. Estrogen metabolism was disrupted with alcohol consumption as consumption increased from 0 to 15 grams/day to 30 grams/day.[40]

One review suggested that acetaldehyde, which is a carcinogenic metabolite of alcohol, may increase circulating hormones, and that this may be one mechanism that explains the link between alcohol consumption and breast cancer specifically.[41] A study of triple-negative breast cancer cells in culture found that even low concentrations of alcohol (0.025-0.1% v/v) led to cellular proliferation (growth and multiplication), migration, and invasion into the growth medium. These changes were associated with alcohol-induced oxidative stress.[42] One study used emerging data on metabolomics to understand the link between 617 metabolites from 55 foods, food groups, and vitamin supplements and breast cancer risk. Of these metabolites, 12 of the 617 were related to alcohol consumption. Ten of these 12 alcohol-related metabolites were among the top 20 metabolites linked to breast cancer.[43]

Studies of gene-environment interactions have shown mixed results. In one study, a polygenic risk score was calculated based upon the presence of 77 single nucleotide polymorphisms. Of several environmental factors studied, alcohol had the strongest multiplicative effect on breast cancer risk. In other words, breast cancer risk was increased most strongly among women with the highest score based upon combined genetic polymorphisms associated with breast cancer who also consumed alcohol.[44] Other studies found no interactions between alcohol and genetic variants, despite seeing increased breast cancer risk with alcohol consumption.[45]

Breast Density

The relationship between breast density and alcohol consumption is explored more fully in the breast density section of this report. However, it is worth noting that the research is inconclusive. For example, one study found no relationship in breast density associated with alcohol consumption.[46] Another study found that women who consumed alcohol were almost twice as likely to have dense breasts.[15] A third study found no overall effect of alcohol consumption on breast density; however, among women with past hormone therapy, those who consumed more than 5 grams of alcohol/day had denser breasts.[47]

Take-Home Message

- Alcohol is causally related to breast cancer, in a dose-dependent manner.
- Risk appears to be higher among heavy drinkers and binge drinkers, but even light drinkers have elevated risk compared to non-drinkers.
- Few studies have explored whether these patterns hold across different racial and ethnic groups. However, results from one study suggest that the risk associated with drinking may be more elevated among Black women than White women.

Alcohol: Context for Interventions

California is the fourth largest wine producer in the world[48] and home to more than 1,000 craft breweries.[49] Despite this, California is not one of the highest high-risk alcohol consuming states: it ranks 22nd in binge and heavy drinking.[50] Still, indirect costs of excessive drinking (lost work productivity, healthcare expenses, criminal justice, and motor vehicle crash costs) amount to $35 billion per year, more than in any other state.[51]

Per capita, Californians drink 2.33 gallons of ethanol in alcoholic beverages a year.[52] This is slightly over the 2.1 gallons per person per year goal (the equivalent of about 448 standard drinks per person per year[53]) set out in the federal Office of Disease Prevention and Health Promotion's Healthy People 2020 report.[54] The 2015-2020 U.S. *Dietary Guidelines for Americans* recommends that if alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and two drinks per day for men—and only by adults of legal drinking age. The Guidelines also recommend that individuals who do not already drink alcohol should not start.[55]

However, research on breast cancer risk related to alcohol consumption brings into question whether this level is still too high. For instance, the World Cancer Research Fund recommends not drinking any form of alcohol (this includes wine, beer, and all forms of liquor) in order to reduce risk of breast and other cancers.[56] Shifting the drinking habits of Californians, whether to one drink a day or total abstinence, will require more education and a cultural shift away from ubiquitous access to alcohol, especially in social settings.

This is no simple task. While there is a great need to raise awareness about the link between breast cancer risk and alcohol consumption, actually changing women's behavior will be difficult. One study found that a mass media campaign was successful in raising awareness about the connection to breast cancer and significantly increased people's support of policies intended to reduce alcohol consumption, but this awareness did not affect the study subjects' motivation to change their drinking habits.[57]

Addressing alcohol consumption among youth is especially important. The National Institute of Alcohol Abuse and Alcoholism notes that alcohol is the most widely abused substance among America's young people.[58] While California's minimum drinking age has been 21 since the end of Prohibition,[59] a 2018 report found that nearly 21%

of youth aged 12-20 in California had consumed alcoholic beverages in the past month.[60] Better enforcement of the minimum drinking age is needed.

In addition to the many ways that drinking can increase risky behavior while under the influence, drinking at a young age sets the stage for long-term challenges: adolescents who start drinking before 15 years of age are at four times the risk of developing alcohol dependence as those who start drinking after 20 years of age.[61,62,63] Among U.S. youth who drink, approximately 50% of those 12 to 14 years of age and 72% among those 18 to 20 years of age drink heavily.[64] Young people who have higher exposure to alcohol marketing appear to be more likely to initiate alcohol use and engage in binge and hazardous drinking.[65]

Fortunately, policies to reduce alcohol consumption have been shown to be effective. In fact, having stronger alcohol policies in general, even those that do not target youth specifically, reduces the likelihood of youth alcohol consumption[66] and heavy/binge drinking overall.[67] Raising prices and reducing availability (e.g., reducing the number of sales outlets) were found to be helpful in reducing binge drinking in particular.[68] In general, stand-alone education programs about the risks of alcohol have been less successful, but a combination of policy approaches and education has potential to reduce alcohol consumption.[68]

Overall, there are many evidence-based approaches to reduce alcohol consumption (See Text Box: The American Society of Clinical Oncology's Recommendations to Reduce Alcohol Consumption); California has embraced a few of these measures, but there are many others that the state could adopt. Compared to other states, California has relatively low taxes on alcoholic beverages: In dollars per gallon, distilled spirits are taxed at $3.30 (20th in the country), beer at $0.20 (25th in the country), and $0.20 for wine (tied with Texas for the lowest).[69] The higher the tax, the more drinking can be expected to go down, especially for younger drinkers.[70] Local governments in California could also use their zoning powers to limit the number of alcohol outlets and the hours of sale.[71,72] One Australian study of 20- and 22-year-olds found that "for each increase in liquor stores over time, alcohol consumption increased by 1.22g/day or 8%, and for each additional club license, consumption increased by 0.90g/day or 6%."[73] Another important piece is improving the public's understanding that the risks of alcohol consumption are both short-term (e.g. higher rates of motor vehicle accidents and neighborhood violence near high concentrations of retail alcohol outlets[74]) and long-term (e.g. increased risk for breast and other cancers over a person's lifetime). Women need to be empowered with the knowledge of the health risk so that they can make informed decisions.

The American Society of Clinical Oncology's Recommendations for Evidence-Based Approaches to Reducing Alcohol Consumption

Below are some of the evidence-based approaches to reducing cancer risk from alcohol consumption recommended by the American Society of Clinical Oncology (ASCO):[75,76]

1. Clinical strategies of alcohol screening and brief intervention: Health care providers can screen adults, including pregnant women, for excessive alcohol use to identify people whose levels or patterns of alcohol use place them at increased risk of alcohol-related harms.

2. Regulate alcohol outlet density: Using regulatory authority to reduce the number of alcohol outlets in a given area (i.e. density) has proven to be an effective strategy for reducing excessive alcohol consumption.[77,78,79,80]

3. Increase alcohol taxes and prices: Increasing taxes, and therefore the overall price of alcohol, has been shown to reduce levels of excessive consumption and related health harms.[81,82,83]

4. Maintain limits on days and hours of sale: Evidence from several studies has demonstrated the positive impact that reducing the number of days or hours that alcoholic beverages are sold generally results in a decrease in related harms.[84,85]

5. Enhance enforcement of laws prohibiting sales to minors: The minimum legal drinking age is 21 years in all U.S. states. Enhanced enforcement of the minimum legal drinking age can reduce sales to minors (younger than 21 years) in retail settings (such as bars, restaurants, liquor stores), thereby helping to reduce youth access to alcohol.[86]

6. Restrict youth exposure to advertising of alcoholic beverages: Early onset of drinking has been associated with an increased likelihood of developing dependence on alcohol later in life,[87] and studies have demonstrated that youth exposed to more advertisements also show increases in drinking levels.[88,89]

In addition to these strategies, ASCO supports "efforts to eliminate pinkwashing in the marketing of alcoholic beverages. Pinkwashing is a form of cause marketing in which a company uses the color pink and/or pink ribbons to show a commitment to finding a cure for breast cancer. Given the consistent evidence that shows the link between alcohol consumption and an increased risk of breast cancer, alcoholic beverage companies should be discouraged from using the symbols of the battle against breast cancer to market their products".[90]

The global alcohol industry spends more than $4 billion each year marketing its products.[91] Federal law allows alcohol companies to largely self-regulate how they advertise. One voluntary industry guideline is to only advertise to an audience that can be reasonably expected to be at least 70% of legal drinking age.[92,93,94,95] However, the industry often does not comply with this guideline.96

Alcohol consumption increases risk for breast cancer. The more you drink, the higher your risk, and even light drinking increases risk.

INTERVENTIONS

Overarching Goal: Significantly expand public education on the link between breast cancer risk and alcohol consumption and expand support and incentives to reduce consumption of alcoholic beverages for girls and women.

Intervention Goal 1

Greatly improve public knowledge of the link between alcohol and breast cancer risk.

Objective 1: Launch a state-wide public education campaign explaining the breast cancer risk from alcohol consumption.

- **Strategy 1:** Require the California Department of Public Health, in consultation with other relevant stakeholders, to develop effective public health messages to raise awareness of the link between breast cancer risk and drinking and to reduce alcohol consumption.
- **Strategy 2:** Develop a distribution plan for the public health messages about drinking and breast cancer that includes public service announcements and various social media platforms.

Objective 2: Revise the *Health Education Curriculum Framework for California Public Schools, Transitional Kindergarten Through Grade Twelve*, which already covers the subject of alcohol use, to specifically include the connection between alcohol consumption and breast cancer risk.[97]

Objective 3: Develop educational materials on the breast cancer-alcohol connection in multiple languages that can be easily adapted to the needs of different communities and distribute them widely though health clinics, community events, and other outreach opportunities.

Intervention Goal 2

Strengthen, fully implement and, where appropriate, enforce measures to reduce alcohol consumption (modeled after American Society of Clinical Oncology's recommendations).

Objective 1: Adopt alcohol screening and education in clinical settings.

- **Strategy 1**: Medical institutions can expand alcohol screening practices from primarily focusing on reducing heavy drinking and addiction to be more inclusive of education on the dose-dependent link to breast cancer risk and other health concerns.

Objective 2: Regulate alcohol outlet density.

- **Strategy 1**: Cities should reduce the number of permits to sell alcohol in retail outlets, bars, or restaurants and ensure that permits that are granted are not concentrated in vulnerable communities.[98]

Objective 3: Increase alcohol excise taxes and designate some of the revenue for alcohol consumption reduction and education activities.

- **Strategy 1:** Raise the California state excise tax on the sale of distilled spirits, beer, and wine to a level comparable to the highest state excise tax rates in the nation.
- **Strategy 2:** Commit a substantial portion of the funds raised from the tax increase toward efforts to educate the public about the health impacts of drinking alcohol, including the impact on breast cancer risk.

Intervention Goal 2 (continued)

Strengthen, fully implement and, where appropriate, enforce measures to reduce alcohol consumption (modeled after American Society of Clinical Oncology's recommendations).

Objective 4: Maintain limits on days and hours of sale of alcohol.

- **Strategy 1**: Oppose efforts (including legislation) to extend bar hours. Legislation to change closing time for bars from 2 a.m. to 4 a.m. in certain cities has been introduced in California on at least two occasions.[99]

Objective 5: Enhance enforcement of laws prohibiting supplying alcohol to minors, both by vendors and adults buying alcohol for minors.

- **Strategy 1**: Ensure local police departments are fully trained and funded to enforce the minimum drinking age of 21. Community members and community-police advisory boards should be fully engaged in setting priorities in how to best enforce this law.
- **Strategy 2**: Increase capacity for campus police or security to enforce the minimum drinking age of 21.

Objective 6: Restrict youth exposure to advertising of alcoholic beverages. [100]

- **Strategy 1**: Cities should prohibit alcohol advertising within 500 feet of all schools, playgrounds, and other places where youth are likely to be present.[101]
- **Strategy 2**: College campuses should further limit and consider banning all advertising of alcoholic beverages.[100] For example, currently California State University allows advertising of beer and wine, but not distilled spirits. This rule could be expanded to be inclusive of all alcoholic beverages.[102]

Intervention Goal 3

Expand research on the link between alcohol consumption and breast cancer.

Objective 1: Support research to better understand the effectiveness of interventions, including educational messages, to reduce alcohol consumption in response to breast cancer risk.

Objective 2: Support research to better understand the mechanisms of how alcohol consumption increases breast cancer risk.

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Breastfeeding

Science Summary

Breastfeeding is a protective factor for breast cancer, with lower risk associated with longer duration of breastfeeding in most studies. Social and cultural barriers lead to lower rates of breastfeeding for U.S.-born Black babies.

What the Foundational Documents Say

Overall, our foundational documents agreed that breastfeeding reduces the mother's risk of breast cancer. The AICR's review concluded that there is strong evidence that breastfeeding reduces the risk of both pre-menopausal and post-menopausal breast cancer for the mother. Overall, the data support a 2% decrease in risk for every 5-month increase in breastfeeding duration.[1] The IBCERCC noted that breastfeeding leads to protective physiological changes in the breast.[2]

The IOM report also noted that breastfeeding reduces risk; however, they indicate that breastfeeding does not occur equally among all women. In the U.S., White women are twice as likely to breastfeed as Black women and their cumulative time breastfeeding is longer.[3] CBCRP notes that lesbians are less likely to breastfeed than heterosexual women (who are also more likely to give birth).[4] The structural inequities that underlie these disparities are addressed in our interventions section.

Other foundational documents discuss concerns that chemicals can be found in breast milk, and as a result, chemicals may make their way to the next generation through breast milk. The unique vulnerability of young children to chemical exposures makes this a particular concern, though breast milk is still the healthiest option for infants compared to formula.[5] Three of the documents further note that some chemical exposures may impair lactation.[2,4,6] The Endocrine Society, in particular, notes that the breast is especially sensitive to endocrine-disrupting compounds (EDCs) "because its complex development involves growth, differentiation, secretory activity, and regression, all orchestrated by hormones, growth factors, and stromal factors."[6] For a brief description of the stages of breast development see BCPP's webpage on this subject.[7]

The Current State of the Evidence

Studies of breastfeeding and breast cancer risk measure breastfeeding in three different ways: duration of breastfeeding, exclusive breastfeeding compared to mixed feeding or formula feeding, and ever versus never breastfeeding. In all cases, the evidence suggests that breastfeeding is protective against breast cancer.

However, in the U.S., Black babies have 20% lower rates of ever being breastfed and of being breastfed at six months. They are half as likely to be breastfed exclusively at six months—14.6% of Black babies are exclusively breastfed at 6 months compared to 26.8% of White babies.[8] Black women may face barriers such as lack of social and cultural acceptance in their communities, inadequate support from health care providers, and unsupportive work environments.[8] For instance, hospital facilities in zip codes with higher than average Black residents had lower rates of five out of the ten recommended Maternity Practices in Infant Nutrition and Care.[8,9] The greatest disparities were found in practices supporting early initiation of breastfeeding, limited use of breastfeeding supplements, and rooming in (allowing mother and child to stay in the same room).[9] While barriers to breastfeeding are common for many mothers, Black mothers have unique or disproportionate barriers. For example, 19.5% of Black mothers reported returning to work as a reason to stop breastfeeding, compared to 8.8% of White mothers.[8]

Duration of Breastfeeding: Most recent studies of breastfeeding and breast cancer risk examine the duration of breastfeeding during a woman's lifespan and associated risk. In a meta-analysis of 27 studies including nearly 30,000 cases of breast cancer, the risk of breast cancer was reduced by more than half among women who breastfed the longest compared to those with the shortest time breastfeeding.[10] A case-control study in Tunisia found a significant trend in risk reduction for increasing duration of breastfeeding.[11]

The protective effects of breastfeeding appear to be additive with the risk reduction conferred from having children. The European Code Against Cancer (a set of personal practices to reduce risk) estimates that breast cancer risk is reduced by about 4% for every 12 months of breastfeeding over and above the risk reduction resulting from parity.[12] In one study, the combination of two or more childbirths and breastfeeding for more than 13 months reduced breast cancer risk by 49% compared to a 20% risk reduction among women who had two or more childbirths regardless of breastfeeding duration.[13]

Multiple studies report reduced overall risk of breast cancer among women who breastfed for longer than 12 months. One meta-analysis of 100 studies found that breastfeeding for more than 12 months resulted in roughly 25% lower risk and that breastfeeding for a shorter duration still conferred reduced risk of 7-9%.[14] Another meta-analysis found that breastfeeding for more than 12 months was associated with 28% lower risk, but that breastfeeding for fewer than 12 months conferred no protection.[15]

- **Longer Duration of Breastfeeding:** Studies of very long total duration of breastfeeding have found mixed results. One study reports that breastfeeding for more than 24 months was associated with 69% lower risk,[16] while another study found that breastfeeding for only 1-2 years was protective compared to longer duration.[17]

Yet another study found a non-statistical reduction in risk among women who breastfed for 74-108 months, and 58% lower risk among women whose cumulative duration of breastfeeding exceeded 109 months (9 years).[11] One study found a 78% decreased risk of luminal B breast cancer among women who breastfed for less than 12 months compared to those who did not breastfeed, but more than doubled risk of Luminal A breast cancer among women who breastfed for more than 12 months.[18]

- **Age/Menopausal Status:** One study found that breastfeeding for 1-12 months reduced the risk of breast cancer among pre-menopausal women but not post-menopausal women.[13] Another study found a non-significant reduced risk of post-menopausal breast cancer among those who started to breastfeed between ages 20-24 and took HRT (as conjugated equine estrogen).

  However, there are some inconsistencies in the research. Post-menopausal women who last breastfed after age 35 had 50% higher risk of breast cancer in the Women's Health Initiative study.[19] In a study of Black women, risk was non-significantly lower among those who breastfed, regardless of age or duration.[20]

- **Subtypes:** Emerging research suggests that breastfeeding may differentially protect against different subtypes. Findings for Luminal A (the most common subtype) have been mixed, with one study finding no effect[18] and one study finding 22% lower risk.[21] For luminal B breast cancer, the first of these studies found a protective effect for breastfeeding up to 12 months but not for breastfeeding for more than 12 months.[18]

  For triple-negative breast cancer (TNBC) however, findings are more consistent and striking. Two studies found overall reduced risk of TNBC ranging from 75% to 31% depending on the study and duration of breast cancer.[21,22] This reduced risk may be especially important for Black women who have higher overall incidence of TNBC. One study found 45% lower risk of TNBC among Black women who breastfed for more than 12 months and no effect on TNBC risk among White women.[21] In another study, Black women aged 22-44 who breastfed for six or more months had 82% lower risk of TNBC.[21]

  In a small, multi-ethnic pooled case-control study of TNBC in California, younger women who had one or more live births and breastfed for more than 24 months had a non-significant decreased risk of TNBC.[23] In the same study, women who had three or more pregnancies but breastfed for less than 12 months or not at all, had more than double the risk of TNBC compared to women who had 1-2 children and breastfed for more than 12 months. In addition, women who had one or more live births and did not breastfeed had double the risk of TNBC compared to nulliparous women (women who did not give birth).[23] While the study sample was too small to stratify the results by ethnicity, the authors report that the prevalence of TNBC among women with 3 or more live births and little or no breastfeeding, was highest for Latinas (22%), Black women (18%), and Asian-American women (15%), and much lower for White women (6%).[23]

Exclusive Breastfeeding: Some studies have measured breastfeeding by comparing exclusive breastfeeding to formula feeding and a mix of formula and breastfeeding. A meta-analysis of 65 studies found that exclusive breastfeeding reduced risk by 28%. Breastfeeding, whether it was exclusive or part of mixed feeding, reduced risk for both pre-menopausal women (14% lower risk) and post-menopausal women (11% lower risk).[24]

A study of women in Japan found no difference in risk among women who fed both breast milk and formula, but 80% increased risk among women who fed their babies only formula.[25] One study in Iran found no differences in exclusive breastfeeding during the first six months of life, compared to mixed feeding.[26] Findings from a cohort study in Mexico suggested that if the rate of exclusive breastfeeding in the first six month increased from 14% to 95%, then the burden of breast cancer cases and economic costs would drop by 14%.[27]

Ever Versus Never Breastfeeding: Studies that assess breastfeeding as "ever breastfeeding vs. never breastfeeding" consistently report that ever having breastfed was associated with reduced risk of breast cancer,[10,14,15,28] and that never having breastfed was associated with a higher risk of breast cancer.[29,30] In a meta-analysis, breast cancer risk was 16% lower among White women and 45% lower among Asian women who ever breastfed.[15]

One study found that among Black women who had ever breastfed, risk of ER- breast cancer was 19% lower, but that breastfeeding had no effect on ER+ breast cancer. Further, ER- breast cancer risk increased with each additional birth among women who did not breastfeed. Women who had four or more births and did not breastfeed had 68% higher risk of ER- breast cancer than women who had one birth and breastfed.[31] In a meta-analysis of 27 studies examining ever breastfeeding and risk of breast cancer subtypes, breastfeeding was associated with 10% lower risk of ER- and PR- breast cancer and 22% lower risk of triple-negative breast cancer among parous women, but no change in risk of hormone-receptor positive breast cancers.[32]

One study estimated that 1.7% of breast cancer cases in Australia could be attributed to breastfeeding for fewer than 12 months.[33]

Nuances and Emerging Considerations

Breastfeeding in Women with BRCA Mutations: The reduced risk conferred from breastfeeding may apply to women with BRCA1 mutations. In one study, breastfeeding for at least one year reduced breast cancer risk by 32% and breastfeeding for two more years reduced risk by 49% compared to women with BRCA1 mutations who never breastfed. Risk among women with BRCA2 mutations was not affected by breastfeeding in this study.[34]

Breastfeeding Infants and Later-Life Risk of Breast Cancer: In addition to reducing the risk of breast cancer for the mother, one study found that Japanese women born prior to 1950 who were exclusively breastfed had a 43% lower risk of breast cancer.[35]

Interaction of Having Children and Breastfeeding on Breast Cancer Subtype Risk: Parity and breastfeeding interact to shape patterns of risk for different breast cancer subtypes. In a small case-control study of Black women, the findings showed intriguing patterns, although none of the findings were statistically significant. Having

children was associated with 18% lower risk of ER+ breast cancer but 92% higher risk of triple-negative breast cancer. However, ever breastfeeding led to 34% lower risk of triple-negative breast cancer, and this pattern held regardless of duration.[36] One hypothesis that the higher rate of triple negative breast cancer in Black women may be associated with lower rates of breastfeeding in this population.

Take-Home Messages

- Breastfeeding appears to be protective for breast cancer, and longer duration is more protective.
- Women who have children and do not breastfeed may have higher risk for ER- breast cancer and triple-negative breast cancer than women who breastfeed, and higher risk than women who do not have children.

Breastfeeding: Context for Interventions

The Centers for Disease Control and Prevention reports that in 2015, 87% of infants born in California were ever breastfed, 67% are breastfed to 3 months old and 40% make it to 6 months being breastfed.[37] These rates are all above the national average, but still leave room for improvement.

Table 3. Centers for Disease Control and Prevention Breastfeeding Rates, 2015[37]

	National	California
Ever Breastfed	83.2%	87.2%
Breastfeeding at 6 months	57.6%	66.7%
Breastfeeding at 12 months	35.9%	40.2%
Exclusive breastfeeding through 3 months	46.9%	53%
Exclusive breastfeeding through 6 months	24.9%	26.3%
Breastfed infants receiving formula before 2 days of age	24.9%	26.3%

Table 4. California In-Hospital Breastfeeding (first 24-48 hours after birth) 2017[38]

	Any Breastfeeding (may include formula and breastfeeding)	Exclusive Breastfeeding
CALIFORNIA	**93.9%**	**69.6%**
African American	86.7%	61.4%
American Indian	89.5%	70.1%
Asian	95%	63.8%
Multiple Race	93%	76.6%
Pacific Islander	88.8%	65.1%
Other	89.9%	64.6%
White	95.3%	81.1%
Hispanic	93.7%	65.5%

Breastfeeding plays a critical role in protecting both the infant and the mother's health, yet like many other breast cancer risk factors, disparities exist. One study by BreastfeedLA found that infants of color in the Los Angeles area are less likely than White infants to be exclusively breastfed at hospital discharge,[39] which has a significant impact on establishing breastfeeding.[40]

What hospital a baby was born in can have a significant impact on whether a baby is breastfed or is breastfed exclusively. The BreastfeedLA study also found that hospitals that did not maintain their Baby-Friendly Status (a successful program to promote breastfeeding launched by the World Health Institute and UNICEF in 1991) saw a decrease in breastfeeding rates, especially for infants of color.[39]

Additionally, how babies are born can impact breastfeeding rates. Babies born at full term and babies born to women who had multiple children had the highest initiation rates for breastfeeding. Important to policy is that

babies born vaginally had a 90.2% rate of breastfeeding initiation, whereas birth by cesarean section had an initiation rate of 73.3%.[41] Hospitals and birthing centers need to practice moderation in providing cesarean births, encouraging live births whenever possible.

California is one of the few states in the nation to provide paid family leave. Studies have found that this six-week, partially paid leave of absence can help increase breastfeeding rates. These increases were noted immediately after the policy was put in place. However, the benefits were mostly available to higher-income working women.[42] One study found that California's paid family leave increased the overall duration of breastfeeding by nearly 18 days and the likelihood of breastfeeding for at least six months by 5%.[43]

Another factor that may influence breastfeeding rates is recent information about the presence of environmental chemicals in breast milk, which may discourage mothers from breastfeeding out of concern for their child's health. While these exposures are certainly of concern, the consensus among researchers and health professionals is that any risk from chemical exposure is significantly outweighed by the benefits of breastfeeding, which include decreased risks of infection, allergy, asthma, arthritis, diabetes, obesity, cardiovascular disease, and various cancers in both childhood and adulthood.[44,45,46]

Despite the clear scientific evidence that breastfeeding is one of the best things women can do for their baby's and their own health, many very personal decisions and factors contribute to whether or not women breastfeed. Some women do not give birth, which may be by choice or may not be medically possible. Some women establish breastfeeding very easily, whereas some babies have a very difficult time breastfeeding for a wide variety of reasons. Some women have a hard time producing enough milk, a factor that can be impacted by chemical exposures.[47] Some women very much want to breastfeed, but do not have a job that allows them to, or they try to work and breastfeed and find it nearly impossible to juggle the many responsibilities. An endless number of factors can influence breastfeeding outcomes. These are extremely personal decisions and experiences, and while all efforts to support babies being breastfed should be made, no woman should be made to feel ashamed for how she ultimately feeds her baby.

Community Input on Breastfeeding

Participants in community listening sessions strongly supported eliminating barriers to breastfeeding. Recommendations were related to a wide range of interventions ranging from systemic to specific changes. Women wanted the security of paid family leave for all kinds of workers whether contract workers or formal employees, whether U.S. citizens or undocumented immigrants. This would allow women the stability to breastfeed and bond with their baby in the early weeks, which is a critical window for establishing breastfeeding. Additionally, they called for a wide range of supports in the workplace to continue breastfeeding.

Just as important was addressing the cultural barriers to breastfeeding, which include discrimination against women who breastfeed in public, sexualizing breasts, relationship pressure to focus on the partnership, the time commitment of breastfeeding and other issues.

Different populations have different breastfeeding support needs

In recent years, breastfeeding rates have improved overall in California; however, the improvements are not equally distributed between different populations. There are unique cultural, historical, logistical and economic barriers for different groups of women in California to breastfeed. Attention should be dedicated to meeting each community's specific needs when promoting breastfeeding and offering support services. For example, lactation support should be offered by people from the same community, in the language of the women seeking support, and financial resources should be dedicated to training women to offer those services. Some specific considerations include:

- **Black Women**: Black babies have the highest infant mortality rate in the country.[48] Breastfeeding can lower mortality rates, and should be highly encouraged.[49,50] However, some Black women experience historical trauma at the thought of breastfeeding as there were extensive practices of forcing enslaved women to breastfeed the White slave owners' children at the expense of her own. Supporting, publicizing and engaging in Black Breastfeeding Week[51] is one important step to support increasing breastfeeding in Black women.

- **Asian Women**: Many Asian-American women face cultural barriers to breast feeding, for example believing that infant formula is better than breast milk or that women should stop breastfeeding sooner than they might want.[52] There is a significant lack of Asian American lactation consultants, and in general, adequate language or cultural support for the varied ethnic backgrounds of Asian American women in California is not always available. The Asian Breastfeeding Taskforce is one effort trying to address these issues.[53]

- **Latinas**: Generally, Latinas tend to initiate breastfeeding at higher rates than the national average, but it varies as to how long they continue. They may experience specific barriers, especially as it relates to how long ago their family immigrated to the U.S.: the longer Latina immigrants have lived in the U.S., the more likely they are to use formula because it is seen as the American way and/or because they see breastfeeding as a practice of poor people. Other barriers specific to lower income Latinas include the need to return to school or work as quickly as possible and not having the support in those places to sustain the practice.[54]

- **Native-American Women**: Native-American women have the second lowest breastfeeding initiation rate when considering race/ethnicity (Black women have the lowest).[55] Generations of trauma from violence, U.S. government's assimilation policies, forcing indigenous people to end their traditional cultural practices, and many other levels of violence are thought to have contributed to decreased breastfeeding rates.[56] This is particularly concerning as Native Americans have especially high rates of obesity and diabetes, which breastfeeding can protect against.[56] Fortunately, there is increasing interest in promoting breastfeeding in Native-American communities,[56,57] and specific resources to support these efforts. See An Easy Guide to Breastfeeding for American Indian and Alaska Native Families as an example.[58]

- **LGBTQI and Gender Queer People**: This community experiences both cultural barriers to breastfeeding (for example, education and promotion of breastfeeding is generally done through a heteronormative and cis-normative lens, leading to feelings of invisibility) and structural barriers (for example, reduced access to health care due to factors such as lower earnings and/or not having access to gender and culturally appropriate medical care).[59] Additionally, very little research has been done on trends and possible interventions to better serve this community.

- **Women with Disabilities**: Women with disabilities may have specific challenges with breastfeeding, including: lack of support, disability-related health considerations, limited information, difficulties with milk production, and difficulties latching.[60] This is a largely understudied area, and research on how to best support women with disabilities who want to breastfeed is greatly needed.

- **Women in Jail, Prison, and Immigration Detention**: California's laws generally grant incarcerated women the right to breastfeed (most often this means they are provided the means to pump breast milk and have a designated family member deliver it to the baby). However, these laws need to be consistently applied. See the Breastfeeding and Lactation Advocacy Toolkit[61] for more details.

- **Young Mothers**: Young mothers, especially teenage mothers, experience particular challenges to breastfeeding. The exceptional stigma for young mothers can make it difficult to breastfeed at work or school. In romantic relationships, concerns about body image and sexual desirability may be a concern while breastfeeding. More emphasis is needed on lactation education for healthcare providers to serve young mothers, and greater enforcement of lactation accommodation laws in schools and workplaces.[62]

- **Low-Income Women**: Numerous challenges exist for low income women, who often need to work multiple jobs, lack adequate health care coverage and maternity leave, lack access to adequate childcare that supports breast feeding, and may face other barriers. Programs to help women get the support they need should be aggressively pursued. Overcoming Barriers to Breastfeeding in Low Income Women[63] offers a range of potential solutions.

There are unique cultural, historical, logistical, and economic barriers for different groups of women in California to breastfeed.

INTERVENTIONS

Overarching Goal: Remove all legal and cultural barriers to maximizing women's ability to breastfeed their babies.

Intervention Goal 1

Create public education campaigns that promote breastfeeding and minimize use of infant formula and include information on the health benefits of breastfeeding to both the child and the mother, including reduced breast cancer risk.

Objective 1: Conduct public education campaigns, including using social media, to promote breastfeeding to pregnant women and young mothers, fathers, and the general public to build general societal support for breastfeeding, while also respecting the right of women to make decisions about their own bodies.

- **Strategy 1:** California Department of Public Health and county public health agencies should aggressively market breastfeeding as the healthiest option for babies and mothers. Materials and ad campaigns should represent the full diversity of California's population and target communities with the lowest rate of breastfeeding.
- **Strategy 2**: The Ad Council should produce and promote culturally appropriate and racially diverse breastfeeding campaigns, developed in consultation with target communities. In addition to pregnant women, messages should be directed to fathers and the general public.

Objective 2: Regulate infant formula advertising in California to prevent targeting of vulnerable communities and require a disclaimer in all ads stating that breastfeeding is the healthiest method of feeding babies.

Intervention Goal 2

Pass and implement policies that support pregnant women and new mothers and offer optimal health benefits for the mother and baby.

Objective 1: Adopt six-month paid parental leave for all new parents employed in California. See Governor Gavin Newsom's proposal as a potential model.

Objective 2: Support the ongoing legislative efforts such as requiring MediCal and health care service plans to provide reimbursement for a variety of breast pumps and ensuring lactation facilities are available in a variety of public locations (see legislation (AB 752) passed in 2019 requiring lactation facilities in certain transit centers). For more policies and legislation that support breastfeeding, see CA advocacy groups including the California Breastfeeding Coalition[65] and BreastfeedLA.[66]

Intervention Goal 3

Create breastfeeding-supportive workplaces for all workers, regardless of employment classification or status.

Objective 1: Adopt a workplace-wide Breastfeeding Friendly Workplace Lactation Accommodation Policy. See BreastfeedLA[66] and LA Best Babies Network[67] for examples.

- **Strategy 1:** Offer employees flexible schedules and possibly flexible assignments to accommodate pumping and breastfeeding needs.
- **Strategy 2:** Create workplaces with the resources and equipment necessary to allow all women (whether employees or contract workers) returning to work to breastfeed. Elements of a breastfeeding-friendly workplace include:
  - Adequate designated lactation rooms that are clean and readily available and have a comfortable seat and preferably a sink. For women who work outdoors, for example farmworkers, ensure easy access to shaded, clean, adequately equipped areas with privacy to pump and an electricity source for pumps and refrigeration.
  - Adequate break time for women to travel to the lactation site, set up, pump, clean up, and refrigerate milk.
  - Access to a refrigerator for breast milk storage.
  - Access to childcare at or near the worksite to allow for breastfeeding, which brings the additional benefit of mother-child bonding. Where feasible, allow babies at the workplace.
- **Strategy 3:** Provide resources to support breastfeeding, such as employee wellness programs, discounted pump rental or purchase programs, and healthcare benefits with lactation services covered.
- **Strategy 4:** Ensure all employers have workplace breastfeeding policies and that employees understand and respect those policies.
- **Strategy 5:** Enforce a zero-tolerance policy for discrimination and retaliation for breastfeeding and/or pumping in the workplace.

Objective 2: Broaden employer understanding of the needs and increase support for breastfeeding and pumping in the workplace. This is particularly important for predominately male-oriented workplaces.

- **Strategy 1:** Hold a summit of employers, business organizations, and other key decision makers to develop a strategy to implement high-quality breastfeeding support programs in the workplace.
- **Strategy 2:** Work with county and state public health departments to implement an employer education program on the benefits of breastfeeding, the business case for breastfeeding[68] and the steps to adopt a breastfeeding-positive workplace.

Intervention Goal 4

Improve breastfeeding-supportive maternity care practices in health care facilities.

Objective 1: Develop a written breastfeeding policy that increases breastfeeding and reduces or eliminates barriers to breastfeeding at all health care facilities. Provide the training and support needed to fully implement the strategies listed below.[69]

- **Strategy 1:** Minimize invasive medical interventions as much as possible, including Cesarean delivery, which can interfere with establishing breastfeeding.[70]
- **Strategy 2:** Unless medically necessary, keep newborns and their mother in the same room post-delivery ("rooming in")[71] and maintain skin-to-skin contact between mother and baby after birth.[70]
- **Strategy 3:** Encourage early breastfeeding initiation[70] and educate new mothers on how to read a baby's cue when they want to breastfeed.[70]
- **Strategy 4:** Discourage distribution of infant formula in birth facilities for postpartum stays and prohibit formula gift packs.[71] Supplement or substitute breast milk with formula or water only when medically necessary or at the mother's specific request.[71]
- **Strategy 5:** Ensure new mothers are aware of options for post-discharge follow-up to support ongoing breastfeeding.[70]

Objective 2: Improve breastfeeding-supportive professional education for doctors, nurses, midwives, nurse practitioners, nutritionists, lactation consultants, doulas and other health care professionals working in maternity care.

- **Strategy 1:** Require participation in in-person and online training opportunities on breastfeeding by health care professionals in this area.
- **Strategy 2:** Distribute clinical protocols developed by experts, such as the Academy of Breastfeeding Medicine, to health care professionals.
- **Strategy 3:** Develop scholarships and grants to support and train women from under-represented groups to offer lactation support to women in health care settings and in their community, including community health educators, doulas, promotoras, and others.

Objective 3: Develop a statewide approach to increasing participation in breastfeeding.

- **Strategy 1:** Encourage healthcare providers and community advocates to participate in community and statewide conferences and events, such as the California Breastfeeding Summit, to learn about current issues and problem solving for California's diverse population.[65]
- **Strategy 2:** Develop scholarships to ensure that health care providers who serve low-income families and women, who are less likely to breastfeed due to systemic or cultural barriers, can receive proper culturally relevant training to increase participation in breastfeeding.
- **Strategy 3:** Develop local and regional working groups in partnership with departments of public health, clinics and other public health care facilities to address the specific breastfeeding needs of the communities.

Intervention Goal 5

Increase new mothers' access to support for breastfeeding after leaving the birthing center.

Objective 1: Ensure new mothers have access to existing support services.

- **Strategy 1:** Eliminate fees for new mothers to receive lactation support and/or medical equipment and supplies (for example, breast milk pumps and milk storage containers).
- **Strategy 2:** Provide free home and/or phone visits with lactation support staff for as long as it takes to establish breastfeeding and with the goal of maintaining breastfeeding until at least 6 months old and longer if desired.
- **Strategy 3:** Ensure services and educational materials are available in all languages represented at the health care facility. CA Dept. of Public Health should take the lead in translating materials into multiple languages.
- **Strategy 4:** Develop and disseminate a resource directory of local lactation support services available to new mothers.[70]
- **Strategy 5:** Improve quality of and access to one-on-one and group peer support programs for breastfeeding that include education, emotional support, encouragement, and problem solving. Whenever possible, these support services should be offered by mothers from the same community, who have breastfeeding experience, and who have been trained in offering peer support.[70]
- **Strategy 6:** Train staff at childcare centers, Head Start programs and other places and institutions where babies spend significant amounts of time to support breastfeeding.[70]

Objective 2: Work with institutions to develop better post-birth services.

- **Strategy 1:** Collaborate with state Medicaid and insurance commissioners to explore ways to increase access to lactation services.[70]
- **Strategy 2:** County health departments should develop walk-in breastfeeding clinics that are available to all new mothers in the community and staffed by trained breastfeeding professionals who are reimbursed for all services provided.[70]
- **Strategy 3:** Create comprehensive, statewide networks to provide home-based or clinic-based follow-up care to newborns in the state.[70]
- **Strategy 4:** Promote the efforts of the California Women, Infants, and Children Association[72] to maximize awareness and access to breastfeeding support services for low income women.

Intervention Goal 6

Expand research on ways to increase women's commitment and participation in breastfeeding and reduce cultural barriers and challenges to breastfeeding.

Objective 1: Expand research on the barriers and possible solutions to promoting breastfeeding in general, as well as focusing on the unique needs of specific populations, such as the Black community, young mothers, women with disabilities, incarcerated mothers and others (See "Different Populations Have Different Breastfeeding Support Needs" text box for more details).

Objective 2: Expand research on the role of breastfeeding in reducing breast cancer risk, with a specific emphasis on understanding whether there is a recommended length of breastfeeding that is especially protective for breast cancer given variables such as age or number of children.

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Chemicals in Consumer Products

Science Summary

Everyday consumer products can contain chemicals linked to hormone disruption and breast cancer. Use of these products can lead to exposures across the lifespan linked to later-life disease with some of these chemicals having the most profound effects when exposures occur prenatally or early in life.

What the Foundational Documents Say

A number of our foundational documents establish the potential for some chemicals to increase breast cancer risk. These reports emphasize concerns about endocrine-disrupting compounds (chemicals that interfere with hormone activity),[1] mammary gland carcinogens (chemicals that are found to increase mammary gland tumors in laboratory studies),[2] and some carcinogens linked specifically to breast cancer.[3]

These reports draw upon research from human, animal, and cell-based studies, since each of these methods has different strengths and limitations and can contribute to our understanding of potential links to breast cancer.[4,5]

Past work has emphasized a life course model,[3,6,4] noting that many chemicals may have the most troubling health effects when exposures happen prenatally or early in life, during vulnerable periods of development. For endocrine-disrupting compounds, effects at very low doses are of particular concern, because the body's own hormones operate on this scale.[1] Other foundational documents have raised concerns that we are all exposed to many chemicals from many sources every day. These mixtures are difficult to study, but research suggests they may have more extensive health effects than single chemical exposures by acting on multiple cancer-relevant pathways.[7]

The Current State of the Evidence

Chemicals in consumer products linked to breast cancer enter the body through inhalation, ingestion and skin absorption. Biomonitoring, a method of measuring pollution in people, has found hundreds of chemicals in people's blood and urine, including chemicals from consumer products. Below we provide examples of chemicals of concern in consumer products.

Legacy Chemicals

Two legacy chemicals, DDT and PCB, illustrate the importance of proactive efforts to reduce chemical exposures. DDT is a pesticide that was used widely in agriculture in the U.S. before it was banned in 1972.[8] Even though its usage has long since been discontinued, people remain exposed to DDT and its derivative DDE because of their persistence in the environment.[1] Studies have demonstrated that exposure during key periods of human development (in utero, childhood, and early adolescence) is associated with a significantly higher risk of adult breast cancer.[9,10]

In 1976, Congress banned the production of new products containing polychlorinated biphenyls (PCBs), but products produced before the ban remain in circulation, and enduring environmental contamination means that individuals are still at risk of exposure. High levels of PCBs in adipose tissue have been associated with increased risk for developing breast cancer,[11] while dietary exposure to fish contaminated with PCBs and metals is associated with increased risk of recurrence.[12]

Chemicals in Current Widespread Use

Bisphenol A (BPA): BPA is an endocrine-disrupting compound that alters key hormonal and developmental processes, including estrogen dependent pathways. It is found in many commonly used consumer products such as plastic food containers, the linings of food cans, and paper receipts.[13] BPA has also been found in indoor air,[14] house dust,[15] and water systems.[16] While BPA is eliminated quickly by the body, the constant exposure from consumer products and the environment results in near-ubiquitous detection in human urine and breast milk.[1] It has also been found in breast adipose tissue of both women with breast cancer and those without.[17] Methodological issues, including the ubiquitous presence of the chemical in our environment and our bodies, makes epidemiological studies of BPA and long-latency diseases like breast cancer difficult, if not impossible, to conduct. However, laboratory studies show BPA alters mammary growth and development in rodents and other mammals and can increase the risk of mammary tumor formation.[18,19,20,21]

Cadmium and Other Heavy Metals: Many heavy metals have been shown to have harmful effects on human health. For everyday consumers, metal compounds can be found in commonly used products like cosmetics, consumed through contaminated food and water, and inhaled through cigarette smoke and car exhaust.[22,23] Even though they are used at levels below regulatory thresholds, many heavy metals are not excreted quickly, and as a result can accumulate in the body.[24] Cadmium is fat seeking, so it accumulates in tissues over time, and is also a metalloestrogen that can activate estrogen receptors.[24] Though inconsistent results have been found in adults, there is concern that exposure to heavy metals during key growth periods prenatally and during childhood can increase risk of breast cancer. Cadmium can be transferred through the placenta to the fetus, raising concerns about prenatal development and subsequent development of breast cancer.[25,26]

Flame Retardants: Polybrominated diphenyl ethers (PBDEs) are a class of chemicals that have been used as flame retardants in household and industrial products.[27,28] Because of California's stringent fire deterrent policies, PBDEs were added to furniture in particularly high levels, leading to California's children having, on average, the highest levels of bioaccumulation of the chemicals in the U.S. and internationally, well above risk-based levels.[29] While they are being phased out of production because of health concerns, these chemicals are still in use and persist almost indefinitely in the environment.[30]

PBDEs accumulate in water, soil, and in the tissue of animals.[27,28] In humans, PBDEs have been found in fat, blood serum, breast tissue and milk, and they can cross the placenta leading to prenatal exposure.[31] Though PBDEs are known endocrine-disrupting compounds, few studies have specifically looked at their effects on breast cancer risk. While some studies have found no relationship between the two, certain PBDEs have been shown to promote estrogenic-like growth of human breast cells and can act in combination with naturally existing estradiol to inhibit the treatment of cancerous cells.[32,33]

Phthalates: Phthalates are a group of chemicals that are used to soften plastics and are found in toys and some medical devices, as well as in many household and personal care products.[34] Phthalates have been detected in human urine and blood samples,[35,36,37] in the amniotic fluid of pregnant women,[38] and in human breast milk.[39,40] They can also pass through the placenta and expose the fetus during development.[41] Because of their endocrine-disrupting properties, phthalates have complex effects on estrogen and androgen hormone systems.[13] As with BPA, the ubiquitous presence of phthalates in our environment and our bodies makes epidemiological studies of phthalates and long-latency diseases like breast cancer difficult to conduct. Epidemiological results have been mixed, varying by characteristics of the study group, the specific phthalates, and the timing of specimen collection.[42] However, consistent with laboratory studies, exposure to dibutyl phthalate (DBP) has been associated with increased risk of ER+ breast cancer.[43] Through epidemiological studies and studies in young rats, several phthalates have been associated with altered and delayed breast development.[44,45] Other phthalates have been found to inhibit breast cancer cell treatment and increase the growth of new cells through in vitro studies.[46,47]

Alkylphenols: Alkylphenols are chemicals commonly used in cleaning products and detergents and are also found in personal care products like hair products and spermicides.[48,49] They and their breakdown products have also been found in samples of household air and wastewater.[50,51,52,53] Human studies have found alkylphenols in human serum and breast milk.[54,55] Rat studies have shown that alkylphenols can alter the development of the mammary gland, and cell culture studies indicate that alkylphenols can increase mammary cell proliferation.[56,57]

PFAS: Per- and polyfluoroalkyl substances (PFAS) are a family of persistent, bioacumulative and toxic chemicals. Perfluorooactanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) are among the thousands of PFAS chemicals. Both PFOA and PFOS have been widely used in many household products for their oil-, grease-, and water-repelling properties and have been shown to be potential endocrine disruptors and carcinogens.[58] Though they are being phased out of production, these chemicals are still in use and persist almost indefinitely in the environment. They have been found at measurable levels in human serum, amniotic fluid, and cord blood samples. PFOA influences both prenatal and pubertal mammary gland development.[59]

Studies from the Ohio River Valley, an area with elevated PFAS exposures due to nearby manufacturing, demonstrated that higher PFOA exposure was associated with delayed breast development and onset of menstruation in girls.[60,61,62]

Pesticides and Herbicides: Some pesticides in current use are toxic or likely endocrine disruptors, which has implications for consumers who ingest produce with pesticide residue or meats and fish contaminated through pesticide run-off. Atrazine is an herbicide still widely used in the United States. In rat studies, atrazine was shown to disrupt normal mammary gland development.[63,64]

Organophosphate pesticides, including malathion and chlorpyrifos may adversely affect mammary gland development.[65] Though many organophosphate pesticides have been banned, those that remain in use are used as the primary insecticide in U.S. agriculture.[66] For children, who are especially vulnerable to exposure as they are still developing,[67] most organophosphate pesticide exposure comes from dietary intake.[66,68] Studies have demonstrated that short-term changes to an organic diet can reduce pesticide exposures.[68,66,69]

Solvents: Solvents, including styrene, methylene chloride, and formaldehyde, are found in consumer products such as building materials, cleaning and personal care products, and cigarette smoke.[70,71,72] Many cleaning and personal care products labeled as containing fragrance contain solvents.[73] Formaldehyde has been found to cause DNA damage in mice[74] and to promote tumor formation and growth.[75] Additionally, when prepubescent mice were exposed to organic solvents, those that experienced high-intensity exposure were later found to have developed mammary tumors.[76] Workplace solvent exposures have also been linked to breast cancer, as described in the "Occupation" section of the Plan.

Aromatic Amines: Aromatic amines are used in a variety of industries and found in most permanent hair dye products, grilled meats, diesel exhaust, and smoke from burning wood.[77,78,79] Aromatic amines can lead to DNA damage in both healthy cells and cancer cells and they mimic estrogen in estrogen-sensitive cancer cells.[78,80,81] Use of hair straighteners and permanent dyes, which contain many chemicals including aromatic amines, was associated with increased risk of developing breast cancer, especially in Black women.[82,83]

Parabens: Parabens are anti-microbial agents found in food, pharmaceuticals, and personal care products and can be absorbed through the skin and the GI tract. As estrogen mimickers, they can increase cell growth and proliferation and inhibit cell death.[84,85,86,87] Since parabens can alter estrogen related pathways to cause abnormal growth in breast tissue, those exposed prenatally and during childhood are especially vulnerable to their negative

health effects.[6] One study of women in the Long Island Breast Cancer Study Project found that the highest urinary level of methylparaben was significantly associated with a 50% higher risk of breast cancer than the lowest level. High levels of propylparaben and the sum of all parabens were also associated with higher risk, but these were not statistically significant.[42]

Nuances and Emerging Considerations

Human observational studies relating exposure to chemicals in consumer products to breast cancer risk provide compelling evidence of their harmful effects. Studies using animal and in vitro models to directly expose cells and tissue to these chemicals help support the conclusions of epidemiological studies and the hypothesis that many chemicals found in consumer products increase the risk of breast cancer. The effects for endocrine-disrupting compounds (EDCs) are seen in low-dose and non-monotonic responses, showing that many hormone-disrupting exposures are more damaging at very low levels and have different resulting effects at different levels.[88,89] In addition, many endocrine-disrupting compounds have a greater impact during prenatal development, during childhood, and at puberty.[13]

In addition to the directly carcinogenic activities from consumer product chemicals, other chemicals have more upstream effects on the body that can lead to an increased risk of breast cancer. Some chemicals have damaging effects on reproductive health and delay activities like breast development and menarche, which suggests these chemicals are disrupting normal hormonal processes.[60,61,90]

Consumers are exposed to a host of different chemicals through the products they use, in addition to other environmental exposures. We know very little about the effects of exposures to such mixtures, but a few studies demonstrate additive or synergistic effects. Thus, screening chemicals for carcinogenic effects one at a time is not adequate to understand risk.[91,7]

Chemical exposures may also trigger epigenetic changes—in other words, changes to gene expression, but not to the actual genetic code—that alter cellular activity, tumor suppression, and mammary gland development. Some of these disruptions in normal physiological processes may ultimately be linked to increased risk of breast cancer.[92,93,62,94]

For those exposures that cause cell damage, there can be changes in the activities of neighboring cells and ultimately in the organization of tissues, as cells are in constant communication with one another. The altered organization of tissues due to cell damage applies to mammary glands and ultimately increases breast cancer risk.[95,96]

Take-Home Message

The combined body of research in humans, laboratory, and cellular studies shows that people are exposed to chemicals from the consumer products they use every day and suggests some of those chemical exposures are associated with increased risk of breast cancer. Extra precautions should be taken during pregnancy, childhood, and adolescence since studies have shown that women and girls are more vulnerable to carcinogens and EDCs during these developmental phases.

Chemicals in Consumer Products: Context for Interventions

Californians are exposed to chemicals linked to breast cancer and other health problems in hundreds of consumer products in their homes, schools, and workplaces, including beauty and personal care products, cleaning products, furniture and carpets, toys, electronics, food and food packaging, textiles, school supplies, and more. Without their knowledge or consent, every day people absorb, ingest, or inhale hundreds of chemicals that migrate out of these products.

The federal government does not require premarket safety testing of the chemicals used in consumer products. Weak and poorly enforced laws, such as the Toxic Substances Control Act, the Federal Hazardous Substances Act and the federal Food, Drug and Cosmetics Act—as well as lack of coordination between the federal agencies with jurisdiction over different product categories—has resulted in a virtual free-for-all in terms of what chemicals manufacturers can and do use in everyday household products. In many cases, regulators don't even know what chemicals are in the products they are tasked with overseeing because of a lack of government-mandated ingredient disclosure.

Over 86,000 chemicals have been registered with the U.S. EPA, and over 40,000 are in active use in commerce today. The identity of almost 20% of those chemicals is hidden from the public as "confidential business information," even if they pose potential health risks.[97] Unfortunately, the overwhelming majority of these chemicals have not been adequately tested for safety, and even fewer have been thoroughly reviewed for their potential impact on breast cancer risk. Endocrine-disrupting compounds (EDCs) are of particular concern given the hormonal sensitivity of some breast cancer types and the impact of EDCs at very low levels, even at parts per trillion. U.S. and international testing protocols do not require adequate evaluation of mammary gland endpoints, one of the most sensitive endocrine-disrupting effects and the most relevant to breast cancer risk.

Government should play a significant role in monitoring and protecting consumers from dangerous chemicals in consumer products. Biomonitoring, a method of measuring pollution in people, has found chemicals from consumer products in people's blood, urine and breast milk. Intervention studies have further shown that when people stop using products containing a particular toxic chemical, their body burden of that chemical goes down. For example, studies have shown significant reductions in the levels of chemicals when behaviors changed for just three days: bisphenol A (BPA) levels went down over 60% and the phthalate DEHP dropped by 50% when food packaged in plastic was removed from the diet of five Bay Area families.[35] Similarly, levels of four endocrine-disrupting compounds were reduced between 25% and 45% when Latina teenagers in the Salinas Valley switched their makeup and personal care products to safer products.[98]

Reductions in the public's exposure to toxic chemicals have also been documented in response to major policy changes and advocacy efforts. Approximately 10 years after polybrominated diphenyl ether (PBDE) flame-retardants were banned in California, Biomonitoring California, one of the premier biomonitoring programs in the world, found a 39% drop in levels of the chemicals found in the breast milk of California women.[99]

Impacts on Already Burdened Communities

Communities of color and low-income communities are disproportionately exposed to hazardous chemicals from numerous sources, including consumer products.[100] For example, low-income Black and Mexican-Americans are more highly exposed to a potentially carcinogenic chemical found in household products such as cheap toilet deodorizers[101] and Mexican-American children in California have higher levels PBDEs, used as flame retardants in consumer products, in their bodies than almost all other people tested worldwide.[102] A study of PBDEs in 6 to 8-year-old girls from California and Ohio found racial disparity in PBDE body burden, with higher concentrations in Black girls compared to White girls.[103]

Evidence also shows that personal care and beauty products marketed to women and girls of color are among the most toxic and add to the already higher burden of chemical exposures many communities of color experience in their neighborhoods. A study by the Silent Spring Institute found 45 endocrine-disrupting compounds in 16 hair-care products marketed to Black women.[104] The study also found five chemicals in these products that are regulated by California's Proposition 65 (chemicals linked to cancer or reproductive harm) or prohibited in the European Union. Product testing conducted by Breast Cancer Prevention Partners in 2018 found 24 chemicals linked to harm in Just for Me shampoo, part of a hair straightening kit marketed to children of color.[73] This represented the highest number of toxic chemicals found in any of the products BCPP tested. The California Safe Cosmetics Program Database,[105] a state program that tracks dangerous chemicals linked to cancer and reproductive harm in personal care products, has documented chemicals of concern in thousands of products sold in the state.[106]

Similarly, products sold in dollar stores—Dollar General, Dollar Tree and 99 Cents Only—are raising concern. Over 31,000 discount retail stores ("dollar stores")[107] across the United States belonging to the major dollar store chains (the giants Dollar General and Dollar Tree/Family Dollar, and smaller chains like 99 Cents Only) often serve as the primary, or only, source of household products and food for many low-income communities. The largest chains collectively operate more stores than Walmart or McDonald's: 75% of the U.S. population lives within 5 miles of a Dollar General store.[108,109] Many communities served by dollar stores are predominantly communities of color or low-income communities that are already disproportionately exposed to chemical hazards, health effects linked to environmental pollution exposures, and substandard or hazardous housing conditions. A report produced by the Campaign for Healthier Solutions[110] found 81% of the dollar store products tested (133 of 164) contained at least one hazardous chemical above levels of concern.[111]

For more information on cumulative exposures to communities, see the "Place-based Chemicals" section.

Ingredient Transparency and Consumer Right-to-Know

Strengthened chemical disclosure and ingredient transparency can be a first step toward safer products. Ingredient disclosure provides consumers with the information they need to make safer and more informed purchases for themselves and their families. Fear that consumers will not buy their products motivates manufacturers to remove toxic ingredients from their products rather than disclose the presence of these ingredients to the public.

California has been a leader in disclosing dangerous chemicals through state polices such as the Safe Drinking Water and Toxic Enforcement Act of 1986 (known as Prop 65) and the California Safe Cosmetics Program, which require the disclosure of chemicals linked to cancer and reproductive harm. Laws recently enacted in California require disclosure of ingredients in cleaning and professional salon products sold in the state.

Regulating Toxic Chemicals in Consumer Products

California has again been a leader in restricting or banning the worst chemicals in products. Over the last two decades, the state has passed laws to ban lead, cadmium, and mercury in various products; BPA in baby bottles and sippy cups; phthalates in toys; and flame retardants in furniture, mattresses and children's products.

However, far too often the targeted industry removes a toxic chemical only to replace it with another chemical that is equally or more toxic, or for which there is insufficient data to evaluate safety. This practice of regrettable substitution has created a "toxic treadmill" of careening from one bad chemical to another. The CA Safer Consumer Products Program is a groundbreaking and unique program that not only identifies chemicals of concern in a category of consumer products—for instance toluene in nail polishes—but also requires manufacturers to conduct a detailed alternatives assessment to ensure that replacement chemicals are actually safer than the ones being removed.

One unintended consequence of policies banning certain chemicals in consumer products is the potential for the older, more toxic articles to end up in low-income communities, a phenomenon known as "downstream dumping." For instance, old couches with high levels of unnecessary and highly toxic flame retardants may end up in secondhand stores, a primary shopping location for low-income families. And even if those products are taken off the primary and secondhand market entirely, which is very difficult from a policy perspective, disposal in waste landfills or incinerators in disadvantaged neighborhoods can still result in adding exposure to already overburdened communities.

Unfortunately in some cases, such as flame retardants in furniture or PFAS in carpets, effective and just disposal solutions simply don't currently exist. Much more research is needed to both understand the dynamics of downstream dumping and develop ways to address it.

Marketing Dangerous Standards

We live in a world that aggressively promotes White beauty standards. Lighter skin, straighter hair and other beauty goals are widely marketed to women, especially women of color, creating societal pressures to use numerous, often harmful beauty products.

A striking example of this is the pressure Black girls and women face to change their natural hair. Black Women for Wellness estimates that Black women in the U.S. spend nearly $9 billion each year on beauty products, twice as much as any other ethnic group.[112] From an early age, sometimes even before elementary school, many Black women begin a life-long quest to chemically change their hair. Straighteners, texturizers, perms, and detanglers all can contain harsh and harmful ingredients, exposing not just the girls and woman using the products, but also the salon workers who spend endless hours doing women's hair. Some of these products are marketed as "natural," though without regulations guiding the truth of these claims, many of these products are anything but natural.

In 2018 California passed legislation banning racial discrimination based on hairstyles at schools and workplaces,[113] but this is only the beginning of a process that allows people's natural beauty to shine. Many Black women still feel pressure to conform to White beauty standards to reduce discrimination and improve their economic security.

There needs to be a shift in the way media presents beauty stands that does not set a White-centric standard and does not seek to stoke internalized racism in women of color. Through regulations that force reformulation of products and a shift in the way all media outlets present and promote beauty to embrace uniqueness and differences, we can reduce pressure to use harmful products to meet unrealistic and oppressive beauty standards.

New, effective media campaigns in advertising, social media, entertainment and other avenues are needed to dismantle expectations that using products that contain harmful chemicals will make us happier, healthier, more beautiful, and more acceptable.

What Individuals Can Do

What can be done to reduce our risk of breast cancer? Awareness and adoption of these prevention tips can help change your daily routine to reduce your risk of the disease. Here are some tips on how you can make simple changes to protect your health.

- **Read ingredient labels.**
  It is perfectly legal to use ingredients linked to cancer, endocrine disruption, and reproductive harm in personal care products, cosmetics, cleaning products and food packaging. Check our Glossary of Exposures to learn more.

- **If you don't know what's in it, don't use it.**
  Labeling loopholes have allowed companies to avoid disclosing ingredients on the labels of household cleaners, food packaging and hair and nail salon products. Buy from companies committed to full ingredient disclosure.

- **Avoid fragrance in everything.**
  Fragrance (or parfum) is a cocktail of ingredients, and each fragrance can include dozens of potentially harmful chemicals. Avoid purchasing and using personal care products, cleaning products, clothing, and home goods with added fragrance as often as possible.

- **Wash your hands.**
  Washing your hands kills germs and reduces exposures to unsafe chemicals. Many chemicals from everyday products end up in household (or workplace) dust. Hand-washing reduces dust on the hands, and as a result reduces exposures to chemicals such as flame retardants and phthalates. Washing your hands for 20 seconds with plain soap, free of antibacterial chemicals, will effectively remove harmful germs.

- **Go fresh, organic, and hormone-free.**
  Choose fresh, organic, and hormone-free foods, when and where these foods are available and affordable, to avoid exposure to pesticides, added hormones, and other possible toxic chemicals in packaged foods. Buying products grown organically reduces pesticide use, which is good for families, farmworkers, and the environment, and eating fresh (or frozen) foods helps you to avoid chemicals like BPA in food can linings.

- **Don't be brainwashed, greenwashed, or pinkwashed**
  Companies use savvy marketing to sell products; so don't let false claims trick you into buying products with harmful ingredients. Watch out for products designed to look like they are good for the environment or natural. This is called green washing—words like "natural" and "safe" have little, if any, meaning without ingredient labels to back them up. So do your research to ensure these products live up to the claims on the label. Be wary of products boasting a pink ribbon, too. Many pinkwashed products contain chemicals linked to cancer, and often do little to prevent or reduce breast cancer.

For more tips: https://www.bcpp.org/our-work/tips-for-prevention/

While these tips are important and helpful, we should never forget that we cannot "shop our way out of the problem." Systemic change is necessary to ensure all of us are safe from harmful chemical exposures.

Community Input on Chemicals in Consumer Products

Community listening session participants were very concerned about the lack of regulation of ingredients in consumer products. They were specifically concerned about the lack of affordable, safe personal care products and household cleaning products, especially products marketed to women of color. Additionally, several women talked about on-the-job exposures, such as working with cleaning products as housecleaners or in custodial roles, or with beauty products as salon workers. Overall, women wanted requirements for products to be safer; clear ingredient labels so they know what is in the products they are using; more affordable, safe options available in their neighborhood stores; and much more public education on the risks of chemical exposures from consumer products.

INTERVENTIONS

Overarching Goal: Ensure that consumer products in California do not contain chemicals linked to breast cancer and that existing products containing toxic chemicals are disposed of in a safe and equitable way.

Intervention Goal 1

Regulate consumer products to disclose, restrict and/or remove chemicals linked to harm to humans or the environment, particularly chemicals linked to breast cancer.

Objective 1: Disclose chemical ingredients in consumer products, providing consumers the right to know what's in the products they buy.

- **Strategy 1**: Pass state laws requiring ingredient disclosure for consumer products, including food packaging, furniture, building materials, electronics, textiles, and school and art supplies.
- **Strategy 2:** Require disclosure of fragrance and flavor ingredients in cosmetics and personal care products, particularly any hazardous chemicals.
- **Strategy 3:** Require disclosure of toxic non-functional constituents and containments in consumer products, particularly those linked to breast cancer.
- **Strategy 4:** Prohibit trade secret protection for any ingredient that harms human health or the environment when requiring ingredient disclosure for consumer products.

Objective 2: Support and strengthen California's unique Green Chemistry Initiative, specifically the Safer Consumer Products Program, based on recommendations from the report *California's Green Chemistry Initiative at Age 10: An Evaluation of its Progress and Promise.*[114, 115]

- **Strategy 1:** Fund and streamline the Safer Consumer Products Program to more efficiently analyze, and where appropriate ban or restrict, hazardous chemicals in consumer products sold in California.
- **Strategy 2:** Pass legislation to provide the Safer Consumer Products Program clear authority to require manufacturers to disclose the chemicals in their product to the Program; to take expedited action when safer alternatives are already available; and to use scientifically sound existing alternatives analyses.

Objective 3: Require the use of a precautionary approach when considering purchasing policies, restrictions or bans of toxic chemicals in consumer products.

- **Strategy 1**: Implement state and local government precautionary procurement policies to reduce or eliminate the use of products containing toxic chemicals, particularly those linked to breast cancer.
- **Strategy 2**: Take a class approach to regulating chemicals in consumer products when the chemical class has inherent characteristics linked to harm to humans or the environment, for example per- and polyfluoroalkyl substances (PFAS) or halogenated flame retardants.
- **Strategy 3**: Ban the use of BPA, phthalates, PFAS and other hazardous chemicals in food packaging sold in the state.
- **Strategy 4**: Prohibit the use and discharge of firefighting foam containing PFAS, a major source of PFAS water contamination in the state.

Intervention Goal 1 (continued)

Regulate consumer products to disclose, restrict and/or remove chemicals linked to harm to humans or the environment, particularly chemicals linked to breast cancer.

Objective 4: Ensure vulnerable populations are adequately considered and protected in any evaluation of the use of toxic chemicals in consumer products, particularly those chemicals linked to breast cancer.

- **Strategy 1:** Enact policies that regulate hazardous chemicals in all consumer products children or women of childbearing age are exposed to, not just products marketed to children.
- **Strategy 2:** Require agencies that assess and/or regulate chemicals in consumer products to explicitly consider safety endpoints linked to breast cancer and to include cumulative exposures to workers and communities when conducting safety determinations.
- **Strategy 3:** Prioritize research, safety determinations, and regulation of products marketed to communities of color and low-income communities.

Intervention Goal 2

Consider the impact of the full life cycle of products—production, use and disposal—particularly on highly impacted communities and workers who manufacture or use the products.

Objective 1: Include exposures and potential harm to workers and the communities around manufacturing facilities when accessing the safety of consumer products.

Objective 2: Consider and control for the potential for "downstream dumping" when developing public policies to label, restrict, or ban consumer products.

Objective 3: Ensure that disposal methods, such as waste landfills, do not disproportionally impact certain vulnerable communities.

- **Strategy 1:** Enact policies at the state and local level requiring zoning and permitting practices to consider cumulative chemical exposures on burdened communities and ensure equitable distribution of disposal facilities.
- **Strategy 2:** Shut down existing California incinerators, which emit toxic chemicals such as the breast carcinogen dioxin.

Objective 4: Fund research to develop processes to properly dispose of consumer products containing toxic chemicals.

- **Strategy 1:** Provide state funding to California universities to research and develop techniques and technologies to destroy or neutralize toxic chemicals, particularly persistent, bioaccumulative and toxic chemicals (PBT) that do not breakdown in the environment.

Intervention Goal 3

Promote programs and media images to counteract discriminatory concepts of beauty that lead women to use more beauty products containing chemicals linked to breast cancer or other health issues.

Objective 1: Promote positive body image and self-esteem for all girls, and particularly girls of color, through K-12 school curricula.

Objective 2: Promote positive images of women of all shapes, sizes, and colors.

- **Strategy 1:** Use state resources to create PSAs with positive messages on beauty and self-worth that counteract negative and discriminatory images. Messages and images must be developed in partnership with the affected communities.

Intervention Goal 3 (continued)

Promote programs and media images to counteract discriminatory concepts of beauty that lead women to use more beauty products containing chemicals linked to breast cancer or other health issues.

- **Strategy 2:** Ensure stock photo sources provide a diversity of images, include photos of women of color with natural hairstyles and women of all shapes and sizes.

Objective 3: Hold media outlets accountable for discriminatory or stereotyping images of women, particularly women of color through social media and market campaigns.

Intervention Goal 4

Support research to identify harmful chemicals linked to breast cancer, and design intrinsically safer chemicals through green chemistry.

Objective 1: Provide additional funding for research on primary prevention and chemical contributions to breast cancer risk by expanding the tobacco tax that funds the California Breast Cancer Research Program to include all tobacco products, not just cigarettes.

Objective 2: Increase funding and staffing for the Office of Environmental Health Hazard Assessment (OEHHA) to build capacity to develop a list of known and suspected endocrine disruptors, including those linked to breast cancer, which will allow advocates to push for disclosure of those chemicals and encourage manufacturers to remove them from their products.

Objective 3: Create and fund green chemistry programs at University of California and California State University campuses. Require that chemistry classes included green chemistry concepts and practices in the curriculum, and support cross-disciplinary training in toxicology for chemists.

Objective 4: Provide funding, through public and private funds, for innovation challenges to spur development of safer chemicals for specific functions, such as preservatives.

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Herbs
We Are Pay What You Can
Salad $3-5
*Arugula
*Spicy Mix
*Seasonal Herbed Heirloom Lettuce Mix
Roots $3-5
*Carrot
*Turnip
*Beet
*Radish $2-4
Greens $2-4
*Kale
*Collards
*Chard
*Tokyo Cabbage
Herbs $2-4
*Basil
*Dill
*Cilantro
*Sage
*Spilanthes
*Mint
*corriander
*Lovage
Seasonal Fair $3-5
*Rhubarb
*Cabbage

Diet and Nutrition

Science Summary

The relationship between diet and breast cancer is complex and still not well understood, as the vast majority of the studies were conducted based on dietary practices later in life. Despite inconsistencies in the overall evidence, the existing scientific evidence suggests healthy dietary patterns may be protective against breast cancer.

What the Foundational Documents Say

The World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) summarize the literature in the Continuous Update Project 2018: Diet, Nutrition, Physical Activity, and Breast Cancer. This project looked only at randomized controlled trials and cohort and nested case-control studies. The Continuous Update Project (CUP) emphasizes a healthy dietary pattern that includes whole grains, vegetables, fruit, and beans; minimizes red and processed meat, fast foods, and other processed foods high in fat, starches, or sugars; and avoids sugary drinks. The CUP points to evidence that suggests increased dairy and calcium intake may be associated with lower risk of breast cancer; similarly, intake of foods high in carotenoids (yellow, orange and red plant pigments) may be linked to lower risk. Some evidence suggests non-starchy vegetables may be protective for ER- breast cancer, while associations with ER+ breast cancer remain inconclusive. The report cites other dietary factors, including overarching dietary patterns, as inconclusive.[1] The other foundational documents quote the CUP's findings on diet and nutrition.

The Current State of the Evidence

The complexity of dietary components and patterns and the challenges in study design may contribute to the lack of clarity regarding dietary factors and breast cancer risk. Complexity is involved in three ways: 1) diets themselves are complex; 2) the relationship between diet and breast cancer is complex; and 3) studying the relationship is complex; for instance, portion size and frequency of meals are not always accounted for, and the accuracy of research participants dietary recall is often unreliable. Still, from overall dietary patterns and macronutrients to individual foods and micronutrients, researchers continue to add to the body of literature investigating dietary influences on breast cancer incidence in order to better understand diet's role in breast cancer risk.

Dietary Patterns

Research on the association between breast cancer risk and various dietary patterns remains largely inconclusive, either from a lack of research on a specific dietary pattern, a lack of consistency in definition of a dietary pattern, or contradictory results. The most well-studied dietary pattern is the Mediterranean Diet. The Mediterranean Diet is typically characterized by an emphasis on seafood, olive oil, and an abundance of plant foods, with a low to moderate consumption of wine and dairy, and a minimal intake of processed foods, red meat, and poultry.[2]

While several studies have found a reduced risk of breast cancer with a Mediterranean dietary pattern,[3,4,5,6,7,8,9,10,11] others found inconclusive evidence.[7,12,13] One showed a decreased risk of high breast density, a known risk factor for breast cancer.[14] Castello and colleagues compared breast cancer risk in three dietary patterns: Mediterranean Diet (high in fish, plant foods, vegetable oil), Prudent Diet (plants, juices, low-fat dairy), and Western Diet (high in refined/processed foods, high-fat dairy, processed meat).[4] While following the Prudent Diet showed no influence in breast cancer risk, following the Western Diet was associated with increased breast cancer risk. In contrast to the Western Diet, this study found that the Mediterranean Diet was protective for post-menopausal women. This inverse association with breast cancer was further supported by Turati et al., who showed that a moderate to high Mediterranean dietary pattern resulted in a lower risk of breast cancer.[9]

In contrast, inconclusive support for the inverse association between the Mediterranean Diet and breast cancer has resulted from a meta-analysis[7] and a review,[12] which suggest the association was only significantly present in case control studies, while non-significant associations were found in cohort studies.[7,12] Updating the meta-analysis using seven more recent cohort studies resulted in evidence of a 6% reduced breast cancer risk with a Mediterranean Diet.[8] Likewise, yet another meta-analysis of 28 cohort studies of cancer—13 on breast cancer—offers further support to the protective association between the Mediterranean Diet and breast cancer risk.[3] Another study found that adherence to a Mediterranean Diet reduced the risk of ER- breast cancer by 40%. They also found a slight decrease in risk of ER+ breast cancer, but that finding was non-significant and could be due to chance. These studies challenge previous equivocal conclusions drawn from a lack of significance in past cohort studies.[7,12] Additional evidence explaining the lack of significance in the past cohort-based studies is needed. A 2019 meta-analysis of cohort and case control studies found a Prudent dietary pattern was associated with an 18% reduced risk of breast cancer which was significant for pre-menopausal but not post-menopausal women.[15]

Three dietary patterns are associated with an increased risk of breast cancer: a Western Diet, [4,15,16] an unhealthy diet,[17] and a diet high in ultra-processed foods.[18] While specific criteria and definitions differ between studies, the Western dietary pattern is commonly described as high in processed meat, refined grains and processed foods, and high-fat dairy.[4,16] An unhealthy diet pattern is described similarly, with an abundance of fat, salt, processed foods, and animal foods.[17] Ultra-processed foods are those including, but not limited to, mass-produced packaged food items, processed meat, processed snacks and breads, convenience and instant foods, and foods exposed to processing and preserving.[18] While the Mediterranean Diet tends to provide a source of healthy fats, the Western Diet includes unhealthy fats, and processed dietary patterns provide sources of saturated and trans-fats; fat type and intake does not seem to explain the differences in breast cancer risk.[19]

Dietary Fat Intake

While some research suggests total fat intake increases risk of breast cancer,[20,21] other studies do not confirm the association.[22,23,24] Monounsaturated fats show inconsistent results with breast cancer risk.[19] Positive associations have been seen with trans-fats and inverse associations with vegetable fat, but those results are not statistically significant.[22] Though dietary n-3 polyunsaturated fat (PUFA) may be associated with reduced risk of breast cancer,[25] the ratio of dietary n-6 and n-3 PUFA intake may be an important factor in risk.[26] One study found an increase in breast cancer risk with a high n-6 and a low n-3 PUFA intake compared to women consuming low n-6 and high n-3 PUFA intake.[26] No association was seen with both high n-6 and n-3 PUFA intake, while a slight decreased risk was seen with low intakes of both in this study, suggesting the interaction between these essential fatty acids may be more important than each individual contribution to risk.[26] The typical U.S. diet may provide 10-fold more n-6 than n-3 PUFA.[27] Certain oils (corn, safflower, sunflower, and sesame); nuts such as pecans, Brazil nuts, and pine nuts; sunflower seeds;[28] and some animal products[29] are examples of foods containing n-6 PUFAs. Flaxseed, walnuts, chia seeds, canola oil, and fish are examples of n-3 PUFA foods.[28] Since the ratio of n-6 and n-3 PUFA may influence inflammation,[30] it is worthwhile to note that research on dietary inflammatory index shows an increased risk of breast cancer with an inflammatory diet, especially in post-menopause.[31,32,33,34] See the "Inflammation" section for more information.

Dietary Carbohydrate and Fiber Intake

Dietary carbohydrate intake[24,35] and dietary glycemic index and glycemic load[35,36,37,38] show inconsistent results regarding breast cancer risk. Unlike dietary fat, all 5 studies investigating dietary fiber show a consistent inverse association with breast cancer.[39,40,41,42,43] In addition to these five studies, another study found an inverse association between flax intake and breast cancer risk.[44] Flax is a dietary source of fiber[45] and plant-based n-3 polyunsaturated fat.[46]

Fruit and Vegetable Consumption and Micro-Nutrients

Note: For more on Vitamin D, see the separate "Vitamin D" section of this Plan.

Current U.S. Department of Health and Human Services (HHS) and U.S. Department of Agriculture (USDA) Dietary Guidelines suggest women consume 3 cups of vegetables and 2 cups of fruit daily, yet on average, adult women in the U.S. do not meet these recommended guidelines.[47]

The impact of fruits and vegetables and micronutrients on breast cancer risk remains controversial. With either contradictory or non-significant results, conclusions on the association between individual vitamins[48,49,50,51] or fruits and vegetables[39,43,52] cannot be drawn at this point. Some evidence suggests protective effects for consumption of alpha carotene[52,53] and isoflavones (which are phytoestrogens).[6,54,55,56,57] While alpha carotene may have an inverse association with breast cancer risk,[52,53,58] risk by tumor subtype remains inconclusive.[59,60] Alpha carotene is one type of carotenoid, or plant pigment, which is found in yellow, orange, and red fruits and vegetables.[61]

The primary source of dietary isoflavones is soy.[62] Although some studies of dietary isoflavones from soy suggest reduced breast cancer risk,[6,54,55,56,57] others are unclear.[24,63,64,65,66] Some research suggests that the protective effects of soy isoflavones on breast cancer risk may be dependent on developmental stage of exposures, with consumption earlier in life offering a more protective effect.[20,67,68] This is supported by research showing an inverse association in populations with life-long dietary patterns typically high in soy foods.[24,63,66]

Dietary Protein Intake

Soy is not only a source of isoflavones, but also a source of plant-based dietary protein. The HHS and USDA dietary guidelines for protein suggest 5.5 ounces of protein daily for individuals consuming a 2,000-calorie-per-day diet.[47] The research exploring dietary protein and breast cancer risk suggests that red and processed meat intake may increase breast cancer risk.[42,57,69,70,71,72,73] While a few conflicting results challenge this view with no or weak associations,[74,75] others provide supporting evidence that red meat intake early in life may lead to breast cancer risk factors such as early menarche[76] or increased breast density.[20]

The associations between other sources of animal protein and breast cancer risk remain inconclusive. While one study found a high fish intake in midlife reduces breast cancer risk compared to low intake,[77] another found no association,[78] and yet another study found an increased risk in White women with tuna intake.[79] Likewise, the relationship between dairy and breast cancer remains inconclusive. While one study found a reduced risk associated with total dairy,[80] another saw a decreased risk in U.S. and Asian populations but not in Europeans,[81] and yet another study contributes inconclusive results.[82] Exploring calcium's role in the dairy debate results in no more clarity. One study supports calcium's role in reducing breast cancer risk in pre-menopause,[83] while another study challenges this with null findings.[84] It is interesting to note that ultra-pasteurization methods may influence milk protein integrity, and therefore may be a factor to consider in evaluating results.[85]

Coffee/Caffeine Consumption

Research on breast cancer risk associations with coffee and caffeine have resulted in mixed conclusions.[86,87,88,89,90] A Canadian cohort study found no association between coffee and total breast cancer risk, but when evaluated by menopausal status, there was an increased risk in pre-menopausal disease.[90] A Swedish cohort study found a decreased risk in total breast cancer and the ER+/PR- subtype with coffee consumption, but found an increased risk with tea consumption.[91] A European cohort study found a decreased post-menopausal risk of breast cancer with coffee, especially in ER-/PR- breast cancers, but no association in pre-menopause with coffee intake, nor with tea intake despite menopausal status.[92] A U.K. cohort study found no association with coffee and total breast cancer risk, but there were non-significant suggestions that associations may vary depending on history of post-menopausal hormone treatment.[89]

Nuances and Emerging Considerations

Teasing apart the complex relationship between diet and breast cancer risk remains a significant challenge for research. Food frequency questionnaires used in data collection may lead to inconsistent results due to errors in characterizing intake. Dietary data collection within a singular time frame does not provide information corresponding to the long-term effects of dietary history. Food nutrients may act together to create health effects, which complicates the study of single nutrients or a specific type of food. The possible interaction between nutrition and lifestyle factors further complicates study design and data analysis.

The effect of childhood and adolescent diets are also beginning to be elucidated. A number of studies, relying on adult recall of adolescent diet, are finding associations with breast cancer risk. A meta-analysis found total fat intake in adolescence was associated with increased risk of pre-menopausal breast cancer, while soy intake in adolescence and childhood was associated with a significantly decreased risk of all breast cancer.[20] Individual studies have found decreased risk with higher total fruit intake in adolescence,[58] and increased risk of pre-menopausal, hormone receptor positive breast cancer with increasing red meat intake in adolescence.[93] More research is needed on the impact of childhood and adolescent diet on later-life breast cancer risk.

An emerging consideration to address in future research may be the effect of the microbiome on isoflavone metabolism. If the gut microbiome influences isoflavone metabolism,[94] then considering the microbiome's indirect influence on the estrogenic effects of isoflavone intake may be worthwhile. Exploring the effects of the microbiome on the absorption and metabolism of other nutrients as well may help shed light on the breast cancer risk and nutrition dialogue. See the "Microbiome" section of this Plan for more information. Other considerations, such as the effect of fiber on estrogen concentrations[95] and the effect of developmental nutrition exposures on breast cancer risk factors including breast density[20] and age at menarche[68] may also be prudent, as discussed in the relevant sections of this Plan. The effect of processing methods on the nutritional integrity of food, such as dairy, should also be explored.

The possible direct and indirect effects of nutrition and dietary patterns across the lifespan may help shed light on nutrition's role in breast cancer risk.

Take-Home Message

- Dietary intake is complex, and research remains largely inconclusive for an association between many individual dietary factors and breast cancer.
- To prevent breast cancer a healthier lifestyle pattern, rather than focusing on individual factors is best. This lifestyle pattern includes maintaining a healthy weight and an active lifestyle, and eating a healthy dietary pattern that emphasizes whole grains, vegetables, fruit, and beans; minimizes red and processed meat, fast foods and other processed foods high in fat, starches, or sugars; and avoids sugary drinks.
- Research suggests that red and processed meat intake may increase risk of breast cancer.
- Dietary fiber may have a protective effect on breast cancer risk.

Eating to Reduce Breast Cancer Risk

While the data on the connection between diet and breast cancer risk are complicated and sometime contradictory, a few themes stand out as dietary recommendations for reducing breast case risk:

- Increase consumption of fruits and vegetables, choosing organic produce when possible.
- Reduce consumption of highly processed foods, foods in packaging that contains hazardous chemicals (such as bisphenol A (BPA) or phthalates),[96] and foods containing growth promoting hormones (such as Zeranol) or pesticides.[97, 98]
- Increase consumption of healthy, plant-based proteins, while reducing consumption of red and processed meats, particularly for children.
- Increase consumption of dietary fiber.

Diet and Nutrition: Context for Interventions

While there is no specific formula for what girls and women should eat to reduce breast cancer risk, generally eating fresh fruits and vegetables—along with a balance of healthy proteins and non-processed carbohydrates—is the basic foundation of a healthy diet. The path to actually doing that, however, is more complex than simply telling people how to eat. People need equitable and affordable access to healthy food at all stages of life.

Unfortunately, California has a lot of work to do to ensure that even basic food needs are met across the state. According to the California Association of Food Banks, California produces nearly half of the nation's fruits and vegetables, yet 1 in 8 Californians,[99] or 4.6 million people,[100] currently lack access to the food they need to lead healthy, active lives. Many do not know where their next meal will come from. This includes 1.7 million children living with food insecurity in California.[99]

There is both a great need and untapped potential to make healthy food more readily available. Studies find that simply having a store that sells healthy food within a half mile of a person's home increases their fruit and vegetable consumption.[101,102] Zoning and planning policies can help address many access barriers (see "Social and Built Environment" for more details), as can community organizing for community gardens; crop sharing; increasing healthy food options in corner stores, bodegas, farmers markets and mobile stores; and other options. The best pathways to increasing healthy food access must be determined in close consultation with affected communities.[103]

In 2017, 10% of California's residents—nearly half of them in working families—used CalFresh (California's version of the federal Supplemental Nutrition Assistance Program (SNAP)).[104] Yet only about 70% of eligible residents take advantage of this assistance.[105] Greater outreach and education is needed to help ensure that everyone

who qualifies and wants to use these benefits knows how and where to access them. But giving people CalFresh benefits helps little if they cannot regularly get to places that sell healthy food. Community members noted that SNAP/CalFresh did not promote healthy eating and they also raised concerns about the fear immigrants feel in using these programs.[106]

Schools are an important frontier in addressing children's nutritional needs. The California Department of Education currently runs the State Meals Program, which supports access to food for needy kids in such a way that it is "not readily apparent that children are receiving free or reduced-price meals."[107] However, there is a lot of room for improving the quality of what is offered, both in terms of nutrition and ensuring kid-friendly options. Church programs that promote healthy eating provide another avenue for effective changes in eating behavior.[108,109,110]

Some of the most exciting work is being done in community land projects and food justice efforts. Groups of people are working together to grow their own food, reclaiming and restoring urban land for farming and gardening by working with permaculture principles, capturing rainwater, and sharing skills. These efforts not only make food more accessible, but also help build connections between people, bring living beauty into neighborhoods, create spaces for community gatherings and rituals, support healthier eating, build Black and Brown leadership in self-sufficiency, and offer many other benefits.[111]

In a state as wealthy and food-rich as California, all people should be able to access affordable foods from their cultural and traditional diets, including traditional meats, vegetables, fruits, grains and spices. In the case of Native Americans, food sovereignty and access to traditional foods are culturally and nutritionally important. Any healthy eating program must be developed in consultation with the people the program is developed to serve.[112,113]

Community Input on Diet and Nutrition

In the community listening sessions, we heard reports of people who lived and worked in or near agricultural fields who could not afford fresh produce. People living in San Francisco reported the need to take multiple buses to shop for healthy food, requiring nearly an hour of travel time. Across the state, communities are plagued with intentionally food deprived areas (sometimes referred to as food deserts)[114] and junk food abundant areas that are flooded with corner stores and fast food restaurants (sometime referred to as food swamps), which especially target young people and communities of color. Of central importance to many communities is the need to invest in economic opportunities so people can afford healthy foods.

Repeatedly, community members called for food security, specifically access to affordable, healthy, culturally appropriate food; education on how to prepare unfamiliar healthy foods; and the sense of connection that comes from growing, sharing, preparing and eating food together. They also want food recommendations that are not discriminatory; for example, the USDA pushes dairy intake, but many people, especially Blacks, Asian Americans, and Native Americans report lactose intolerance.

INTERVENTIONS

Overarching Goal: Ensure access to safe, nutritious foods, which can help reduce the risk of breast cancer, for all Californians by increasing access to culturally appropriate, nutritious, affordable food while also providing economic opportunities so people can afford food.

Intervention Goal 1

Eliminate intentionally food-deprived areas (sometimes referred to as "food deserts") and junk food abundant areas by following affected communities' leadership in creating healthy food communities.

Objective 1: Work with local zoning and planning boards, public health departments and city or county representatives to improve options for healthy eating and reduce availability of fast and highly processed food.

- **Strategy 1:** Conduct a community needs assessment, with leadership from the local community, to evaluate the food environment and identify potential interventions and barriers to change.
- **Strategy 2:** Invest in programs to promote local food security, such as free or low-cost community gardens[115] (with uncontaminated soil)[116] and urban farms;[117] education on building planters, portable gardens (for renters), and roof-top gardens; free or low-cost seed access; gardening tool libraries; and other supports for communities and individuals to grow their own food.
- **Strategy 3:** Create and invest in local initiatives to support corner stores selling fresh fruits and vegetables. See the National Healthy Corner Stores Network[118] for more details.
- **Strategy 4:** Eliminate legal barriers to people growing their own food on available land, for example in front yards or sidewalk strips.
- **Strategy 5:** Invest in community-driven businesses that offer healthy food. For example, invest in mobile markets[119,120] that sell affordable and culturally appropriate food or programs that support business leadership development and microcredit options for community members to launch healthy food businesses.
- **Strategy 6:** Provide support for community food and crop swaps. For example, cities can host, or community members can organize, crop swap events. Promote technologies like Cropswap[121] that help people organize themselves to share and trade food they have grown.
- **Strategy 7:** Create and support programs that invest in locally owned food-related businesses and other commercial enterprises to build local economies and provide economic opportunities to support people's ability to afford healthy food. These programs should include a special focus on supporting un- and under-employed people in building their economic autonomy.
- **Strategy 8:** Work with existing grocery stores to promote healthy purchasing options with improved product availability, sales, and promotions.[122]
- **Strategy 9:** Create zoning ordinances that serve as barriers to establishing fast food and unhealthy food outlets, for instance by limiting available licenses, controlling the density, and creating school buffer zones[123] for fast food restaurants.[124] For existing fast food restaurants, ban drive-through services.[125] See ChangeLab Solutions[126] and Develop Healthy Food Zone Ordinances[127] for more information.
- **Strategy 10:** Implement soda taxes and other disincentives for people to consume unhealthy food and beverages. See Berkeley's soda tax[128] as an example.

Intervention Goal 1 (continued)

Eliminate intentionally food-deprived areas (sometimes referred to as "food deserts") and junk food abundant areas by following affected communities' leadership in creating healthy food communities.

- **Strategy 11:** Develop policies to limit the marketing of unhealthy foods, particularly to children and adolescents.[129]

Objective 2: Expand access to farmers markets that sell affordable and culturally appropriate food.

- **Strategy 1**: Establish farmers markets in areas where communities want them and ensure that food is affordable and culturally relevant to the local population. The Ecology Center created a Farmers Market Finder,[130] available in English and Spanish.
- **Strategy 2:** Support ongoing expansion and promotion of Market Match,[131] which allows CalFresh benefits to be used at 288 farmers markets across the state.
- **Strategy 3:** Provide culturally appropriate cooking and nutrition classes and educational materials at farmers markets to ensure that local people know how to use the items sold there.

Intervention Goal 2

Invest in childhood nutrition and life-long healthy eating habits.

Objective 1: Continuously improve options for healthy eating at all public schools through programs that are available to all students and/or families.

- **Strategy 1:** Make Universal Breakfast mandatory in all school districts across the state and provide reliable funding streams to make this possible. See Berkeley Unified School District[132] as an example. This approach de-stigmatizes kids who are eating subsidized school breakfasts while ensuring all kids are able to start the day with a nutritious breakfast, which can support their academic performance.[133]
- **Strategy 2:** Develop healthy school lunch programs with leadership from students to ensure the food being offered includes options the students will want to eat. See the Oakland Good Food purchasing program[134] as an example of how to ensure food is nutritious (including fresh fruits, vegetables, and healthy protein sources, and excluding processed foods), sustainably produced, and when possible, locally sourced.
- **Strategy 3:** Offer free or discounted hot meals at after-school programs.
- **Strategy 4:** Provide free or low-cost summer breakfast and lunch programs when school is out while not requiring income or residency documentation for any child.
- **Strategy 5:** Provide adequate funding to ensure that meals and snacks offered at California's Child Development Programs[107] (preschools) are healthy.
- **Strategy 6:** Develop more school gardens, with gardening, nutrition and cooking curricula at all grade levels. Ensure soil is free from contamination by testing the soil and using raised beds where appropriate.
- **Strategy 7:** Ensure schools are preparing food that comes in non-toxic packaging to prevent unsafe chemicals from leaching into otherwise healthy food.

Objective 2: Provide education for K-12 students on the importance and elements of a nutritious diet, including overeating, portion size and evidence of early life nutrition's impact on immediate health as well as long-term endpoints, such as the potential impact on breast cancer risk decades later.

Intervention Goal 2 (continued)

Invest in childhood nutrition and life-long healthy eating habits.

Objective 3: Ensure access to healthy food for adults in workplace and community settings, particularly foods that support breast cancer prevention.

- **Strategy 1:** Serve healthy food at workplace cafeterias and functions.
- **Strategy 2:** Develop community kitchens and meals that bring seniors together to cook and eat in community and provide healthy prepared food to take home with them.

Objective 4: Promote good gardening, nutrition and cooking education to support individual and family health.

- **Strategy 1:** Ensure that nutrition and cooking programs linked to food assistance programs, such as Women, Infant and Children (WIC) and CALFresh, offer culturally appropriate nutrition and cooking options and education.
- **Strategy 2:** Continuously improve outreach and education about the CAlFresh program to ensure access to everyone who qualifies and wants to use the program. See Transform CALFresh[135] to learn about current efforts.
- **Strategy 3:** Ensure immigrants both are able to and feel safe enough to access CalFresh if they desire.

Intervention Goal 3

Expand understanding and support for nutritious traditional diets of Native Californians.

Objective 1: Ensure food sovereignty for California's Native-American people by restoring and protecting food systems that support Indigenous self-determination, wellness, cultures, values, communities, economies, languages, and families, and that rebuild relationships with the land, water, plants, and animals.[136]

Objective 2: Support educational efforts for all Californians on the benefits of Native American traditional diets and the value of food as medicine.[137]

Intervention Goal 4

Encourage or require institutions to provide, and ensure universal access to, healthy food that can reduce breast cancer risk.

Objective 1: Require state agency and state-supported programs to adopt healthy food purchasing policies, such as the Good Food Purchasing guidelines.[138]

Objective 2: Require all University of California and California State University campuses to develop programs and services that address student food insecurity. See UC Berkeley's Food Pantry[139] or UC Irvine's Basic Needs Hub[140] as examples.

Objective 3: Encourage health care institutions to offer options to support healthy eating.

- **Strategy 1:** Work with Federally Qualified Health Centers to develop programs to make it easy for patients to access healthy food, for example, community supported agriculture[141] or culturally appropriate, affordable farmers markets.
- **Strategy 2:** Work with other major health institutions to promote healthy eating, including providing healthy meals in hospitals. See Kaiser Permanente's farmers markets[142] and California's Plant-Based Meals law (SB 1138)[143] as leading examples.

Intervention Goal 4 (continued)

Encourage or require institutions to provide, and ensure universal access to, healthy food that can reduce breast cancer risk.

Objective 4: Work with agricultural companies to develop worker food programs.

- **Strategy 1:** Provide incentives for farmers to provide their workers with access to surplus crops.
- **Strategy 2:** Develop programs for farmworker communities to have access to community gardens to grow supplemental food.

Objective 5: Require state correctional facilities to provide nutritious meals[143] to inmates and establish communal gardens to improve access to healthy food and teach job skills.[144]

Objective 6: Ensure the health of community food banks and food pantries while building economic opportunities to reduce people's reliance on food banks over time.

- **Strategy 1:** Ensure ongoing state funding[145] to support food banks.
- **Strategy 2:** Maintain or improve tax incentives for the California Food Bank's Farm to Family program[146] to continually expand access to fresh fruits and vegetables that food banks can provide to food pantries and other food assistance outlets.

Intervention Goal 5

Support research on the connection between diet, breast cancer risk, and systemic changes that result in people eating healthier diets.

Objective 1: Expand research to better understand the connection between diet and nutrition and breast cancer risk, including a focus on the impact of early life/adolescent diet and how diet interacts with other risk factors.

Objective 2: Expand and fund research on the most effective interventions to improve access to and consumption of healthy foods, including prospective cohort studies to gather data on improving healthy eating habits as it relates to breast cancer risk.

- **Strategy 1**: Study programs that promote eating healthy food options beginning during prenatal development and throughout the lifespan.
- **Strategy 2:** Collect longitudinal data on the effects of education on nutrition, school meal programs, school and community garden access, and other interventions specifically focused on lifelong eating habits to reduce breast cancer risk.
- **Strategy 3:** Increase funding to evaluate community food access and food justice efforts that seek to improve access to healthy food in underserved communities.

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Ionizing Radiation

Science Summary

Ionizing radiation is an established risk factor for breast cancer, and minimizing radiation dose to breast tissue is critically important, particularly in girls and young women.

What the Foundational Documents Say

The President's Cancer Panel Report, the Institute of Medicine (IOM) Report, and the IBCERCC Prioritizing Prevention Report all considered ionizing radiation an established risk factor for breast cancer. Evidence cited included increased risk of breast cancer associated with:

- Radiation exposure from the atomic bombings of Hiroshima and Nagasaki;
- Therapeutic radiation to the chest; and
- Radiation exposure to the breast associated with diagnostic imaging.

All three documents emphasize that minimizing radiation dose to breast tissue is critically important, particularly in girls and young women, but also in older women. All point out that, in the general population, the largest source of exposure to ionizing radiation is from medical diagnostic procedures, highlighting the need to ensure imaging studies are justified and optimized to use the least amount of radiation required for the clinical questions that are being asked, and to adjust the doses to patient requirements (for example, body size).

The President's Cancer Panel report further emphasizes the impact of radiation exposure from: air travel; work in the nuclear industry; and nuclear weapons production, use, and testing exposures to military personnel and civilians, as well as communities surrounding or downstream from testing and related activities. These exposures are largest in subsets of the population.

The documents also raised concern about exposure to naturally occurring radon gas in homes.

The Current State of the Evidence

The literature since 2012 has further cemented concern over ionizing radiation and breast cancer. Recent research has emphasized medical radiation and environmental contamination, whether through pollution or nuclear disasters.

Medical Radiation Exposures

Radiation exposures from diagnostic medical imaging have increased more than seven-fold over the last few decades.[1] The most recent National Council of Radiation Protection report suggests a slight decrease in the average annual exposure to medical imaging, mostly due to slight decrease in fluoroscopy. The largest contributors to radiation exposure from medical imaging are computed tomography and nuclear medicine. Over 85 million computer tomography (CT) scans are performed annually in the U.S., and thus a large number of women are exposed to CT-associated radiation.[2] Additionally, the radiation doses used for diagnostic imaging are highly variable across different facilities,[3] meaning some women will be exposed to far higher doses than medically needed. This contrasts with radiation exposure from mammography, which is standardized across facilities. The risks of breast cancer have shown to be elevated among women who are exposed to radiation from medical imaging.[4]

Recent research has continued to highlight the risks for later-life breast cancer in young girls treated with radiation therapy for childhood cancers. Treatment of hemangiomas with medical radiation has been shown to increase later-life risk[5] and particular concern has been raised for girls who undergo radiation treatment for cancers before age 15 or around puberty.[6] One study found an aggregate breast cancer incidence by age 40-45 of 13-20% for women treated with radiation as children—similar to BRCA mutation carriers (10-19% aggregate incidence by age 40) compared with 1-2% aggregate incidence by age 45 in the general population.[7]

Chest radiation, particularly in women treated for Hodgkin lymphoma around puberty (10-16 years of age), increases risk of breast cancer with risk increasing as early as eight years after the radiation exposure. Median time between radiation and diagnosis was found to be 15-20 years.[8] The authors of this study recommended that those treated with cumulative doses ≥20 Gy chest irradiation (a measure of the dose received) should undergo annual screening for breast cancer after age 25 or eight years after exposure, whichever comes last. They also stated that those treated with cumulative doses ≥10 Gy in fields affecting breast tissue should be counseled for similar surveillance.

Some concerns have been raised over the use of radiation in mammography screening for breast cancer. However, a large Norwegian study concluded that the risk of radiation-induced breast cancer and breast cancer death due to mammographic screening was "minimal." They estimated one radiation-induced death compared to 350 lives saved per 10,000 women (followed from ages 50-85) and a total lifetime risk of radiation-induced breast cancer of 10 per 100,000 women.[9] Mammography exposures to younger women who are BRCA mutation carriers and are screened regularly is concerning because of their increased risk of breast cancer. BRCA mutations are located in DNA repair genes, and women with these mutations are therefore more susceptible to DNA damage by ionizing radiation. One study found a 90% increased risk of breast cancer in BRCA1/2 carriers exposed to any diagnostic radiation before the age of 30, and advised the avoidance of ionizing radiation screening for young women with BRCA1/2 mutations, suggesting instead the use of magnetic resonance imaging (MRI).[10]

Nuclear Disasters

Researchers have studied survivors of the 1986 Chernobyl nuclear disaster. One study found up to three-fold increased breast cancer risk in survivors,[11] while another did not find a significant increase. The latter study concluded that breast cancer incidence had gradually increased in Ukraine and the regions near Chernobyl before and after the accident but that the breast cancer increase was not significant in contrast to data on thyroid cancer which had increased significantly.[12]

Recent research has found that male breast cancer is also elevated in survivors of atomic bombings in Japan. The authors suggest male breast cancer should be included in the IARC assessment of ionizing radiation and considered as an occupational cancer for which compensation can be claimed.[13]

Environmental Radiation Exposure

Environmental contamination from legacy radioactive pollution continues to be an issue as highlighted in the President's Cancer Panel report; however, little research specific to breast cancer has been published.

Looking at nuclear power plants in Taiwan, no significant difference was seen in breast cancer rates between plant-vicinity and non-plant-vicinity groups.[14]

A study looking at environmental radon exposure found increased exposure was not associated with breast cancer risk overall. However, women in the highest quintile of exposure (compared to the lowest quintile) had a suggested (non-significant) 38% elevated risk of hormone receptor negative tumors with no association seen for hormone receptor-positive breast cancer. The study also found a significant interaction between radon exposure and region of residence. In this case, women with high radon exposures residing in western regions of the U.S. had a 47% increased risk of invasive breast cancer compared to those with lower exposures (highest versus lowest thirds of exposure levels). In comparison, higher radon exposure was not associated with increased risk of invasive breast cancer in the Northeast, Midwest or South of the U.S.[15]

Studies in Iraq have concluded that the Gulf Wars of 1991 and 2003 left a legacy of pollution with radioactive depleted uranium from munitions in many regions of Iraq. The effects of these munitions may be causing the increase in cancers seen in these regions.[16] Given the strong connection between radiation and increase risk of breast cancer, more research focused on environmental exposures is needed.

Nuances and Emerging Considerations

In addition to its direct carcinogenic impacts, radiation can also interact with, and in some cases trigger or amplify, the impacts of other breast cancer risk factors. These include tobacco, chemicals or chemotherapeutic agents, and host factors such as age at exposure, gender or reproductive history.[17] For instance, studies in rats have shown that the effect of ionizing radiation can interact with exposures to chemical carcinogens and estrogen to cause additive or synergistic effects.[18,19]

Take-Home Message

- Ionizing radiation is an established risk factor for breast cancer.
- Minimizing radiation dose to breast tissue is critically important, particularly in girls and young women.
- Occupational exposures to radiation have decreased but worker protections must continue to be prioritized.
- Environmental contamination through legacy radiation pollution may contribute to increased risk of breast cancer.

Ionizing Radiation: Context for Interventions

Californians are exposed to radiation from a range of sources: some natural, some medical, some from military and industrial activity. Many exposures are medical necessities, however other procedures may be unnecessary. There has been a movement within the medical world to curb the use of radiation imaging, to both reduce exposures and curb health care costs.[20,21] Exposure to ionizing radiation cannot be totally avoided, but whenever possible, any unnecessary exposures to ionizing radiation should be eliminated.

Medical Radiation Exposures

Medical imaging—including x-rays, mammograms, CT scans and fluoroscopy—expose people to ionizing radiation. Mammography is currently the only area of medical imaging technology that undergoes close federal oversight as a result of the federal Mammography Quality Standards Act, established in 1992. The law set standards enforced through strict accreditation, certification and inspection of equipment and personnel at mammography facilities.[22] The law also requires assessment of physician performance, including measures of accuracy on interpretation.

CT scans are of the greatest concern for radiation exposure because of their higher doses and frequent use. Approximately one CT scan is performed per four individuals annually in the U.S., and the radiation dose is high for these examinations, up to 500 times the level of an x-ray radiograph.

CT scans are widely used across the population, including on children. There are no comprehensive standards or guidelines for how to set the radiation doses of CT scans. There is general agreement that doses should be as low as reasonably achievable, but there are no guidelines on how to do this and no organizations responsible for collecting information on CT scans and radiation exposure. This is a critical area for reform.

While medical imaging plays an important role in medical care, options to reduce the amount of exposure should be pursued. Only medically necessary imaging should be done and the lowest dose of radiation possible used; imaging equipment should be properly maintained and calibrated; and radiological technicians should be trained to minimize multiple procedures. When possible, ultrasound, medical resonance imaging (MRI), or an x-ray, should be used over a CT scan to reduce exposure to ionizing radiation.

Additionally, occupational exposures for the workers who administer various forms of medical imaging must be better

studied and addressed.[23,24] Fluoroscopy in particular exposes medical workers to higher levels of ionizing radiation,[25,26] though clinicians are not likely to be adequately trained in how to safely administer these techniques.[27]

Currently, patients are left to advocate for themselves on the need for imaging procedures, placing a great burden on people who generally have limited understanding of these technologies. Reforming and better regulating medical imaging holds great potential for reducing exposure to ionizing radiation. Studies on the most effective interventions are limited, and taking a multi-pronged approach (including policy, training, and quality control audits) may offer the greatest potential to reduce risk.[28,29] While standards should ultimately be set at the federal level, California has acted to limit exposure to medical radiation. In 2005, the state enacted Assembly Bill 929 (AB 929), Quality Assurance for Radiological Equipment, to require the California Department of Health Services to adopt quality assurance standards that include testing on all radiation-emitting equipment to ensure that the lowest possible dose of radiation is used without sacrificing imaging quality.[30] In 2010, California also led the nation on a bill (SB 1237) amending the Public Health Code to require reporting of the radiation dose used for CT to be included in the medical record.[31] However, no resources have been provided to analyze what these doses are and whether they are being reduced in association with this reporting requirement. California must continue to be a leader in setting standards for medical professionals and institutions to follow.

Minimizing Exposure to Medical Radiation

Medical patients need to be their own advocates. But when it comes to minimizing exposure to medical radiation, there is not simple path. The Centers for Disease Control and Prevention suggest that when it comes to medical imaging, doctors and radiation experts can help reduce your exposure to and risk of harm from diagnostic ionizing radiation by:

1. Checking to see if you have had a similar test done recently that can provide them with the background information they need;
2. Checking to see if a test that does not use ionizing radiation (for example, ultrasound or MRI) can provide similar information;
3. Making certain the least possible amount of radiation needed to obtain a good-quality image is used for your procedure.

Damage from medical imaging and all sources of ionizing radiation are thought to be cumulative over a lifetime. Patients should have a way to track the frequency, type, and radiation dose of all medical imaging, starting from birth. The University of California-San Francisco has created a website with information and tools to help people understand the doses of medical radiation to which they are exposed and approaches to try to limit those exposures where possible, including how to talk to their clinical providers about how to minimize their doses. Go to https://knowyourdose.ucsf.edu/ to learn more.

Nuclear Disasters

California is not immune to the impact of nuclear disasters, from within or outside the state. In 1959, a nuclear meltdown occurred in Ventura County at the Santa Susana Field Laboratory that went largely under-reported until decades later, when the Three Mile Island Nuclear Plant meltdown occurred.[33] Currently the only nuclear power plant still operating in California is Diablo Canyon Nuclear Power Plant near San Luis Obispo.[34] Due to concerns about its proximity to three fault lines,[35] it is scheduled to be permanently closed by 2025.[36]

Ionizing radiation knows no political boundaries. Nuclear disasters outside the state can and have affected California. Ionizing radiation from the 2011 nuclear disaster at the Fukushima Daiichi Nuclear Power Plant in Japan has reached California. In 2015 the National Academy of Sciences released a study indicating that Fukushima's radioactive plume had reached North American continental waters[37] and was detectable in marine life.[38] Traces of the radiation have been found in California's wine.[39] To date, the state's Department of Public Health reports that there are no health and safety concerns to California residents.[40] However, since no level of exposure to ionizing radiation is safe, global efforts are needed to eliminate nuclear risks and identify all other options to reduce or eliminate other exposures to ionizing radiation.

Environmental Radiation Exposure

Radon is a naturally occurring radioactive gas. Compared to many other parts of the country, California does not have consistently high radon levels, in part due to underlying levels of radon and in part due to the way houses are built, as they are less insulated than in colder parts of the country resulting in less trapped gas.[41] However, some areas in California, such as around Ventura County, have a potential for higher levels of radon exposure. People who live in these areas may want to get their house and, if relevant, water wells, tested. The Environmental Protection Agency's Radon Zone Map provides information on radon levels.[41] The California Department of Public Health has tips on how to get houses tested[42] and the Environmental Protection Agency has resources on what to do if radon is detected.[43]

Military and Industrial Sites: The Wall Street Journal identified 22 military and industrial locations in California that were at one time, and possibly still are, contaminated with residual radioactivity.[44] One site on the UC Berkeley campus, has been cleaned up. The rest are at different stages of remediation, though it is difficult to track all the statuses systematically as cleanup for these sites may be referred to a range of state and federal agencies. Many of these sites are located near highly populated areas, such as San Diego, San Francisco and Los Angeles, and near fault lines. Recent wildfires have raised concern about the burning of radioactive waste sites.[45,46]

INTERVENTIONS

Overarching Goal: Minimize, and where possible eliminate, exposure to all ionizing radiation, particularly in girls and young women.

Intervention Goal 1

Minimize exposure to ionizing radiation from medical imaging.

Objective 1: Minimize patient exposure to ionizing radiation from medical imaging.

- **Strategy 1:** Establish best medical practice that encourages the use of MRI, ultrasound, or other non-radiation technologies instead of x-ray mammography for routine surveillance of women at high risk for breast cancer, especially young women with the BRCA mutation. Require health insurance to pay for these procedures.
- **Strategy 2:** Promote public education on the risks and benefits of different medical imaging technologies and information on when to advocate for lower-risk options. Health institutions should encourage patients to use the UCSF Know Your Dose Website (http://knowyourdose.ucsf.edu).
- **Strategy 3:** Ensure full implementation and compliance with the Quality Assurance for Radiological Equipment law (AB 929) to ensure all medical radiological equipment in the state is properly maintained and calibrated to minimize exposures in medical imaging.
- **Strategy 4:** Fully implement the CT dose recording and analysis requirements of the California Public Health Code, including resources to analyze the data.
- **Strategy 5:** Require health care institutions to establish best practices for appropriate health care provider access to previous medical images to avoid duplicate imaging procedures.
- **Strategy 6:** Strengthen regulations requiring health care institutions to adequately train health care providers and technicians in how to administer medical imaging.
- **Strategy 7:** Strengthen regulations requiring that health care institutions adequately document lifelong exposure to medical imaging, including the dose of ionizing radiation used in each procedure, in medical charts.
- **Strategy 8:** Establish—and update as new technology becomes available—standards and benchmarks for appropriate radiation doses for different technologies as well as guidelines for when to opt for alternative lower radiation medical imaging. Priority should be given in establishing best practices for reducing the use and radiation dose of CT scans. Hold medical institutions accountable for meeting benchmarks. The California Medical Board should support efforts in these areas.[47]
- **Strategy 9:** Advocate for federal standards for all medical imaging that uses ionizing radiation to meet the same high standards as mammography.
- **Strategy 10:** Enact legislation that would require hospitals to calculate radiation doses adminstered and report anonymized data publicly.

Intervention Goal 1 (continued)

Minimize exposure to ionizing radiation from medical imaging.

Objective 2: Minimize occupational exposure to ionizing radiation from medical imaging (many of the recommendations that pertain to reducing patient exposure may also apply to occupational exposures).

- **Strategy 1:** Educate health care workers on the risks of medical imaging, especially fluoroscopy, which is especially high-risk for worker exposure to ionizing radiation.[26,27]
- **Strategy 2:** Train health care providers and technologists on appropriate use of medical imaging equipment, shielding, and other protective techniques for reducing radiation exposure and available alternatives that do not use ionizing radiation.[48,49,50]
- **Strategy 3:** Track lifelong exposures to ionizing radiation from workplace exposures.[24]
- **Strategy 4:** Hold employers and, where appropriate employees, accountable for meeting or exceeding standards and benchmarks for safer medical imaging.

Intervention Goal 2

Establish standards and best practices for all occupations where workers might be exposed to ionizing radiation. While each profession may have specific needs, some guidelines that apply to multiple occupations are listed here.

Objective 1: Redesign work and workplaces to eliminate use of ionizing radiation wherever possible and ensure proper storage, handling, processing, and disposal of radioactive substances, particularly where workers are in contact or proximity to those substances.

Objective 2: Provide the most protective shielding and protective equipment to minimize exposures.

Objective 3: Educate workers on the full potential impact of exposures to ionizing radiation, including risk from cumulative exposure over the course of a lifetime, and train them to minimize or eliminate exposures to the greatest extent possible.

Objective 4: Ensure comprehensive record keeping of workplace exposures and doses of ionizing radiation, creating records for individual workers that are transportable to other jobs over the course of his or her work life.

Intervention Goal 3

Clean up current or former military or industrial sites that are contaminated with radioactive waste.

Objective 1: Expedite remediation of sites with radioactive contamination across the state by dedicating adequate funding, setting enforceable deadlines, coordinating state and federal efforts, and ensuring transparency in the process and outcomes.

Objective 2: Require full transparency to residents, developers, and other interested parties of potential radioactive contamination in communities.

Objective 3: Ban residential and commercial development or the development of public spaces such as parks on or near sites contaminated with radiation without adequate cleanup.

Objective 4: Provide financial and logistical assistance to relocate businesses or individuals/families who currently live or work on contaminated sites.

Intervention Goal 4

Expand research to identify ways to reduce exposures to ionizing radiation.

Objective 1: Expand research to develop new, effective methods for detection of breast cancer that do not involve exposure to ionizing radiation.

Objective 2: Expand research on medical imaging to quantify doses, harms, and the effectiveness of approaches to lower those doses.

Objective 3: Expand research on interventions to reduce or eliminate worker exposures to ionizing radiation. Industries include aviation; health and science technology; health care, including nursing, radiological technology, radiology and certain medical specialties; laboratory work; nuclear power/nuclear fuel fabrication; fossil fuel extraction and refining; transport of radioactive materials; and other work with radiation.

Objective 4: Expand research on renewable energy technology and options to support California's commitment to addressing climate change without increasing pressure to expand nuclear power generation in the state.

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Light at Night

Science Summary

Light at night may affect breast cancer risk through circadian rhythm disruption and/or reduced melatonin production, which are influenced by shiftwork, exposure to artificial light at night, and sleep duration.

What the Foundational Documents Say

The International Agency for Research on Cancer (IARC) considers night-shift work a probable human carcinogen.[1] Carcinogenic effects are most likely through circadian rhythm disruption and suppression of melatonin. Studies reviewed in the foundational documents have shown increased incidence of breast cancer in those exposed to artificial light at night and those working night shift. Variations in exposure, duration of shift work, and effect on breast cancer incidence exist.[2]

The Current State of the Evidence

The circadian rhythm is a natural cycle that influences cell processes. The natural 24-hour cycle of light and dark in a day provides for synchronization of our circadian rhythms. One's circadian rhythm affects the production and release of hormones, like melatonin, and gene expression which can influence breast cancer risk.[3]

Artificial Light at Night

Artificial light at night is a concern for circadian disruption. A study of 164 countries found that those with the highest light at night exposure had a 30-50% higher risk of breast cancer.[4] A nationwide study in the United States showed a 14% increase in risk of breast cancer in areas identified as the top quintile of outdoor light at night. A 5% increase in breast cancer was associated with each interquartile increase of 31.6 units of radiance (nanoWatts/centimeter square/steradian) of cumulative outdoor light at night.[5] Similar results showing an association between exposure to outdoor light at night and breast cancer risk were demonstrated by studies in Georgia,[6] California,[7] and Connecticut, U.S.;[8] South Korea;[9] and Madrid and Barcelona, Spain.[10] The type of outdoor illumination may matter, with night light in the blue spectrum[10] and light from strong illumination sources resulting in increased incidence of breast cancer.[11]

Artificial light indoors that is not related to working night shift may also be a risk factor, though studies are limited. One study showed some indication between breast cancer risk and keeping the lights on while sleeping, sleeping during the day, and leaving the curtains open, but results were not significant.[12] White, et al.'s 2017 study used data gathered through the large Sister Study cohort, which also showed an association between leaving the lights or television on while sleeping and a higher risk for ER+ breast cancer.[13]

Night-Shift Work

Night-shift work has been described as the most disruptive factor to the circadian rhythm.[14] A meta-analysis of 13 studies found a 48% increase in the risk of breast cancer among airline cabin crews and other night-shift workers.[15] A combined analysis of studies from Australia, Canada, France, Germany, and Spain showed an increase in risk for ER+ breast cancer for pre-menopausal, but not post-menopausal, women who had ever worked night shift of at least 3 hours. The risk was increased for women who worked night shifts of greater than 10 hours and for women who worked three or more night shifts per week, with the greatest effects for women who worked 3 or more hours a week for at least 10 years. Two years after termination of night-shift work, risk for developing breast cancer was significantly reduced compared to women still actively enaged in night-shift work.[16]

Results varied based on the duration of night shift. A large cohort study in Denmark found no association between breast cancer risk and fewer than six years of night-shift work.[17] An increased association between breast cancer and working at least six years in a night-shift position was found in a study of the Danish military, with increasing risk associated with increased years of night-shift work.[18] In Sweden and Germany, studies showed an association between working night shift for more than 20 years and risk for breast cancer.[19,20] This was also found in Canada, where an increased risk of breast cancer was found with a duration of night-shift work of 30 or more years.[21] A Spanish study showed a positive dose-response relationship between cumulative night shifts and risk for breast cancer.[22]

Rotating shifts also resulted in increased risk. A study in Western Australia found a 22% increase in breast cancer risk associated with working phase shift, which includes day and night shifts.[23] Long-term rotating day and night shift was classified as the most disruptive and resulted in a higher risk, based on a case-control study of Danish nurses.[24]

A population-based prospective cohort study in China found no association between working night shift and breast cancer, even accounting for duration, frequency, and cumulative time.[25] A meta-analysis of 10 studies showed no association between night-shift work and breast cancer, including those with a long duration.[26]

Sleep Duration

Sleep duration and characteristics were evaluated for association with breast cancer with widely varied results. The Sister Study, a large prospective cohort study, found that sleep duration had little association, yet women who reported difficulty sleeping four or more nights a week were at an overall increased risk for breast cancer.[13] A small case-control study found that not getting adequate sleep, or less than 6 hours a night, was highly associated with breast cancer.[27] However, a meta-analysis of six studies found no association between sleep duration and breast cancer risk.[28]

Risk may also vary by hormone receptor status of breast cancer tumors. Data from the Breast Cancer Detection Demonstration Project showed no association between sleep duration and overall breast cancer risk. This study did, however, find a decreased risk of ER+PR+ breast cancer and an increased risk of ER-PR- breast cancer, with shorter duration of sleep (less than 6 hours), although results were not statistically significant.[29] Another study found that Black women who slept for less than 8 hours nightly were at an increased risk of ER-PR- breast cancer.[30] Women who had the least sleep variability were found to have mean estradiol levels that were 60% lower. Estradiol may increase the risk for breast cancer because of higher lifetime exposure to endogenous estrogens.[31]

Melatonin

Melatonin is a hormone related to the circadian rhythm. Typically, there are higher levels of melatonin at night as a natural aspect of the sleep-wake cycle. Melatonin may act directly to reduce the risk of breast cancer by halting the spread of cancer and growth-inhibitory mechanisms, or indirectly by regulating reproductive hormones, including estrogens.[32]

Several studies have used 6-sulfatoxymelatonin (aMT6s), a melatonin metabolite present in urine, to measure levels of melatonin. A study of night-shift workers demonstrated that they have lower levels of melatonin (as measured by aMT6s) during both daytime sleep and nighttime sleep on off-days. Among these workers, levels were 62% lower during daytime sleep, and 42% lower when they slept at night on off-days, when compared with day-shift workers.[32] In a meta-analysis of five studies, an increase of 15ng/mg urinary aMT6s was associated with a 14% reduced risk of breast cancer.[28] The Nurses' Health Study also found that higher levels of aMT6s were associated with lower risk of overall breast cancer.[33] Several large prospective studies cited in a literature review also showed this association.[34]

Nuances and Emerging Considerations

Race and Ethnicity

A large study in Georgia found an increase in breast cancer risk related to light at night for White but not Black women. The researchers discuss the possibility that eye pigmentation may affect sensitivity of melatonin production to light suppression.[6] Asian night-shift workers were found to have less disruption of melatonin levels than their White co-workers. On off-nights, White night-shift workers averaged a 47% reduction in melatonin, measured by 6-sulfatoxymelatonin (aMT6s) urinary levels, whereas Asian night-shift workers only had an 18% reduction. This suggests that Asian shift workers may be at reduced risk for cancer related to shift work.[35]

Time Zones

Circadian disruption and subsequent higher breast cancer risk was associated with being in the western part of a time zone in 11 U.S. states. This association may be caused by the mismatch of circadian rhythms (set by environmental time—sunrise, solar noon, sunset) and time zones, leading to increased exposure to light later in the day.[36] A study of flight attendants showed a positive exposure response between time zones crossed and breast cancer risk in women with three or more children, although this was a small subset of the flight attendant population.[37]

Gene Expression

Researchers are studying how light at night can influence gene expression. Phosphodisterase 6 (PDE6), a protein found in the eye that plays a role in the transduction of light (converting light that hits the eye into neural activity), and genes that control circadian rhythm were found to be expressed in breast cancer tissues.[38] One study found an association between genetic variation of circadian gene pathways and the risk for post-menopausal breast cancer.[39] However, another study found no association between single-nucleotide polymorphisms in circadian genes and breast cancer.[21] Steroid receptor-negative human breast cancer xenografts growing inside rats showed that circadian rhythms and melatonin regulated the uptake of linoleic acid (an essential fatty acid) and oxidative and proliferative actions. Exposure to dim light caused a reduction in melatonin that inhibited these rhythms, causing increased tumor growth and metabolism.[40]

Interactions

Circadian disruption may increase other risk factors for breast cancer. Urinary levels of 8-isprostane, a marker of oxidative stress, were found to be 8.2% higher in women with less than 6 hours of sleep, when compared with those getting more than 8 hours of sleep per night. Levels were 25.5% higher in women working night shift than in those working day shift.[41] Women that worked night shift for more than 15 years had 25% higher mean breast density than those who had never worked night shift.[42] A German case-control study identified that this population—night-shift workers—were more likely to be nulliparous.[20] Stress, breast density, and parity are identified risk factors for breast cancer.

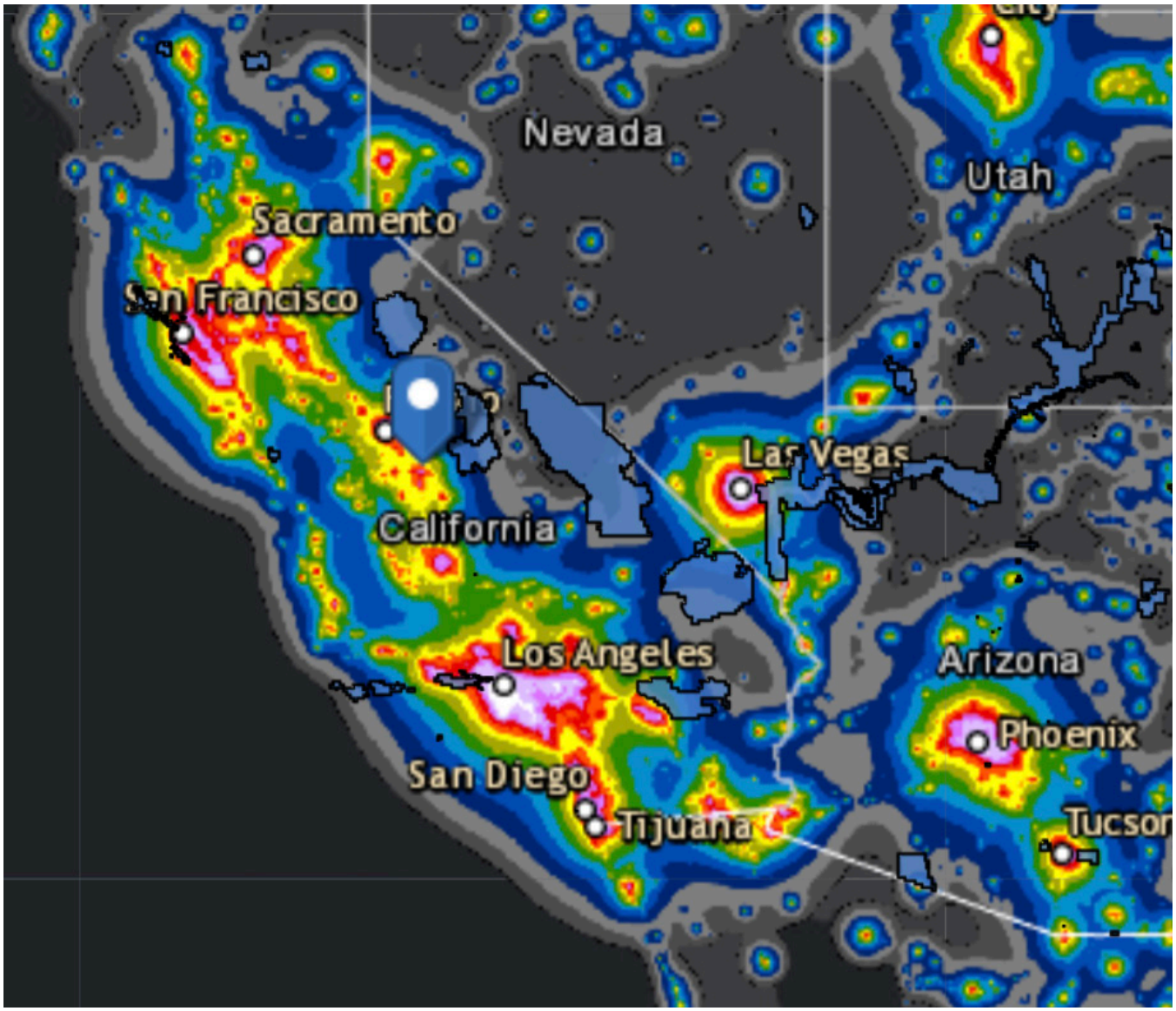
Take-Home Messages

- Circadian-rhythm disruption and melatonin suppression are linked to breast cancer risk.
- Exposure to outdoor and indoor light at night at home or in the workplace can increase breast cancer risk.
- Long-term night-shift and rotating day/night-shift workers are at a greater risk.

Light At Night: Context For Interventions

People can be exposed to light at night in a wide range of ways. In some cases, reducing these exposures is as simple as turning off the lights or TV. In other cases, it requires addressing a range of issues that impact people's work and the way our society functions. The New World Atlas of Artificial Night Sky Brightness[43] shows the extent and intensity of light pollution around the globe, with the Light Pollution Figure that follows, showing where light at night is especially intense in California.

Figure 6. Light Pollution in California[43]



Occupational Light at Night

A significant of concern is shift work. Unfortunately, there is limited data on how many people work night shifts. The U.S. Department of Labor Bureau of Labor Statistic's most recent data are from 2004, when it was estimated that approximately 15 million people in the U.S. work evening, night, rotating, or irregular shifts.[44]

Shift workers play important roles in our society and economy, but many people working these night shifts are economically disadvantaged. The Urban Institute estimates that 60% of all workers with nonstandard schedules have earnings below the median of the typical American worker, and 40% have earnings that are lower than those of 75% of all workers.[45] Shift work can also be a source of stress from family conflict[46] because of the difficultly connecting, sharing responsibilities, caring for children and other issues.

California faces the specific challenge of increasing emphasis on agricultural work at night.[47,48] This is not a new practice, but it is expected to grow as climate change leads to elevated daytime temperatures. Balancing the different concerns of risk of heat exhaustion or stroke from daytime field work and risks from working in evenings and nights—exposure to artificial light at night, risk of accident from reduced visibility, potential for increased risk of sexual assault, and other concerns—is complex. CalOSHA is considering standards for night-time agricultural work, though the effort is not currently considering breast cancer risk from exposure to light at night.[48,49]

Without significant changes to our economy, California can expect to continue to have night-shift workers for the foreseeable future. As a result, it is important to focus on a range of possible mitigation efforts that can at least reduce the risks from exposure to occupational light at night.

Ambient Light at Night

As the map above indicates, considerable light pollution exists where people live in high concentration. Streetlights, office buildings, stores, and other facilities are significant sources of ambient light. In some areas, factories, packaging and shipping depots, and other businesses that run all night often have bright lights shining outdoors. Many people live near highways. All of these sources of light can be mitigated through implementing best practices and/or changing city and county ordinances for lighting.

Additionally, people are often exposed to light at night in their houses. See Personal Tips for Reducing Risk of Exposure to Light at Night for details.

Community Input on Light at Night

Community members were surprised to learn about the link between light at night and breast cancer risk. Participants identified a wide range of possible ways that this impacts their lives. Very few women in the listening sessions personally worked night shifts, but they were concerned for their larger network of friends and family who did, and some noted living near facilities that operate overnight with bright lights. Importantly, many women

understood that they could change some personal practices immediately, such as not falling asleep with the light or television on, using sleeping masks, or using blackout curtains, but these actions were not adequate to address the problem as a whole.

Personal Tips

Whenever possible, people should take personal action to reduce light at night exposure or its impact. Some actions individuals can take include:

- Get outside during the day. The more daytime sunlight people get, the more they can offset the impact of exposure to light at night.[49]
- Turn off screens (TV, smart phones, tablets, etc.) at least 2 hours before bedtime.
- Take advantage of "night shift" display options on devices,[50] and if buying new devices, check to see if this option exists before purchasing.
- Sleep in as dark a room as possible by using blackout curtains, a sleep mask, or other means to block out light.
- If you need to use lights at night, consider using red light bulbs.
- If possible, maintain a regular schedule of activity and rest, going to sleep and waking up at the same times each day.

INTERVENTIONS

Overarching Goal: Reduce breast cancer risk by eliminating all unnecessary exposure to circadian rhythm-disrupting light at night and promote action to mitigate the impact when it cannot be avoided.

Intervention Goal 1

Increase worker awareness of these issues. Develop workplace policies, with worker involvement, to reduce, eliminate, or mitigate unnecessary exposures to light at night.

Objective 1: Develop and implement interventions to reduce the impact of light-at-night exposure for workers.

- **Strategy 1:** Develop workplace policies that allow workers to voluntarily reduce their night-shift work without putting workers at risk of losing their job or lowering their income.
- **Strategy 2:** Develop workplace policies that limit the number of night shifts people work per week, the number of consecutive night shifts, and possibly the maximum number of years of night-shift work. More research is needed to determine the specific recommendations as it relates to breast cancer (see Intervention Goal 4).
- **Strategy 3:** Change shift cycles to be less disruptive. Examples include creating a 3 p.m.-to-3 a.m. shift so that it is dark when workers return home;[51] creating a forward rotation schedule where the shifts start at different times each day—for example, day one starts in the daytime, day two starts in the evening, and day three starts at night;[54,52,53,54,55] providing at least 11 hours off between shifts to allow for rest;[56] and offering workers self-scheduling options so they can control when they rest.[56]
- **Strategy 4:** Wherever possible, switch to dim lighting and/or red lighting[54] in work areas that do not require strong, bright light to be effective and/or safe. In agricultural settings, develop policies that balance the need to work at night to escape extreme heat with enough light to avoid accidents and maintain safety, with the goal of minimizing the potential increased breast cancer risk presented by light at night.
- **Strategy 5:** Wherever possible, minimize or eliminate the use of blue-wavelength lighting and/or provide protections such as taking breaks, offering glasses/goggles that protect from blue light, or providing screen filters for computers or other devices.
- **Strategy 6:** Where appropriate, provide safe, dark spaces for naps.
- **Strategy 7:** Establish 24-hour childcare at workplaces (wherever possible) to reduce the number of young mothers who work permanent night shift because of difficulty finding childcare providers who can accommodate changing shift-work schedules.[56]

Objective 2: Provide clear education to workers on the risk of light at night exposure and ways to reduce its impact.

- **Strategy 1**: Incorporate education on the risks of exposure to light at night into nursing and medical curriculum so health-care providers are educated before they start their careers.
- **Strategy 2**: Provide on-the-job training for health-care providers on the link between light at night and breast cancer, and encourage them to share the information with people who work night shifts.

Intervention Goal 1 (continued)

Increase worker awareness of these issues. Develop workplace policies, with worker involvement, to reduce, eliminate, or mitigate unnecessary exposures to light at night.

- **Strategy 3:** Offer training and educational materials to workers about the link between light at night and breast cancer risk, with a special emphasis on providing examples of actions they or their employers can take in the workplace to reduce the risk. Also provide education and support for workers to develop healthy sleep habits when off the job.
- **Strategy 4:** Educate union leadership on the connection between light at night and breast cancer risk and how to mitigate those risks, so they are prepared to support workers' requests for protection.

Objective 3: Encourage and promote exposure to daytime natural light, which can offset the harm of exposure to light at night.[57]

- **Strategy 1:** Educate people, especially people who work night shifts, about the benefit of exposure to daylight, and encourage them to seek it out at times appropriate to their optimal sleep schedule.
- **Strategy 2:** For indoor workers, position people near windows and/or skylights as much as possible.
- **Strategy 3:** Maximize design options for access to natural light in new construction or during remodeling.[58,59]
- **Strategy 4:** Where possible, give workers access to rooftops, patios, or other outdoor spaces for breaks and provide items that draw people to use the spaces, such as seating, tables, plants, fountains, etc.
- **Strategy 5:** Encourage meetings to take place outdoors or near windows, and, where possible, encourage people to host walking meetings.

Intervention Goal 2

Reduce or, where possible, eliminate light at night where people live.

Objective 1: Design public lighting to minimize impact on residential areas.

- **Strategy 1:** Replace outdoor lights with those that are only as bright as necessary, only light the area necessary, are shielded to minimize glare,[60] and, when appropriate, have motion sensors to turn on only when people are in the area.
- **Strategy 2:** Adopt city- or county-wide model lighting ordinances[61] which set standards that reduce glare, light trespass, and skyglow (brightness of the sky due to light pollution).[62] The city of Borrega Springs, the only designated "Dark Sky Community" in California, provides a model.[63]

Objective 2: Support individuals in reducing their exposure to municipal light at night.

- **Strategy 1:** City and county health departments should provide educational materials in health clinics and at public education and outreach events on the dangers and protective actions related to light at night.
- **Strategy 2:** City and county health departments should offer free or reduced-price blackout curtains for people living in areas with extreme municipal lighting.
- **Strategy 3:** Make free blackout curtains and/or sleep masks available to people living in public housing where light at night is an issue.

Intervention Goal 3

Expand research on the connection between light at night and breast cancer, as well as possible interventions and their effectiveness.

Objective 1: Support research on the etiology of how light at night increases breast cancer risk.

Objective 2: Support epidemiologic research that measures the specific quantity and quality of light and its connection to breast cancer and other health impacts.

Objective 3: Support research to identify the most effective interventions to reduce breast cancer and other health risks from light at night, including optimal shift-work patterns, particularly for industries that rely on shift work, such as health-care, public safety, and emergency services, and manufacturing.

Objective 4: Support research into ways to limit outdoor light pollution from industries that function at night, such as warehouses, refineries, and ports; options for municipalities and residents to reduce outdoor light; and other ways to reduce the impact of exposure to light at night generally.

Objective 5: Support research that identifies practices and technologies to eliminate all unnecessary sources of light at night in the workplace, municipal uses, and home use (such as computer and TV screens), and/or reduces the risk from these exposures.

Objective 6: Support research to develop outdoor lighting that balances offering warmer light spectrum while maximizing energy efficiency, as well as the minimum amount and location of light that still ensures public safety.

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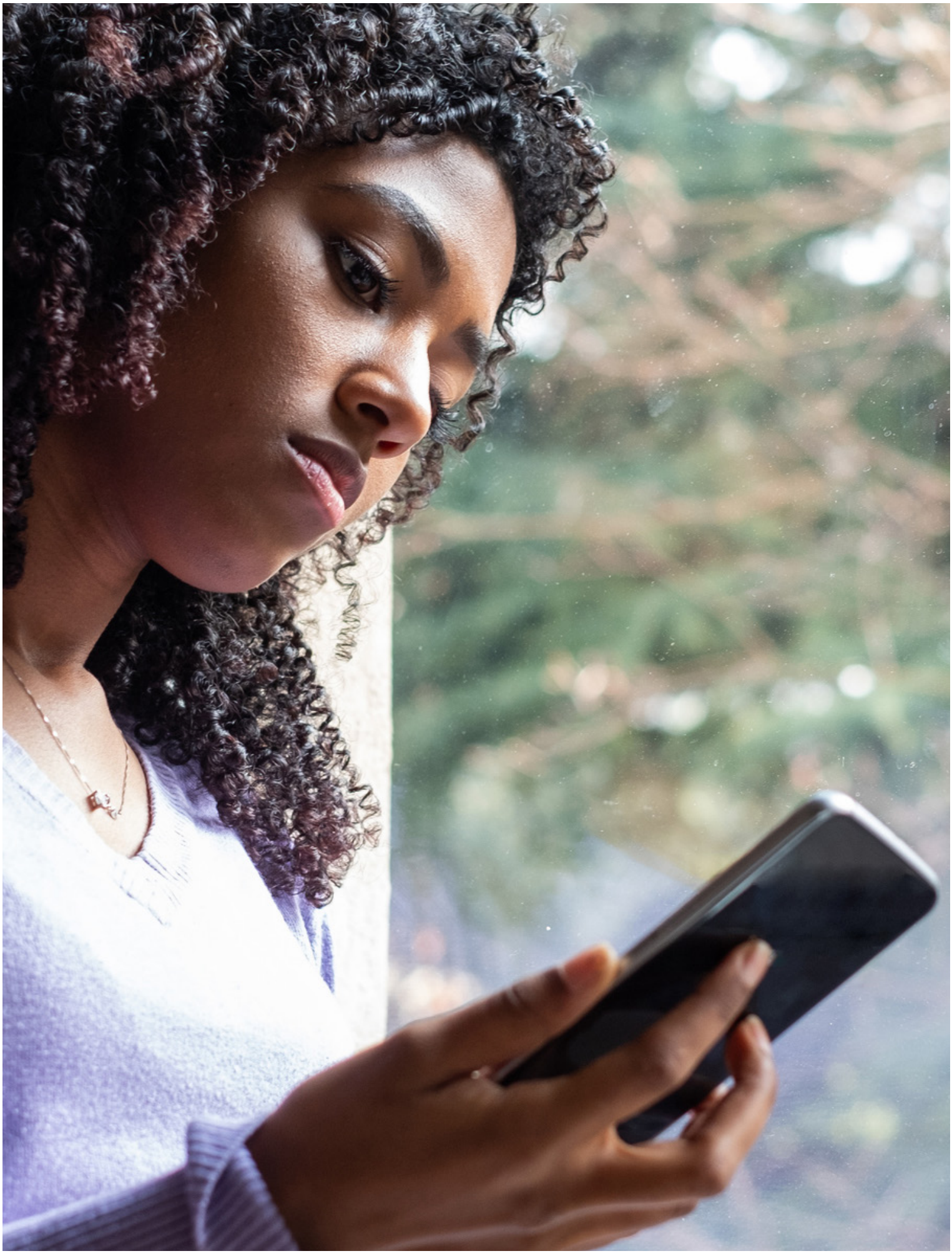


Non-Ionizing Radiation

Science Summary

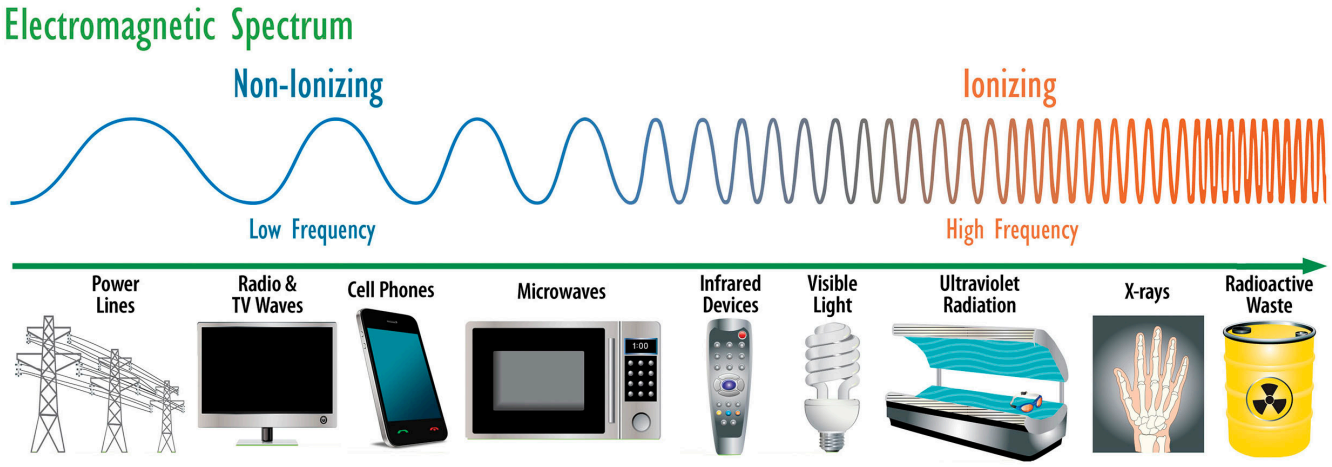
Research on non-ionizing radiation and breast cancer has yielded mixed results. Currently radiofrequency (cellphone) radiation does not appear to be linked to breast cancer although more research is needed on modern 4G and 5G technologies. High chronic occupational exposures to extremely low frequency electromagnetic fields (ELF-EMF—from power lines and electrical appliances) may be associated with increased risk of male breast cancer. Exposure to high ELF-EMF may be linked to increased risk of pre-menopausal breast cancer, but more studies are needed that directly measure radiation exposure.

Background

Non-ionizing radiation exists along a spectrum of frequencies, with radiofrequency radiation (RF) and extremely low frequency electromagnetic fields (ELF-EMF) being two kinds of non-ionizing radiation to which people can be regularly exposed. RF is emitted by cellular and cordless phones, cell antennas, Wi-Fi antennas, radar, and broadcast transmission towers while ELF-EMF is emitted by electric powerlines and from electrical appliances.

The International Agency for Research on Cancer (IARC) has evaluated ELF-EMF and RF and concluded that radiofrequency electromagnetic fields (RF-EMF) were "possibly carcinogenic to humans (Group 2B)"[1] on the basis of limited evidence of an increased risk of glioma. ELF-EMF were evaluated as "possibly carcinogenic to humans (Group 2B)"[2] based on limited evidence of an increased risk of childhood leukemia.

Figure 7.



Source: https://www.niehs.nih.gov/health/topics/agents/emf/index.cfm

What the Foundational Documents Say

As for research on possible links between non-ionizing radiation exposures and risk of breast cancer, both RF and ELF-EMF were addressed in the President's Cancer Panel report. It concluded that there were no consistent or conclusive data on the cancer risk due to RF exposures, despite considerable research. With ELF-EMF, the report did not mention a link to breast cancer but cited conflicting evidence of a link between living near electric power lines and childhood leukemia.

The IOM report and the CBCRP Gaps (2013) document addressed only ELF-EMF. They both reported inconclusive data on increased female breast cancer risk from ELF-EMF exposure. The IOM noted no association between risk of breast cancer and ELF-EMF exposure from household exposures and appliances, including electric blanket use (once raised as a source of concern). Both reports pointed to occupational ELF-EMF exposure as a potential factor among men with breast cancer but highlighted that results are mixed with some studies in the early 1990s finding an association but later studies finding no relationship. The IOM recommended further research on occupational exposure to ELF-EMF and male breast cancer as well as potential effects of timing of exposure through the life course on breast cancer risks.

The Current State of the Evidence

RF/Cellphone Radiation

Concerns about cancer risk associated with RF exposures from cell phones have mainly focused on brain cancers and other tumors of the head and neck.[3] There has been very little research examining possible effects of RF exposures on breast cancer risk. In an evaluation of a purported cancer cluster in a neighborhood near a cell phone base station, no increased risk for developing breast cancer was found.[4] A single case-control study in the Central African Republic looking at behavioral factors and breast cancer reported an increased risk when cellphones or

money were kept in bras, as well as increased risk associated with several dietary and behavioral factors.[5] A case study report from California reported on four young women who developed breast cancer after regular prolonged habit of carrying their cellphones in their bras.[6] Given the very small number of patients, more research is needed to ascertain if this is a real effect.

A lab study that looked at breast cancer cells exposed to sources of mobile phone and Wi-Fi frequencies at different distances found increased oxidative stress, apoptosis (cell death), and overload of intracellular calcium ions (Ca2+) when sources were within 10 cm (4 inches) of the cells. The authors suggested that using cellphones and Wi-Fi sources more than 10 cm away could mitigate against these effects.[7]

ELF-EMF/Magnetic Fields

More studies have examined ELF-EMF and magnetic fields and breast cancer risk.

Looking at environmental exposures (power transmission lines, power equipment, and appliances), results have been mixed. Some studies have found no excess risk from living near power lines.[8] However, two meta-analyses of 23 and 16 case-control studies, respectively, found up to 10% increased risk of breast cancer overall with increased exposure. When the results were stratified by menopausal status, the effect of increased exposure was limited to pre-menopausal breast cancer.[9,10] No other associations were seen, and the authors pointed to the need for better epidemiological studies incorporating more accurate exposure assessment.

A third meta-analysis of 42 global studies found conflicting results from European and U.S.-based research. The authors concluded that there was a slight increased risk for pre-menopausal breast cancer but only in studies where exposures were measured directly. Again, they called for future epidemiology studies to include direct measurement of exposures.[11]

Looking at occupational exposures of women, overall data do not suggest that occupational exposures to non-ionizing radiation increase risk of breast cancer in women.[12,13,14]

For male breast cancer, a meta-analysis of 18 studies published from 1991-2005 found a significant 30% increase in risk of male breast cancer with EMF exposure.[15] However a more recent (2016) study in Canada found no clear association between occupational magnetic field exposure and male breast cancer.[16]

Nuances and Emerging Considerations

Interaction with Other Agents

Lab experiments with animals have indicated that exposure to ELF-EMF may increase mammary tumor incidence when exposure is in combination with other carcinogenic agents.

One study found that rats exposed to 0.1 Gy of gamma-radiation (ionizing radiation) plus a magnetic field of 1000μT (micro Teslas) had a significantly increased incidence of mammary adenocarcinomas than rats exposed to 0.1 Gy of gamma-radiation alone.[17]

Other studies of lifetime exposures of Sprague Dawley rats to ELF-EMF continuously or intermittently found increased mammary tumors for EFL-EMF in combination with formaldehyde or acute low-dose gamma-radiation but not with ELF-EMF alone. The authors pointed to a possible role of ELF-EMF as a cancer enhancer in the presence of other chemical and physical carcinogens.[18]

Changes in RF Radiation Exposures

Cell phone radiation exposures are changing rapidly as new generations of the technology develop—in less than 30 years, cellular networks went from 2G[19] to 3G and 4G[20] to 5G,[21] with large changes in the bandwidths and frequencies of the RF used.[22] Current research looking at possible impact on cancer incidence has focused on 3G frequencies, and research on the more modern bandwidths and frequencies has not yet been undertaken. More research is needed to ascertain the health impacts, including breast cancer risk, of these bandwidths and frequencies, while recognizing that these newer technologies will soon be surpassed by updated generations of cellphone capabilities.

Difficulties in Epidemiological Research

Due to the ubiquity in cell phone use globally, it is challenging to conduct high quality studies of health effects because of the lack of a control (unexposed) population.

Take-Home Message

- Although links have been made between RF and other types of cancer, studies are insufficient to draw any conclusions about potential links between RF radiation and breast cancer. More research is needed on modern 4G and 5G technologies.
- High chronic occupational exposures to ELF-EMF may be associated with increased risk of male breast cancer. More research is needed to examine the link between occupational exposures and female breast cancer.
- Exposure to high environmental ELF-EMF may be linked to increased risk of pre-menopausal breast cancer, however more studies are needed that directly measure radiation exposure.

High chronic occupational exposures to ELF-EMF may be associated with increased risk of male breast cancer.

Radio Frequency Radiation: Breast Cancer Risk is Unclear, but Other Risks Exist

Concerns about RF (especially cellphone) radiation and health effects have been raised for many years and numerous research studies are considering and expanding the scientific literature in this area. As noted above, a link to breast cancer has not been clearly established though more research is needed, including on modern 4G and 5G technologies. This is reflected in the intervention goals and objectives for breast cancer prevention below.

There is some evidence of associations for 2G and 3G radiation with other cancers. Epidemiology studies of human populations have mostly looked at the incidence of gliomas (brain cancers), acoustic neuromas (benign tumors in the cells of the nerve responsible for hearing—also known as vestibular schwannomas), meningiomas (usually benign tumors in the membranes that cover and protect the brain and spinal cord), and parotid gland tumors (tumors in the salivary glands).[23] These studies have not shown a consistent or clear association of cellphone radiation and these cancers, though individual studies have shown some associations for subgroups of people—including those under 20 years of age and people who used cellphones for more than ten years. However, a number of studies have looked further at these subgroups and not found associations.[23]

In 2018, the National Toxicology Program (NTP) published the results of a long-term laboratory study of 2G and 3G radiation exposure of rodents. That study found that high exposure to 900MHz RF radiation (in the range of 2G and 3G phones) was clearly associated with tumors in the hearts of male rats (malignant schwannomas), with some evidence of association with tumors in the brains of male rats (malignant gliomas) and tumors in the adrenal glands of male rats (both malignant and benign). There was no clear association of RF radiation with tumors in female rats or male or female mice.[24] In an extension of this study, brain structures involved in cognition and memory showed DNA damage, although the mechanisms underlying this result are currently unknown.[25]

NTP is currently evaluating the existing literature on the higher frequencies intended for use in the 5G network and is working to better understand the biological basis for the cancer findings reported in these studies with 2G and 3G technologies.

The cancer-inducing results of RF exposure in the NTP study were replicated in a large study, exposing rats to RF radiation from prenatal time through natural death.[26]

Tips for Individuals and Public Health Educators

More research is needed to determine the extent of the breast cancer impacts of non-ionizing radiation exposure of existing and future cellphone and wireless technologies. However, given the associations with other cancers seen in sub-populations in some studies, precautionary measures to reduce exposures may be warranted and are easily undertaken:

1. For Individuals

- Avoid carrying powered on cellphones next to your body, including in your bra. RF exposures decrease exponentially with distance.
- Use earbuds/microphone or other equipment (e.g., speaker phone or headset) so that you don't hold the phone next to your head when on a call.
- Minimize use of cellphones by children.
- Send texts instead of calling by cell phone when possible.
- Don't sleep with a cellphone near your head.
- When possible, do not use smartphones to download large files or stream videos. If you do these things, keep the phone away from your body.

For more ideas and further exploration of ways to reduce your exposure to RF, see the California Department of Public Health advice on reducing exposure: https://www.cdph.ca.gov/Programs/CCDPHP/DEODC/EHIB/CDPH%20Document%20Library/Cell-Phone-Guidance.pdf

2. For Public Health Educators

- Develop and support messaging to be used by physicians, especially pediatricians and general practitioners, about potential risks of holding phones close to their heads and wearing cell phones in pockets or bras.
- Develop and support similar messaging for K-12 teachers of health and science classes.
- Support PSA materials that draw from cell phone company manuals that advise against using cell phones close to the body.

Non-Ionizing Radiation: Context for Interventions

Exposure to non-ionizing radiation is widespread in California, affecting nearly all residents. While the evidence linking it to breast cancer risk is inconclusive, many people none-the-less express concern about risk in general and breast cancer risk specifically. Primary exposures of concern come from cell and smartphone use, wireless intensification, close proximity to 4 and 5G antennas/facilities, electric transmission (e.g. power lines), and certain occupational exposures.

Cell and Smartphones

In 2017, the California Department of Public Health issued guidelines on how to reduce exposure to radio frequency energy from cell phones. They stated, "Although the scientific community has not reached a consensus on the risks of cell phone use, research suggests long-term, high use may impact human health."[27]

While data on cell phone use is not available specifically for California, the Pew Research Center estimates that 96% of people in America own a cellphone of some kind, and that smartphone ownership is now 81%, up from 35% when they surveyed in 2011. Ownership was not equal but was still quite high across genders, income and education levels, races, and rural/suburban/urban use. In other words, cellphones, and increasingly smartphones, are ubiquitous.[28] Common sense measures to reduce exposure make sense, even if the science remains inconclusive about the link between cell phone use and breast cancer.

Inequities in broadband access are leading more people to use their smartphones for their high-speed internet access,[29] which can increase the exposure to RF with some high intensity uses.

Electric Transmission

California has thousands of miles of electricity transmission and distribution lines, reaching far and wide into residential, industrial, and rural areas.

In response to public concern over ELF-EMF exposures from utility transmission and substation projects, the California Public Utilities Commission (CPUC) has taken some actions to address ELF-EMF concerns.[30] Seven measures were ordered in the CPUC's November 1993 decision and affirmed in the January 27, 2006 decision:

- No-cost and low-cost steps to reduce EMF levels: When regulated utilities design new projects or upgrade existing facilities, approximately 4% of the project's budget may be used for reducing EMFs. The CPUC did not set specific reduction levels for EMFs.
- New designs to reduce EMF levels: The CPUC's Advisory and Compliance Division and Safety Division held workshops for utilities to develop EMF design guidelines for new and rebuilt facilities. The guidelines incorporate using alternative sites, increasing the size of rights-of-way, placing facilities underground, and using other suggested methods for reducing EMF levels at transmission, distribution, and substation facilities.

- Measurement of EMFs: Uniform residential and workplace EMF measurement programs were also designed in the workshops; they are available to utilities and their customers. Other utility companies are also encouraged to use them.
- Education and Research: The CPUC wants the public and groups having a financial or basic interest in EMFs to become involved in developing education and research programs. These programs are established and managed by the California Department of Public Health (CDPH). CPUC-regulated utilities and municipal utilities use ratepayer funds to pay for their share of development costs for the following programs:

  a. EMF Education: This $1.49 million program will provide credible, meaningful, consistent, and timely EMF information to electric utility customers, employees, and the public. CDPH will coordinate a uniform EMF education program to supplement, but not duplicate, those that most electric utilities already have. Utilities without programs are expected to implement one as soon as possible.

  b. EMF Research: This program will provide for utility participation in state, national, and international research that benefits ratepayers.

  c. Other Research: Utilities are authorized to contribute to federal experimental research conducted under the National Energy Policy Act of 1992.

Occupational Exposures to Extremely Low-Frequency Electromagnetic Fields (ELF-EMF)

According to the National Institute for Occupational Safety and Health (NIOSH), "Workers may be exposed to high magnetic fields if they work near electrical systems that use large amounts of electric power (for example, large electric motors, generators, or the power supply or electric cables of a building). High magnetic fields are also found near power saws, drills, copy machines, electric pencil sharpeners, and other small electric appliances. The strength of the magnetic field depends on equipment design and current flow, not on equipment size, complexity, or voltage."

Despite studies finding increased risk of male breast cancer in workers occupationally exposed to high ELF-EMF over long periods, there are currently no specific OSHA or Cal/OSHA standards that address extremely low frequency (ELF) fields.[31] NIOSH has a publication on EMFs in the workplace (available at https://www.cdc.gov/niosh/docs/96-129/) that includes examples of voluntary measures employers and workers can take to reduce exposures, but there are no official recommendations.

INTERVENTIONS

Overarching Goal: Reduce and where possible eliminate ELF-EMF exposure linked to breast cancer and expand research on the link between non-ionizing radiation (both ELF-ELM and RF) and breast cancer risk.

Intervention Goal 1

Reduce occupational exposures to ELF-EMF linked to breast cancer in both men and women.

Objective 1: Identify occupations that are of higher concern related to ELF-EMF exposure and monitor exposures.

Objective 2: Direct Cal/OSHA to develop and disseminate recommendations on reducing exposures in the workplace using the NIOSH suggestions as a starting point.[32]

Objective 3: Implement policies, through Cal/OSHA regulation or legislatively, to require ELF-EMF reduction in workplaces of highest concern.

Intervention Goal 2

Reduce environmental exposures to ELF-EMF around homes, schools, public spaces, and workplaces.

Objective 1: Direct CPUC to re-examine and update its 2006 EMF policy based on research conducted over the last 13 years.

Objective 2: Assess ELF-EMF exposures in planning decisions and incorporate exposure mitigation measures.

Intervention Goal 3

Expand research on the connection between non-ionizing radiation and breast cancer risk.

Objective 1: Expand funding for research on 4G and 5G radiation and breast cancer.

Objective 2: Expand funding for research to monitor ELF-EMF exposure in communities and occupational settings, especially to identify any areas of elevated concern.

Objective 3: Expand funding for research on occupational exposures to ELF-EMF and breast cancer risk for women.

Objective 4: Expand funding for research to understand the biological mechanism on timing of exposure to ELF-EMF and breast cancer risk.

Objective 5: Increase research on public exposures to ELF-EMF from utilities (powerlines and substations) and breast cancer incidence, including direct measurement of exposures.

Exposure to non-ionizing radiation is widespread in California, affecting nearly ALL residents.

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Occupation

Science Summary

Work in specific occupations and some workplace exposures have been linked to increased risk of breast cancer, and research in this area continues to grow more sophisticated.

What the Foundational Documents Say

Research on occupation and breast cancer has been limited due to small numbers of women in occupational and workplace exposure studies.[1] Recent reports have raised concerns about workers' exposures to unique mixtures of chemicals at work[2] and suggested that workers may be exposed through multiple routes, such as through both skin absorption and inhalation.[3]

Some communities may be disproportionately affected by workplace exposures due to the cumulative effects of work in local industries, along with residential proximity to those industries, socio-economic status, and other social factors.[4,5]

The Current State of the Evidence

Several occupations have been linked to increased risk of breast cancer in multiple studies. However, the association of a given occupation with increased risk of breast cancer does not provide information about why or how that occupation may increase risk. Workers in many occupations are exposed to multiple chemicals, ionizing radiation, sedentary work, and occasional or routine night-shift work, all of which have been associated with an increase in breast cancer risk. More research is needed to explore and increase understanding of workplace exposures; however, we have sufficient evidence of a connection to breast cancer risk to take action.

Agriculture

Studies of agricultural work and breast cancer have found mixed results, with most studies finding null results. However, one study found a 71% increased risk of ER- breast cancer, but no effect for ER+ breast cancer.[6] Another study found no effect for those who worked in agriculture for fewer than 10 years, but more than doubled risk for those who worked for more than 10 years.[7]

Flight Attendants

Flight attendants are one of the most extensively researched occupational groups. Studies from around the world have consistently found elevated risk of breast cancer, with most studies reporting 37-50% increased risk,[8] and meta-analyses in the past five years have found similar estimates.[9,10]

Medical and Healthcare Professions, Including Physicians and Nurses

Nurses have historically been cited as an occupational group at higher risk for breast cancer. The most recent data, however, are mixed. The most compelling data suggest that long-term work as a nurse may increase risk, with one study finding a 70% higher risk among those in the profession for more than 10 years,[11] and another finding a 28% higher risk among those who worked as a nurse for more than 25 years.[12] Yet another study found nearly tripled risk among women who had recently left nursing (within five years), but no elevated risk among those who left the field more than 15 years ago, and who were nurses for a shorter period.[13]

Several studies have found increased risk among physicians, although some studies have found no increased risk. Among those studies reporting elevated risk, estimates range from 35-40% higher[14,15] to nearly triple the risk, among orthopedic surgeons specifically.[16]

While contemporary radiological technicians do not appear to have elevated risk for breast cancer, those who began working in the early years of the field were found to have twice the risk of the general population.[17] Changes in radiation dosage and safety precautions likely reduced this risk over time. Laboratory workers may also have elevated risk; one study found 67% higher risk among laboratory workers with a 20-year latency,[18] while another found 40% higher risk among those who worked in a chemical laboratory for more than 10 years.[19]

Production Workers, in Sectors Such as Auto Plastics, Canning, and Metal-Working

Some production jobs may confer elevated risk. One study found more than five times the risk of pre-menopausal breast cancer for women working in food canning.[6] The same study found women in metal-working professions had double the risk for ER+/PR+ breast cancer.[6] Studies of paper production and printing have found mixed results, but one study found tripled risk among printing machine operators.[20] Women working in auto plastics were shown to have almost five times the risk of pre-menopausal breast cancer and more than double the risk of post-menopausal breast cancer.[6] Finally, while studies of textile workers have been mixed, several studies have found elevated risk of breast cancer.[20,21,22]

Retail and Sales

Studies examining risk among workers in retail and sales consistently found elevated risk of breast cancer, ranging from 40% increased risk to more than doubled risk.[15,20,23,24,25]

Teachers

Some of the earliest studies of occupation and breast cancers cited teachers as an occupation with elevated risk. More recent studies are more equivocal. One study found teachers had 30% higher risk overall. However, only women who had at least one live birth showed elevated risk when they analyzed the data based upon reproductive history.[25] One study found 50% higher risk among school administrators.[26]

Occupation and Exposures

Several workplace exposures were linked to increased risk of breast cancer:

Chemicals used in the workplace may increase risk of breast cancer. Solvent exposure appears to increase breast cancer risk by 40-50%,[27] especially in women who have not had children[28] and for estrogen-receptor negative/progesterone-receptor negative (ER-/PR-) breast cancers.[20] Both benzene and trichloroethylene have been linked to roughly doubled risk of male breast cancer.[29]

Some pesticides, such as chlorpyrifos,[30] terbufos,[30,31] methyl bromide,[31] malathion,[30,32] dieldrin,[33] and chlordane,[32] have been associated with increased breast cancer risk, ranging from 1.5 times to nearly 4 times the risk, among women who mixed and applied pesticides. One study found that the combined chemicals in pesticides caused an increased incidence of breast cancer in younger Latina farm workers. The chemicals that these workers were exposed to included 2,4-D, malathion, and chlordane.[34]

Other chemicals linked to elevated risk include ethylene oxide (75% to tripled risk),[35,36] PCBs (specifically, exposures among women of color increased risk by 33%),[37] chlorinated compounds (doubled risk),[38] and metal-working fluids (13-33% higher risk).[39,40]

Night-shift work is one of the most well-studied exposures. Long-term night-shift work is consistently linked to modestly increased risk.[41,42,43] Researchers are beginning to explore whether different patterns of shift work have different effects on breast cancer risk. This exposure is explored in more detail in the section "Light at Night."

Ionizing radiation is also linked to increased risk of breast cancer, especially among those with higher exposures[17] and with specific genetic profiles.[44,45,46] The associations among those occupationally exposed (such as flight attendants and health-care workers) are consistent with ionizing radiation exposure from any source, which is explored in more detail in the "Ionizing Radiation" section.

Job strain or stress[47,48,49] and long work hours[50] conferred added risk in the range of 40- 60%. Overall psychosocial stress is explored in the "Stress" section of the Plan.

Sedentary work is linked to 20-50% increased risk of breast cancer,[51,52] while workplace physical activity is protective for both younger women[53] and post-menopausal women.[54,55,56]

Data are conflicting regarding occupational exposures to non-ionizing radiation and passive smoking. These exposures are explored in more detail in other sections of the Plan.

Nuances and Emerging Considerations

Many studies were not able to measure or account for other important risk factors for breast cancer, such as menopausal status, family history, body mass index (BMI), smoking behavior, alcohol consumption, or reproductive patterns. Accounting for variations in reproductive history, smoking, alcohol consumption, and BMI may be particularly important, since these factors may correlate with occupation. Similarly, race/ethnicity and childhood socio-economic status may affect occupational opportunities, job roles, and exposures. More research is needed that includes sufficient numbers of women to assess whether specific groups experience higher exposures of concern on the job.

Evidence in some occupations suggests that some work exposures early in life affect later breast cancer risk,[28,39,57] and that long-term work in some occupational fields may confer added risk.[11,12,58,59,60,61,62,63]

As the President's Cancer Panel expressed in 2010,[4] new and thorough assessments of workplace exposures linked to cancer that integrate new research models and endpoints are needed. Having medical professionals collect workplace exposure history is needed to advance research in the field.

Take-Home Message

Some occupations and occupational exposures may be linked to elevated risk of breast cancer.

Future research and ongoing studies should include women from different racial, ethnic, and socio-economic backgrounds in adequate numbers to study variations across groups. In addition, research on occupation needs to assess exposures from jobs held in adolescence and early adulthood, examine the risk of different breast cancer subtypes, and examine the risk of pre- and post-menopausal breast cancer.

Occupation: Context for Interventions

Nearly 8 million women are part of California's workforce, the majority of whom are employed in lower-paying jobs.[64] Women's occupational risk for breast cancer, especially for women of color, has been largely under-studied.[64] However, existing research shows the connection between breast cancer risk and occupation can be understood through numerous lenses: chemical exposure; stress, including around job security and fair wages, threats or acts of sexual and physical violence, and lack of power to advocate for oneself; challenges with time and accommodation for breastfeeding; light-at-night exposure; and many other issues. Below are highlights of some of the specific concerns in these areas:

Wage Inequality

California's female workforce faces many of the challenges that exist nationally. The Institute for Women's Policy Research released their Status of Women report in 2018 and found that women in California have median annual earnings of $45,000. Broken down by race, we see racial discrimination at play: White women earn 77% of what White men earn, Asian women 73%, Black women 62%, Native-American women 50%, and Latina women

just 43 cents for every dollar earned by White men.[65] These figures likely do not fully represent information about undocumented or informal workers. If current trends continue, women in California will not see equal pay until the year 2043.[67] The economic stress and insecurity that women face remains a significant concern for Californians and may increase breast cancer risk (see the "Stress" section for more information).

Chemical and Radiation Exposure

A groundbreaking research project led by the California Department of Public Health and the California Cancer Prevention Institute has begun to map the details of women's exposure to chemicals and radiation in the workplace. They looked at potential chemical exposures of 6.6 million women in the state and found:

- Around 1.7 million women may be exposed to solvents in the workplace, including nearly 200,000 informal workers who may be especially vulnerable;
- Maids and housekeeping cleaners, a workforce that is 81% Latina (not including informal workers), may be exposed to antimicrobials, phthalates, and pesticides;
- Many Black women work as personal care, nursing, or other aides, with potential exposure to antimicrobials, fragrance ingredients, and combustion products; and
- Cashiers, many of whom are teenagers, may be exposed to the endocrine-disrupting compound bisphenol A in cash register receipts and fragrance ingredients.[66]

The California Division of Occupational Health and Safety (Cal/OSHA), the agency responsible for enforcing federal and state regulations for protecting worker health, is woefully underfunded and understaffed.[67] While Cal/OSHA does have some stronger provisions than the federal OSHA, those provisions and the lack of enforcement still fail to adequately protect workers. The entire system of attempting to regulate workplace exposures one chemical at a time is completely unworkable, given the complexity and the time it takes to set a single Permissible Exposure Level (PEL) as well as the sheer number of chemicals in the workplace.

Given the lack of resources at Cal/OSHA, other state agencies must step up to help protect workers. The Occupational Health Branch (OHB) of the state Department of Public Health[68] has a number of programs, such as the California Safe Cosmetics Program and the Hazard Evaluation System and Information Service (HESIS)(https://www.cdph.ca.gov/Programs/CCDPHP/DEODC/OHB/HESIS/Pages/HESIS.aspx), designed to identify hazardous circumstances and prevent injury and illness on the job; OHB should be adequately funded. In addition, California's Department of Public Health, Office of Environmental Health Hazard Assessment, and Department of Toxic Substances Control must expand their domains to include a specific focus on occupational exposures to better inform their decisions and recommendations regarding safe exposure levels.

With the state agencies that should be protecting workers lacking sufficient resources and authority to provide that protection, unions have stepped up to create programs and informational tools to help workers reduce dangerous chemical exposures. One example is Putting Breast Cancer Out of Work,[69] an interactive curriculum developed by BlueGreen Alliance (BGA) in collaboration with other organizations such as Breast Cancer Prevention Partners and the United Steelworkers. This training, led by BGA union trainers, explains the role of chemicals in breast cancer and other chronic diseases, discusses workplace practices and policies to reduce those exposures, and provides participants a set of tools and informational resources. One of those resources is the ChemHAT database, which allows workers to research potential health impacts of the chemicals they are exposed to at work and which includes a specific section for breast cancer resources.[70]

Interventions related to workplace chemical exposures will be addressed in this section. Interventions related to radiation will be addressed in the "Ionizing Radiation" section.

Light at Night

Light at night poses a significant breast cancer threat to women. Shift workers are especially at risk due to the disruption in their sleep cycles. However, while not required by federal law, night-shift work may offer higher pay, called shift differentials, that make it economically advantageous for women.[71] As a result, interventions must be reviewed and balanced against the potential for unintended consequences regarding women's earning power. Relevant interventions will be explored further in the "Light at Night" section of this Plan.

Breastfeeding

Women often go back to work while they are still breastfeeding. Community listening session participants with jobs as varied as farmwork and office work noted challenges related to breastfeeding at the workplace. Interventions related to breastfeeding and work will be addressed in the "Breastfeeding" section.

Discrimination

Employment discrimination can lead to fewer opportunities for women, and particularly for women of color. Racist policies or attitudes against Black women's natural hair can lead to either lost opportunities or extreme pressure to treat hair with dangerous chemicals to straighten it. As mentioned elsewhere, as people of color earn higher-paid positions at work, they may experience significantly higher stress and health impacts due to both chronic and acute discrimination.[72] Interventions related to discrimination are noted in several relevant sections of this Plan.

Sexual Harassment and Violence in the Workplace

Sexual harassment and violence in the workplace remain major concerns,[73] especially for less economically secure women such as farm workers, domestic workers, hotel workers, and others. Interventions related to these issues will be addressed in the "Stress" section.

Power in the Workplace

Critical to all the workplace-related concerns is the ability for workers to have collective power. Unions play a critical role in educating, empowering, and lobbying on behalf of people's right to a fair and safe workplace. When it comes to health and safety at work, it is easy to suggest that workers be educated on these issues, but if workers have no power to change their work conditions there are real limits to what is possible. Across the country, unions have been under attack, with an effort to reduce worker's rights and reduce the political power of unions to protect workers. As of 2018, only about 15% of California workers were unionized, down 7% since 1983.[74]

Workers, particularly women, who fear losing their jobs are unlikely to have the power or security to advocate for workplace safety. For instance, a 2014 report, The Glass Floor: Sexual Harassment in the Restaurant Industry, found that 90% of women in the restaurant field, particularly those dependent on customer tips, experienced sexual harassment, and many on a weekly basis. Only a fraction of those workers report the harassment.[75] Workers—and particularly women workers—need enough power, whether through unions or other workplace-organizing strategies, to advocate for their safety on the job and to compel employers to protect them.

Ultimately though, California must improve the laws and regulations protecting all workers and provide state agencies the mandate and resources to fully enforce them. Given the relative power of corporations versus workers in our society, only government can provide the necessary protections.

Overall, there is much more work to be done to understand exactly what the breast cancer risks are for working women in California, but enough information exists to take proactive, health-protective measures to ensure that women's working environments are safe.

Community Input on Occupational Exposures

Community listening session participants noted that regulations overall are not strong enough to protect worker health, and they lacked confidence in government agencies to adequately enforce existing regulations or levy fines that actually act as a deterrent. Community members firmly believed that to see any tangible improvements, a firewall is needed between industry and the regulators.

Participants also noted that exposures in the workplace are also "place-based," and that workers exposed on the job are often also exposed in their community.

Transitions in California's industries and workforce must prioritize benefiting the communities that have suffered from limited economic opportunities and that experience the greatest impact from industrial pollution and climate change.

California's Just Transition: Protecting Health, Creating Justice and Safe Jobs for All

California, like much of the rest of the world, is functioning in an unsustainable model of infinite growth and consumption with little regard for life-supporting ecological systems or human dignity. Many solutions proposed to address climate change and other pressing societal issues are often based on market-based approaches that benefit corporations and their leadership. For instance, California's carbon cap-and-trade program has allowed corporations to continue to emit greenhouse gases while concentrating those emissions in economically disadvantaged communities that are already highly impacted.[76] These policies were designed by and continue to benefit the fossil fuel and other industries at the expense of overburdened and disenfranchised communities.

While California continues to be a global leader on climate change, many of the proposed policy changes fall short. Ultimately, a shift is needed from an extractive economy to a regenerative economy based on renewable energy and implemented through a just transition.

It is beyond the scope of this Plan to propose details of a comprehensive overhaul of all of California's industries, but all actions inspired by this Plan should be guided by a Just Transition framework, which Climate Justice Alliance[77] describes as:

Just Transition is a vision-led, unifying, and place-based set of principles, processes, and practices that build economic and political power to shift from an extractive economy to a regenerative economy. This means approaching production and consumption cycles holistically and waste-free. The transition itself must be just and equitable; redressing past harms and creating new relationships of power for the future through reparations. If the process of transition is not just, the outcome will never be. Just Transition describes both where we are going and how we get there.

Transitions in California's industries and workforce must prioritize benefiting the communities that have suffered from limited economic opportunities and that experience the greatest impact from industrial pollution and climate change. Making industry more sustainable while destabilizing communities is not an acceptable shift toward a healthier world. (See Four Pillars for a Just Transition report for more information.[78])

INTERVENTIONS

Overarching Goal: Support workers' right to a healthy livelihood by reducing exposures and conditions that increase risk for breast cancer.

Intervention Goal 1

Implement workplace policies and practices, following the Hierarchy of Controls, to protect workers and reduce breast cancer risk.

Objective 1: Develop workplace interventions to reduce exposure to breast carcinogens.

- **Strategy 1:** Require companies to assess their workers' exposure to chemicals and other risk factors in the workplace (e.g. radiation and light at night) and annually report to state agencies tasked with protecting workers such as Cal/OSHA and CDPH.
- **Strategy 2:** Require companies to implement inherently safer materials and technology to reduce workplace hazards, specifically those hazards linked to breast cancer risk. (For example: CA Process Safety Management of Petroleum Refineries, focused on protecting worker safety through inherently safer practices).[80]
- **Strategy 3:** Ensure employers implement needed controls to reduce exposure to chemicals linked to breast cancer when safer alternatives are not available.
- **Strategy 4:** Provide incentives for companies to invest in research to innovate new and safer materials and manufacturing processes to reduce harmful exposures.

Objective 2: Strengthen California's laws to protect the most vulnerable workers.

- **Strategy 1:** Amend California law to provide OSHA protections to temporary and contract workers, for instance domestic workers and day laborers, to protect them from workplace breast cancer risks.
- **Strategy 2:** Establish ambient air pollution standards to protect outdoor workers, with specific requirements set for high-risk situations such as working outdoors during wildfires or other disaster situations. Include comprehensive, enforceable worker-safety practices for those who do work outdoors (for example, providing adequate safety gear).
- **Strategy 3:** Develop regulatory mechanisms to require information from Safety Data Sheets (SDS) to inform enforcement around exposure protections. (Currently SDSs offer information, but there are no requirements for the information to influence practice.)

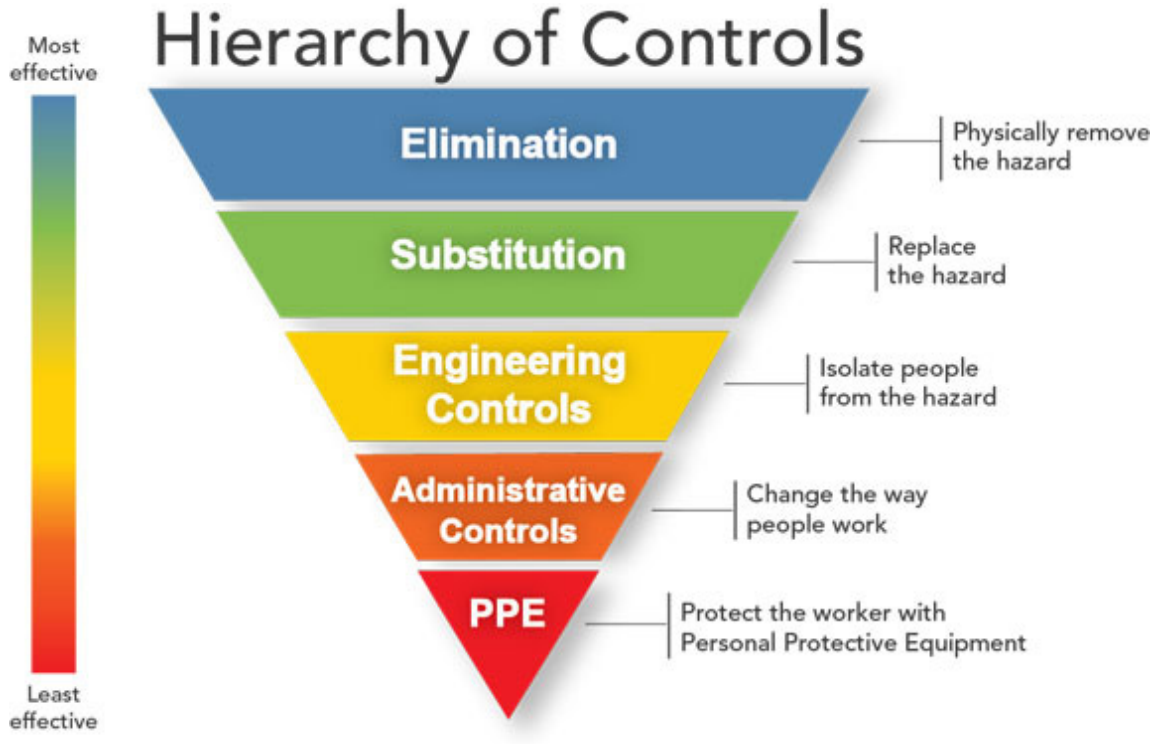
Objective 3: Educate employers and workers on the link between workplace hazards and increased breast cancer risk.

- **Strategy 1:** Educate employers on available governmental lists of breast carcinogens. Adequately fund ongoing updates to these databases.
- **Strategy 2:** Provide technical assistance and implement policies to teach employers how to eliminate or reduce risks to their workers using the Hierarchy of Controls, which prioritizes systemic change over the use of personal protection equipment (PPE). For example, teach salon owners how to properly ventilate to reduce worker exposure to chemicals in salon products.
- **Strategy 3:** Educate workers about their rights in the workplace, current safety regulations, how to advocate for themselves, and how to properly protect themselves (such as proper use of PPEs) to reduce hazardous exposures, including those linked to breast cancer.

Intervention Goal 1 (continued)
Implement workplace policies and practices, following the Hierarchy of Controls, to protect workers and reduce breast cancer risk.

- **Strategy 4:** Ensure employers provide workers easy access to Safety Data Sheets (detailed informational documents on physical and chemical properties prepared by the manufacturer or importer of a hazardous chemical)[81] in people's native languages and without fear of retaliation.
- **Strategy 5:** Promote the Chemical Hazard and Alternatives Toolbox (ChemHat)[82]—an Internet database with easy-to-use information on how workers can protect themselves against chemicals—to workers and employers to help identify alternatives to breast cancer carcinogen use.
- **Strategy 6:** Create and promote educational programs to workers and employers on breast cancer risk in the workplace and ways to reduce that risk. See Putting Breast Cancer Out of Work[83] as an example initiative.
- **Strategy 7:** Ensure women can seek information, report violations, and request education and workplace changes to protect themselves from breast cancer risks without retaliation.

Figure 8.



Source: NIOSH[79]

Intervention Goal 2

Strengthen the institutions and laws that protect workers from on-the-job health hazards that can increase risk for breast cancer.

Objective 1: Strengthen workers' rights by protecting the right to unionize.

- **Strategy 1:** Support legislation that protects and strengthens workers' right to collective bargaining and unions, such as the California Labor Federation's agenda.[84]
- **Strategy 2:** Ensure enforcement of those protections, such as Senate Bill 866,[85] which protects workers' rights to manage membership dues and sets the terms of maintaining and withdrawing membership.[85]

Objective 2: Ensure that California's worker protection agencies have the authority, capacity, and strength to protect workers.

- **Strategy 1:** Ensure adequate staffing of the California Division of Occupational Safety and Health (Cal/OSHA),[86] including inspectors who operate independently from industry's influence and who are held accountable for enforcing laws and regulations that reduce breast cancer risk.
- **Strategy 2:** Provide adequate resources for the California Department of Public Health's Occupational Health Branch to track potential hazardous and work to prevent harm.[68]
- **Strategy 3:** Expand Cal EPA's Office of Environmental Health Hazard Assessment and Department of Toxic Substances Control authority and mandate to include a specific focus on and requirement to consider occupational exposures when assessing the hazard and acceptable exposure level to chemicals or other workplace risk factors, particularly exposures related to breast cancer risk.
- **Strategy 4:** Ensure that the California Department of Industrial Relations Retaliation Complaint Investigation Unit (RCI)[87] is adequately staffed and responsive to requests for help, so workers can make complaints without fear of discrimination or retaliation.
- **Strategy 5:** Develop more streamlined approaches to regulating chemicals and other workplace risk factors, such as light at night and radiation exposures. For example, regulate classes of chemicals instead of individual chemicals where appropriate.

Objective 3: Expand requirements for health-care providers in California to consider and document occupational exposures to better understand risks and how to protect workers.

- **Strategy 1:** Expand the requirements for health-care providers to include occupational history on intake assessments and screening forms to identify workplace exposures over women's lifetime. Include information in electronic health records so it can be accessed, while protecting patient confidentiality, to better document and understand workplace hazards—including those linked to breast cancer risk across industries and jobs.
- **Strategy 2:** Expand the occupational health training requirements in medical and nursing schools, include occupational health in Continuing Education requirements, and develop and distribute resources for clinicians.
- **Strategy 3:** Ensure employers have access to and use occupational hygienists who are trained to recognize workplace factors linked to increased risk of breast cancer.

Intervention Goal 3

Support workplace equity to ensure all women have economic security and the ability to advocate for workplace safety.

Objective 1: Ensure that workers are paid livable, equitable rates.

- **Strategy 1:** Support equal pay for all women regardless of race and ethnicity by continuously strengthening and enforcing the California Equal Pay Act.[88]
- **Strategy 2:** Ensure compliance with California's minimum wage requirements, which will incrementally increase to $15 per hour by 2022 or 2023, depending on the size of the business.
- **Strategy 3:** Promote local efforts to increase the minimum wage beyond state requirements. To see the list of more than 20 cities that have already done this, go here: https://www.laborlawcenter.com/education-center/california-minimum-wage-requirements/.

Objective 2: Continually strengthen and enforce the nearly 50 laws[89] that prohibit discrimination and retaliation against employees and job applicants in California.

Intervention Goal 4

Support research to better understand women's occupational breast cancer risk and how to reduce those risks.

Objective 1: Fund research that expands knowledge around which industries expose workers to risk factors linked to breast cancer, as well as the mechanism and level of those exposures.

Objective 2: Fund research that identifies ways to make workplaces inherently safer, isolate people from hazardous exposures, and, when necessary, determine the most effective personal protective equipment.

- **Strategy 1:** Fund research on ways to eliminate hazardous chemicals and practices from workplaces, with an emphasis on breast cancer risks.
- **Strategy 2:** Fund research focused on actions specific workforces—such as salon workers and janitorial workers—can take to protect themselves immediately.
- **Strategy 3:** Fund research to determine if proposed changes in work practices could disadvantage women, including how to best protect pregnant workers from exposure to harmful chemicals without creating a discriminatory environment.

We must ensure that California's worker protection agencies have the authority, capacity, and strength to protect workers.

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Pharmaceutical Hormones: Hormone Replacement Therapy, Oral Contraceptive Pills, Infertility Treatments

Science Summary

Use of combined estrogen plus synthetic progestin (E + P) hormone replacement therapy for post-menopausal women has been found to be a risk factor for breast cancer, while estrogen only therapy for women who have had a hysterectomy is seen as protective. The relationship between use of oral contraceptive (OC) pills and breast cancer risk is nuanced regarding duration and timing of use and formula preparation, but the consensus is that OCs should be taken for the shortest duration of time possible to avoid increased risk of breast cancer.

What the Foundational Documents Say

Pharmaceutical hormones include those that imitate or are natural forms of, endogenous sex hormones (estrogen, testosterone, progesterone) and they come in a variety of forms and purposes. These hormone or hormone-mimicking compounds bind to the respective hormone receptor and may affect risk of breast cancer.[1]

The foundational documents, specifically the AICR Continuous Update Project, the IOM report, and the IBCERCC, speak to the use of pharmaceutical hormones as a risk factor for breast cancer. The IBCERCC reports that the greatest amount of proliferation of cells is in the post-menopausal breast, and therefore the greatest increase in risk for developing breast cancer occurs in women receiving combined E + P hormone replacement therapy (HRT) when compared to no HRT or estrogen-only therapy.

Estrogen only therapy is given only to women who have had a hysterectomy because it increases the risk of endometrial cancer. The Women's Health Initiative (WHI) was one of the large trials that found E + P use to be a risk of breast cancer. Following publication of these results there was a significant decline in ER+ breast cancer incidence rates among white post-menopausal women that was widely attributed to reductions in use of this form of HRT.[2,3] The IOM report specifically states that in post-menopausal women, use of E + P increases both incidence of and mortality from breast cancer.[4] In concurrence, the AICR reported that combined estrogen and progesterone (E + P) preparations of HRT increase risk of breast cancer.[5]

In terms of oral contraceptives (OCs), the AICR reports that OCs containing both E+P can cause a slightly increased risk of breast cancer in current and recent users.[5] The IOM report concurs with this statement, adding that an increased risk of breast cancer from OC is based on the formulation of the pills. Importantly, risk associated with OC use is small, especially considering the large population of young women who use OCs prior to menopause, with risk decreasing shortly after discontinuation of use.[4]

The Current State of the Evidence

The main body of research surrounding pharmaceutical hormones as a risk factor for breast cancer comes from a select group of trials conducted in the 1970s to the early 2000s. The breadth of these dates reflects changing formulations and dosages, particularly for oral contraceptives. The 2002 WHI trials followed post-menopausal women aged 50 to 79 years, with one arm of the study receiving only conjugated equine estrogen (CEE; a synthetic form of estrogen) and the other arm receiving both CEE and medroxyprogesterone acetate (MPA, a synthetic progestin that is functionally and structurally similar to the natural progesterone). Follow-up to this study ranged from 3-10 years and has been critical in determining the association between hormone therapy and breast cancer. In the E + P arm of the trial, there was a 28% increase in risk of breast cancer. The trials were stopped after 5.6 years due to this adverse health effect.[6] The drop in breast cancer incidence observed since 2002 is attributed to the release of the WHI trial data and the subsequent decrease in HRT use.[7]

In 1996 the Million Women Study, a large observational study, recruited 1 in 4 U.K. women born in the years of 1935-1950 to study the effects of hormone therapy.[8] The study found an increased risk of 30% for women taking estrogen only therapy and a two-fold increase for women taking E + P. These larger effects may reflect the lack of control of other factors that influence breast cancer risk.[9] Lastly, the 1990 E3N-EPIC French cohort study was one of the first studies to consider bioidentical compounds, natural forms of estrogen and progesterone produced from plant derivatives, in place of synthetic hormonal therapy. This study remains controversial as follow up later in the women's lives shows increased breast cancer risk while the results at the time (i.e. 1990) showed no increased risk. These four trials changed the course of hormone therapy administration and oral contraceptive formulations, and served as the pioneers in a field not well understood by clinicians, scientists, and the actual patients using the hormones.

While HRT use has been the subject of large studies, use of OCs has a more limited body of research examining the relation to breast cancer. However, the Nurse's Health Study, a very large and groundbreaking cohort study that studied OC and hormone therapy use and its effects, started in 1976 and occurred in phases of 4-6 years. Its goals were to account for changes in OC formulations, age of use and effects on health outcomes. This study produced a large body of information relating to how current vs. past use and different doses and formulations of OCs impact risk of breast cancer. The findings related to hormone therapy echo those of the WHI.

The state of the evidence that follows reflects our scoping review of the literature since 2012. Most of this work is based upon the four major cohort studies described above, and includes reviews, meta-analyses and re-analyses of these projects and their respective follow up data.

The findings from these follow-up projects are often contradictory. This may be due to lack of data, differing analyses of the same data, changing pharmaceutical formulations that are no longer in use, and limited follow up after trials.

As scientists and clinicians aim to understand the emerging nuances that are associated with the administration of pharmaceutical hormones (family history, duration of use, timing, formulations, risks/benefits), the repeated use of historical trial data shifts the accuracy and conclusions of many of the reviews. Analyses of the effects of hormone therapy also yield contradictory results depending on timing of use, risk benefit assessments, and the use of bioidentical compounds. Oral contraceptives have the most contradictions in terms of the impact of timing of use, formulation, and family history on breast cancer risk.

Hormone Replacement Therapy

Hormone replacement therapy (HRT), in the form of estrogen or combined E + P, is often used by women in their 50s-70s to alleviate the negative effects of menopause. A major 2019 meta-analysis on the data of over 100,000 HRT users found that all forms of HRT, except vaginal estrogen only therapy, led to an increased risk of breast cancer.[10] Further analyses of the WHI trials data confirm that combined hormone therapy is a risk factor for breast cancer while estrogen only therapy is protective for hysterectomized women.[11,12,13,1,14,15] Several reviews looking at a host of other studies support this finding.[7,16,17,18,9,19,20,21,22,23,24,25,26]

The following discussion is a summary of reviews concerning hormone therapy with the majority basing results off the main body of trials discussed above. In the WHI trials, the increased risk posed by E + P formulations persisted even after discontinuing the hormonal therapy.[12] A reanalysis of the results of the WHI trial found that for combined (E+P) HRT, the risk of breast cancer was elevated throughout the length of use, reaching a 3-fold risk after 5 years.[26] A more recent meta-analysis of HRT focused studies found that among current users of combined HRT, there was a 60% increased risk of breast cancer for 1-4 years of use with the risk increasing to two-fold after 5-14 years of use. Beyond 5 years of use, daily use of progestin-based HRT led to a higher risk of breast cancer than less frequent use of progestin.[10]

A reanalysis of the WHI trials found that estrogen only therapy was protective of breast cancer for hysterectomized women, although results were only statistically significant for women less than 5 years after menopause.[1]

A review found that for women with an intact uterus who are taking estrogen only therapy, longer duration of use could increase risk of endometrial cancer and hyperplasia.[15] In addition, another review found that estrogen therapy should not be taken as a preventative measure against breast cancer for women with family history of the disease or genetic mutations including BRCA1/2.[18]

A major debate in the field of analyzing HRT risk involves understanding timing of use. The "timing hypothesis" differentiates between starting hormone therapy immediately after menopause or waiting for some years to pass, and considering the risks/benefits of each scenario.[20,21,22] One review defends the immediate post-menopausal use of HRT for protection against coronary heart disease (CHD); however, the authors acknowledge

that women may have breast carcinomas that are not immediately apparent and clinically detectable around the time of menopause. These carcinomas may be aggravated by estrogen or progestin therapy. Waiting 5 years after menopause to initiate HRT use allows already present occult breast carcinomas to go through apoptotic cell death, as the cells will have been estrogen deprived.[27,26] On the other hand, a different review critiquing the results of the WHI trials found that the relationship between HRT initiation and risk of breast cancer was not significantly influenced by age or time since menopause.[28]

Interactions with Race and BMI: A reanalysis of the WHI trial data analyzing race/ethnic identification and HRT use found that Black women have higher increased risk of breast cancer (38%) when taking combined HRT compared with White women (29%).[13] While studies report that estrogen only therapy is more protective for Black women than White women, they do not consider the confounding factor that Black women are more likely to have undergone hysterectomies and bilateral oophorectomies.[1]

A separate review of women in Korea and HRT use found that breast cancer incidence after the age of 50 was lower than in other countries and that estrogen only HRT use was not significantly affecting Korean women's risk for breast cancer. This study highlighted the lower incidence of breast cancer after the age of 50 in Korean women compared with both other Asian countries and women of the United States.[29]

In terms of Body Mass Index (BMI) and weight, the Million Woman Study found that combined HRT had a proportionately greater adverse effect on lean women than it did in obese women. Leaner women not taking HRT had lower rates of breast cancer than did heavier women. Use of HRT increased risk for all participants, resulting in a constant rate for all participants regardless of BMI.[30] However, the WHI study did not find any difference in breast cancer risk by BMI levels, either in Black or White women.[13]

Hormone Replacement Therapy and Subtypes: The body of research correlating HRT use with breast cancer subtypes is inconsistent, with few studies showing significant associations. A review concerning HRT and breast cancer subtypes found that all HRT formulations were consistently associated with an increased risk of ER+ breast cancer.[31] More specifically, in current users of HRT, ER+ breast cancers were significantly increased, but there was no significant effect of past use of HRT on ER+ breast cancers.[32,33] One study cited in the review found that there was a significant correlation to triple-negative breast cancer (TNBC) only for current users of HRT, however more research needs to be done concerning HRT administration and its connection to TNBC.[32,34] In another study, combination HRT was associated with increases in both ductal and lobular breast cancer risk.[31]

The Multiethnic Cohort Study, which includes women of Japanese-American, Native-Hawaiian, African-American, and Latina descent, analyzed subtypes of breast cancer across race and use of hormonal therapy. It found that across different ethnicities HRT was associated with ER+/PR+ cancers, but not TNBC.[35]

Studies looking at HER2+ breast cancer risk and HRT administration have found no association.[32]

Despite reanalysis of trial data to identify associations between HRT and race and studies like the Multiethnic Cohort Study, more research is required to look at the associations between women of historically underrepresented ethnicities (Latina, Black, Native American, Asian, Native Hawaiian and Pacific Islander), hormone therapy use, and breast cancer subtypes.

HRT and Protective Effect of Physical Activity: Physical activity is known to have a risk reducing effect on breast cancer. A meta-analysis examining the effect of HRT use on the protective effect of physical activity found that HRT use negated the protective effect of physical exercise.[36]

Oral Contraceptives (OCs)

The effects of OCs on breast cancer risk vary with duration of use, timing, and formulation. The first Nurses' Health Study (1976-1992) found that pre-menopausal women who were current OC users had a 50% higher risk of breast cancer.[37] Pre-1975 formulations, with high dose components, were thought to account for this increased risk. The NHS II (1989-2001), which was conducted 10 years later and followed a new cohort of women who had started OC use in adolescence/early adulthood, found that current OC users had a 33% higher risk of breast cancer due to triphasic preparations (3 different doses of hormones over the month of use) with the progestin levonorgestrel.[32,38] Two separate reviews also found that triphasic preparations of OCs with levonorgestrel among younger women were associated with the highest increase in breast cancer risk.[39] A separate meta-analysis found an 8% increase in ever users compared with never users and a 24% increase in current users compared with never users.[40,41,42] The risk remained highest within 5 years of use and then diminished over time such that after 10 years of discontinuing OCs, no detectable increased risk was found.[43] By contrast, a study in Denmark found that for women over 55, long (> 10 years) duration of prior use of OCs led to a significant two-fold increase in breast cancer risk.[42]

In terms of different formulations, a review found that the use of depot medroxyprogesterone only OCs did not affect breast cancer risk for women under the age of 35.[42] A separate meta-analysis found no association between risk of breast cancer and OCs in terms of duration and timing of use.[44]

Family History of Breast Cancer and BRCA1/2 Mutations: Most reviews analyzing the effect of taking OCs on the risk of breast cancer for women with prior family history of breast cancer or with BRCA1/2 mutations have not found OCs to be a strong risk factor, although some interactions were found pertaining to duration of use[43] and formulation.[44] A 2013 meta-analysis found no increase in breast cancer risk for those with the BRCA1/2 mutations using combined E + P OCs.[43] A meta-analysis of five studies found that pre 1975 formulations of combined OCs (higher doses) dramatically increased risk of breast cancer, while use of more contemporary OC formulas did not increase breast cancer risk for women with BRCA1/2 mutations.[44] A review conducted by The American College of Obstetricians and Gynecologists found that most studies and meta-analyses did not show an association between oral contraceptive use and risk of breast cancer; however, one case control study found that women with the BRCA1 mutation have an increased risk of breast cancer if they used OCs for longer than five years before the age of 30.[45]

Oral Contraceptives and Subtypes: A review of OC use and increased risk of different breast cancer subtypes found no significant relationship between OC use and ER+, HER2+ breast cancer risks, but did report an association with increased risk of TNBC in middle aged (45-64 year old) women who started taking OCs before age 18.[32] A separate review and meta-analysis found a significant 21% association between OC use and TNBC.[46] More research is needed on the mechanism underlying OCs effect on TNBC.

IUD and Implants: There is limited research on the effects of levonorgestrel releasing intrauterine devices (IUDs) and implants and their possible relationship to risk for breast cancer. However, a retrospective analysis of a population-based study did not show any association between use of levonorgestrel releasing IUDs and breast cancer.[42]

Infertility Drugs

Most studies have found no significant relationship between in vitro fertilization (IVF) exposures or the use of Assisted Reproductive Technology (ART) and breast cancer,[47,48,49] however a few studies have found differing results.

Some studies have indicated an elevated risk for women exposed to high doses of clomiphene citrate (used to stimulate hormones that support ovulation)[50] although others have shown no association.[51] However, the results were significant only when the incidence of breast cancer was compared with the general population of women, but not with the more appropriate control of women with ovarian infertility who have not been treated with fertility drugs.[52]

An Australian study found that women who started hospital infertility treatment at a young age (24 years) and required IVF had a 1.5-fold increased risk for breast cancer. Risk was not elevated in women who commenced treatment at age 40 and required IVF.[51]

A woman's potential to implant all transferred embryos may be associated with breast cancer risk. A Dutch study of IVF treated women found breast cancer risk was 1.44 times higher in mothers of multiples than in mothers of singletons. Risk was highest in women who gave birth to multiples from all embryos transferred and not significantly raised for those with multiples after incomplete embryo implantation.[53] However, some studies have not seen this association[54] and others have noted nuances by genes,[55] the infant's sex,[56] and breast cancer subtype (with elevated risk of only HER2-enriced breast cancer in pre-menopausal women).[57]

Emerging Nuances and Considerations

Alternatives to Traditional HRT Formulations

While most studies have focused on the use of synthetic estrogens and progestins, recent research has started testing the use of the natural forms of the hormones, also called bioidentical compounds, mainly focusing on progesterone.

Some studies have posited that natural progestins, in the form of micronized progesterone (miP4), are safer to use compared to synthetic progestins. However, a follow up on the E3N-EPIC cohort study found an increased risk of breast cancer with long-term use of micronized progesterone and estrogen, up to 47% for 5-10 years and 92% for >10 years.[9,17,19,58,59] The mechanistic activity of miP4 is also under debate. Studies have suggested that miP4 promotes the growth of small breast carcinomas that first appeared during the fertile stage of the woman, while other studies have shown that miP4 reduces breast cell proliferation.[58]

Another HRT alternative to synthetic progesterone for non-hysterectomized women currently being researched is a combination of conjugated equine estrogen (CEE) and bazedoxifene (BZA). BZA, a Selective Estrogen Receptor Modulator (SERM), counters estrogenic effects on the endometrium, acting in place of progesterone.[28] The function of SERMs is to have an anti-estrogenic effect on estrogen receptors in the breast, reducing breast cell proliferation. A trial studying the effects of CEE + BZA found no increased risk of breast cancer although the follow up period for this trial was only one year.[28]

Although hormone therapy alternatives are becoming increasingly popular given the increased risk of breast cancer from synthetic HT, more research is required for the long-term effects on breast cancer risk.

Endometrial Cancer

Peri-menopausal and pre-menopausal women who have undergone bilateral oophorectomy or hysterectomy for treatment for endometrial cancer often experience early menopausal symptoms. A systematic review on the use of HRT to treat menopausal symptoms of women treated for endometrial cancer advises using a risk-benefit assessment in choosing between an estrogen-only therapy and a combination therapy.[59] Endometrial cancers are known to be estrogen sensitive, making estrogen only therapy a risk factor for endometrial cancer if there are residual cancer cells post treatment or the woman has only had an oophorectomy and the uterus is intact. The addition of progesterone improves the prognosis for endometrial cancer; however, the addition of progesterone increases risk of breast cancer creating the need for a risk-benefit analysis for each woman.[59]

Thyroid Dysfunction

In a meta-analysis of six studies pertaining to thyroid hormone replacement therapy for hypothyroidism, hormone administration did not affect breast cancer risk.[60]

Testosterone Therapy for F2M Transgender People

There is currently limited research on androgen treatment of female to male transgender people, however a recent review found that there is a marked reduction of glandular tissue and an increase of fibrous connective tissue in the breast following testosterone treatment. The administered testosterone can partially aromatize to estradiol, which can be a risk factor for those who have not gone through a mastectomy.[61] One report found that those who have undergone mastectomy may develop cancer in residual breast tissue ten years after the breasts are removed.[61] There is also a dearth of information on possible effects of estrogen treatment on breast cancer risk in male to female transgender persons, although a few cases have been reported. In these studies, the incidence of breast cancer in the transgender community did not exceed the expected risk for age matched members of the general public.[62,63]

Take-Home Message

- Combined HRT use should be avoided or used for the shortest time possible due to evidence of increased risk of breast cancer.
- Formulations and duration of use should be considered when using oral contraceptives, and as a precaution, be administered for the shortest time possible.

Pharmaceutical Hormones: Context for Interventions

Hormones are prescribed as contraception, to control menopausal symptoms, and to address infertility. The interventions explored in this section focus on contraception and menopausal hormone replacement, both of which have been linked to breast cancer.

Women have found methods to control fertility for thousands of years. Plant-based extracts provided some of the first hormonal and biochemical means of family planning.[64] Many compounds were known to be effective for contraception and that knowledge was shared among women. Modern science has demonstrated that some of these remedies have contraceptive benefits.[64] Efforts to identify and synthesize hormones date back to the early part of the 20th century. Bisphenol A (BPA), an endocrine-disrupting compound widely used in consumer products, was investigated as a hormone replacement in the 1930's,[65,66] although it was never used for this purpose. Diethylstilbestrol (DES), a synthetic estrogen linked to rare vaginal cancers and breast cancer, was synthesized in 1938 and used (ineffectively) as an anti-miscarriage drug.[67] DES use caused cancers not just in the women who took the drug, but also in their daughters and granddaughters.

By 1960, the first oral contraceptive pill was approved for use.[64] The first pill, Enovid 10, contained notably higher concentrations of hormones than today's oral contraceptives (OCs). These levels were higher than needed to prevent pregnancy and had more side effects than lower dose contemporary formulations.[68]

Today, OCs are the most frequently used form of effective, reversible contraception; nearly 82% of sexually active women aged 15-44 report having used OCs at some point in their life. Women also use OCs to alleviate menstrual irregularities and dysmenorrhea.

In 2012, 75.4 million women in the United States were in the reproductive age range of 15-50 years.[69] In California, birth rates among adolescents are on the decline, with 2018 rates 11% lower than in 2015-2016. This is attributed to improved access to reproductive health services, increased contraception use, and public health education.[70,71]

While one of the goals of this Plan is to minimize the impact of OCs on breast cancer risk, it is important to support women's autonomy around their reproductive health. This should include providing unbiased information on the risks and benefits of oral contraceptives and other birth control methods.

Hormone Replacement Therapy

As of 2010, approximately 64 million women in the United States were post-menopausal.[69] As many as 85% of women experience some symptoms during menopause,[72] which can include hot flashes and night sweats; vaginal atrophy; and changes in sleep, mood and sex drive.[25] For some women, these changes are extreme and significantly affect their quality of life. The use of conjugated equine estrogen (CEE) was introduced in U.S. in 1942 to help manage these symptoms,[25] and treatments have evolved significantly over time.

Until 2002, the use of combined estrogen plus synthetic progestin (E + P) hormone therapy was recommended to counteract peri-menopausal symptoms and decrease the risk of developing some chronic diseases such as cardiovascular disease and osteoporosis. However, two significant clinic trials released results between 2002 and 2003 that indicated increased risk of breast cancer and stroke with these therapies.[73,74] Because of these trial results, the prevailing wisdom about HRT shifted, use of this form of HRT dropped dramatically and quickly, and the result was a significant drop in the rate of breast cancer. Ongoing follow up of the women recruited for these studies continue to enhance our understanding of menopause, HRT use, and health risks and behaviors of older women.[75,76]

Through a California statewide registry and California Health Interview Survey of almost 3 million women, researchers confirmed that combined HRT increases the risk of breast cancer in post-menopausal women, and that stopping use of the combination pill leads to decreased risk of developing breast cancer. Decreased incidence in breast cancer was highest (22.6%) in groups with the greatest decline in using HRT, reducing to 13.9% in moderate HRT use, and smallest (8.8%) with least decline in HRT use.[77]

Most recent recommendations suggest that short-term use of HRT can be safe for many women. The Endocrine Society's guidelines suggest that short-term use may be safe for many women under age 60 who are fewer than 10 years from the onset of menopause.[78] They recommend a shared decision-making approach between the health care provider and each woman and that health care providers screen for both cardiovascular and breast cancer risk as part of this individualized planning.[78] While short-term hormone use may be acceptable for symptom management,[79] researchers and medical professionals agree that prescribed hormones are not recommended to prevent chronic disease, due to lack of efficacy and other risks.[78,80]

Standard formulations offer a set dosage and purity of active hormones. Considerable interest in bioidentical formulations has emerged since 2003, with the assumption that specially compounded formulations, usually from estrogenic plant-based sources (phytoestrogens), could have fewer risks. However, these formulations are less consistent and the American College of Obstetricians and Gynecologists recommends against their use.[79] The National Institutes of Health's National Center for Complementary and Integrative Health website summarizes the research and guidelines on bioidentical, compounded formulations and other complementary therapies,[81] reflecting similar conclusions.

As the science review indicates, most of the data on HRT is based on studies of primarily White women. Research needs to consider women of all ethnic and racial backgrounds. Almost no research exists on the impact of hormone therapies for transgender people, whether androgen therapy for female to male transitions or estrogen therapy for male to female transitions.

INTERVENTIONS

Overarching Goal: Better understand how various forms of pharmaceutical hormone treatments impact breast cancer risk and provide clear public education and health care provider guidelines on how to minimize breast cancer risk while using hormone treatments.

Intervention Goal 1

Create comprehensive educational materials that incorporate current research on hormonally active medications, including the potential risks such as breast cancer.

Objective 1: Provide education to women in the pre-menopausal range about the natural process of menopause, potential menopausal symptoms and ways to ameliorate or manage those symptoms without hormone therapy.

Objective 2: Provide unbiased information to women in California on the risks and benefits of oral contraceptives and other birth control methods.

Intervention Goal 2

Provide ongoing education to health care providers who prescribe hormones and ensure they provide accurate patient counseling regarding hormone therapies and the use of oral contraceptives, including discussing the benefits and potential risks, such as breast cancer risk.

Objective 1: Educate health care providers about the association between oral contraceptives and hormone replacement therapies (including bioidentical formulations) and breast cancer.

- **Strategy 1:** Support health care providers by providing education regarding alternative approaches to manage menopausal symptoms.
- **Strategy 2:** Provide guidance on dosage and duration of HRT when other symptom management approaches are not successful, including referencing recommendations from professional organizations (e.g., American College of Obstetricians and Gynecologists).
- **Strategy 3:** Provide guidance on optimal dosage and duration of oral contraception use to minimize breast cancer risk.

Intervention Goal 3

Fund and support research that expands our understanding of menopause and the effects of hormone therapies for different populations and in different contexts, particularly as this pertains to breast cancer risk.

Objective 1: Support research that expands our understanding of the natural trajectories of menopause in order to support deeper understanding of the experience of menopause, symptoms, and women's needs.[82]

Objective 2: Support research into optimal OC and other birth control methods that minimize breast risk.

Objective 3: Support research that considers race in terms of HRT and oral contraceptive usage and breast cancer risk (including duration, breast cancer subtype, and age at first use).

Objective 4: Support research that rigorously tests the usage of bioidentical compounds as HRT alternatives, explores the mechanistic impact of progestin on the breast, and considers potential impact of infertility drugs on breast cancer risk.

Objective 5: Support research that deepens understanding of the health effects of puberty blockers and hormones that support transitioning by transgender persons, including the impact of hormone therapy on breast cancer risk.

- **Strategy 1:** Develop studies that affirm individuals' gender identities, while understanding the health risks of long-term hormone use and how to mitigate them.

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Physical Activity

Science Summary

Physical activity reduces risk of both pre- and post-menopausal breast cancer, with vigorous physical activity being the most protective.

What the Foundational Documents Say

The IOM report[1] listed physical activity as a probable preventative factor against post-menopausal breast cancer based on the conclusions of the 2007 WCRF/AICR report, which was further confirmed by the more recent 2018 WCRF/AICR Continuous Update Project (CUP) report.[2] This report on diet, nutrition, physical activity, and breast cancer found:

- strong evidence that undertaking vigorous physical activity (e.g. running or fast cycling) decreases the risk of pre-menopausal breast cancer;
- limited evidence that being physically active (including occupational, recreational, walking, and household activity) may decrease the risk of pre-menopausal breast cancer; and
- strong evidence that being physically active (including vigorous physical activity) decreases the risk of post-menopausal breast cancer.

The Current State of the Evidence

The 2018 WCRF/AICR report[2] conducted a systematic literature review of physical activity and breast cancer incidence, which included only randomized controlled trials, cohort, and nested case-control studies published before 2017.

The literature reviewed here includes observational (case-control and prospective cohort) studies as well as other epidemiological studies on physical activity and breast cancer from 2012 to 2018—including those cited in the WCRF/AICR report. The findings broadly supported the conclusions of the WCRF/AICR CUP (2018), with some additional details.

Sedentariness/Lack of Physical Activity

Physical inactivity, often described as sedentariness, has been related to a 1.5–2.8 times higher risk of breast cancer compared to regularly active women in a number of studies.[3,4,5,6] In one study, increased sedentary time was associated with an 80% increase in breast cancer risk independent of whether the woman participated in some moderate-to-vigorous activity.[7] Another study, which focused on occupational sedentariness, found increased risk of breast cancer compared with mixed or non-sedentary occupations.[8] A study of Black women found higher total time spent sitting (≥10 versus <5hrs/day) was associated with increased breast cancer risk, with stronger associations for hormone receptor-negative tumors. Sitting 10 or more hours a day was associated with increased risk, regardless of physical activity level.[9]

Other studies have not found associations between breast cancer and sedentary behavior.[10,11,12] However, a number of country-specific studies have concluded that between 5% and 18% of breast cancers in the population could be attributed to physical inactivity,[13,14,15,16,17] and that meeting the WCRF/AICR physical activity recommendations could ameliorate this increased risk.[18]

Racial Differences

Studies examining physical activity and breast cancer risk by race or ethnic origin are sparse, though some data are emerging on Black women:

- In a nested case-control study from the Southern Community Cohort Study, increased time in sedentary behaviors was associated with significantly increased odds of breast cancer among White women but not among Black women. Similarly, higher total physical activity decreased breast cancer risk among White women but not Black women. This difference was magnified when the analysis was limited to post-menopausal breast cancer. However, among Black women, those with the highest level of sports/exercise had a 27% reduced risk of breast cancer compared to those reporting no sports/exercise in the previous decade, although due to low numbers in the study, the finding was marginally significant.[19]
- In other studies, more than two hours per week of vigorous activity by Black women was associated with decreased risk of breast cancer,[20,21] as was higher adherence to the WCRF/AICR physical activity recommendations.[22]
- A study of indigenous African women in Nigeria, Cameroon, and Uganda found that physical activity at any intensity was significantly associated with up to 60% reduced breast cancer risk in both pre- and post-menopausal women. This inverse association was strong for lean women, and less strong but still significant for overweight women. Among obese women, physical activity did not affect breast cancer risk.[23]

Subtype Differences

Recent studies have stratified data by tumor receptor subtypes. Physical activity appears beneficial among all subtypes, but many studies have found the effects are stronger for hormone receptor-positive than for hormone receptor-negative tumors.[24,25,26,27,28,29,30] In contrast, two studies did not see significant differences in the association with decreased risk across different ER/PR subtypes.[31,32] One study looking at the androgen receptor status of tumors (an aspect rarely considered in studies) found that physical activity decreased breast cancer risk by 33% in AR- tumors but did not significantly affect AR+ tumors.[33] More research is needed to determine this effect.

Nuances and Emerging Considerations

Age at Activity

A number of studies have indicated that although physical activity at any age is beneficial, higher physical activity during adolescence and early adulthood is strongly protective against breast cancer including among BRCA1 and 2 mutation carriers.[34,35,36,37,38]

One study found that women who had been athletes in the past had a 40% reduced risk for developing breast cancer during 15-year follow-up. The risk of developing breast cancer was almost twice as high in non-athlete groups.[39]

Vigorous Versus Moderate Activity

Recent studies have also strengthened the WCRF/AICR conclusions that vigorous activity is more protective. One study found that the recommended 10 Met-hours per week was associated with a 4% reduction in breast cancer risk.[40] A metabolic equivalent of task (MET) is a metabolic unit used to quantify the intensity of physical activity, which is defined as the ratio of the metabolic rate during exercise to the metabolic rate at rest. The breast cancer reduction role of leisure time physical activity dropped dramatically below the recommended 10 MET-hours per week. The studies cited above on effects in Black women also support a more protective role of vigorous physical activity.

Figure 9.

Moderate-intensity Physical Activity (Approximately 3-6 METs) Requires a moderate amount of effort and noticeably accelerates the heart rate.	**Vigorous-intensity Physical Activity (Approximately >6 METs)** Requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate.
Examples of moderate-intensity exercise include:	Examples of vigorous-intensity exercise include:
• Brisk walking	• Running
• Dancing	• Walking / climbing briskly up a hill
• Gardening	• Fast cycling
• Housework and domestic chores	• Aerobics
• Traditional hunting and gathering	• Fast swimming
• Active involvement in games and sports with children / walking domestic animals	• Competitive sports and games (e.g. Traditional Games, Football, Volleyball, Hockey, Basketball)
• General building tasks (e.g. roofing, thatching, painting)	• Heavy shovelling or digging ditches
• Carrying / moving moderate loads (<20kg)	• Carrying / moving heavy loads (>20kg)

Source: World Health Organization

https://www.who.int/dietphysicalactivity/physical_activity_intensity/en/

Interactions

A number of interactions are beginning to be examined in recent studies:

- Body Weight: Studies looking at the interaction of physical activity and body weight on breast cancer risk have provided mixed results. One study found that the protective effects of exercise were mainly seen in women who were a healthy weight and not among women who were the overweight and obese.[42] Another study found that the reduced breast cancer risk in women working in active jobs was strongest among overweight, post-menopausal women with ER+ tumors.[43]
- Hormone Replacement Therapy (HRT now termed Menopausal Hormone Therapy): A large meta-analysis of studies found that the protective effect of physical activity in post-menopausal women was confined to women who never used HRT.[32]
- Diabetes: One case-control study of women in Mexico found that moderate-intensity physical activity could substantially ameliorate the increased breast cancer risk observed in diabetic women.[44]

Take-Home Message

- Physical activity at any age is protective against breast cancer and should be facilitated from childhood through adulthood by systemic policies at local, regional, and national levels.
- Vigorous physical activity is more protective but even moderate physical activity can significantly reduce breast cancer risk.

This cannot be overstated: Californians need more physical activity.

Physical Activity: Context for Interventions

A recent study by UCLA Center for Health Policy Research found that only 31% of children ages 5-11 and 18% of adolescents ages 12-17 in California meet the physical activity guidelines of engaging in at least one hour of physical activity every day. Of particular importance to breast cancer prevention, girls aged 8-17 were considerably less active than boys the same age.[46]

The U.S. Office of Disease Prevention and Health Promotion found that the amount of activity adolescents get is actually declining. Between 2011 and 2017 U.S. adolescents who met physical activity guidelines declined from 28.7% to 26.1%. Among adolescents, no racial or ethnic group has achieved the Healthy People 2020 physical activity goal of 31.6% meeting the guidelines. Specific to adolescent females, 18.5% met physical activity guidelines in 2011, but only 17.5% did in 2017.[47]

These rates are troublingly low. Physical activity is critical to a child's overall development and ability to learn and thrive.[46] Specific to breast cancer prevention, low physical activity rates do not set girls up for life long healthy habits: high childhood activity levels is a key predictor of a high level of adult physical activity.[48]

A survey of schools in all California counties found, on average, there were only 0.6 physical education (PE) teachers for every 500 students. Half (51%) of districts did not have elementary PE teachers, and districts with more Black and Latino youth were disproportionately lacking in PE teachers. Having more PE teachers per students is associated with increased student fitness.[49] Exploring physical fitness test results[50] by county wealth[51] also demonstrate that there are noticeable distinctions, with wealthier counties tending to have kids performing at higher fitness levels than poorer counties.

While our education system is already stretched thin and underfunded,[52] our schools need to do better. California needs to fund programs that offer equitable access to physical activity that engages all kids in moderate to vigorous activity. It is especially important to engage girls in activities they enjoy. This is a critical investment in setting the compass of girls' health for the rest of their lives.

Physical Activity Versus Exercise

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure.

Exercise is a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.[45]

A major concern for the sedentary behavior of children is the huge increase in screen time—including both TV watching and new digital media such as mobile devices. Research shows that 63% of U.S. children spend over two hours a day on recreational screen time,[53] and that screen time begins as early at 4 months of age.[54] Limited screen time does provide some benefits, however research shows that the amount of screen time U.S. children and adolescents are engaging in is significantly higher than health professionals recommend and can lead to numerous negative outcomes, including increased sedentary behavior, obesity, lack of recommended sleep time, and increased risk of attention problems, anxiety, and depression.[55] The American Academy of Pediatrics has issued guidelines for age appropriate levels of screen time.[54] More education of parents about the risks of excessive screen time, including its impact on reduced physical activity, is critical.

Physical activity appears especially breast cancer protective for post-menopausal women.[56,57,58,59] Adult women in California also fall woefully below physical activity recommendations. In 2018, U.S. Department of Health and Human Services (HHS) increased their federal physical activity guidelines to recommend that, for substantial health benefits, adults should sit less and get a weekly minimum of 150–300 minutes of moderate intensity or 75-150 minutes of vigorous physical activity or a combination of both, and do strength training twice per week[60] (this reflects a recommendation of doubling both moderate and vigorous activity from the 2008 standards).[61] Yet, according to a 2014 CDC report, less than 25% of Californians met even the lower 2008 physical activity guidelines.[62] Of women aged 18-64, only 19.1% hit those goals. Having a job was not the major barrier—21.5% of working women in California met the goals whereas only 15.5% on non-working women did.[63]

As discussed elsewhere in this Plan, barriers to physical activity are often more pronounced in communities of color. New research suggests that racism reduces people's available time for exercise and other activities due to factors such as slower access to services, less leisure time, discrimination leading to longer times to finds jobs or apartments, and many other aspects of daily life.[64]

Addressing many of the other societal and structural issues addressed in this Plan can support increased physical activity: built environments that reduce commute times and provide green space, affordable housing, livable wages so people don't have to work more than one job, access to healthy food so they have energy to exercise, and adequate healthcare to ensure they feel well enough to exercise.

Given the promise of physical activity to be a protective factor against breast cancer throughout a woman's lifetime, as well as positively impacting numerous other health concerns, and the abysmally low rates of physical activity for girls and women in California, great emphasis should be placed on developing interventions that support active lifestyles and reduce barriers to physical activity. And as with many risk factors addressed in this Plan, physical activity is interrelated with several others, such as "Body Weight" and "Social and Built Environment;" combining interventions across issues is likely to be even more effective at reducing breast cancer risk.

Community Input on Physical Activity

Throughout the community listening sessions, many barriers to physical activity were identified including that people need access to green space, safe neighborhoods, walkable and bikeable neighborhoods, childcare support, and time outside of work that is not in competition with other responsibilities such as child or elder care.

In addition to these factors, stories from the Central Valley revealed a specific concern: Valley Fever. Valley Fever is caused by naturally occurring fungus found in dirt which, when disturbed through activities like construction or agriculture, becomes airborne. Symptoms vary widely, but the fungus usually infects the lungs and can cause respiratory symptoms including cough, fever, chest pain, and tiredness.[65] Valley Fever can go away naturally or with treatment, though some cases require extended treatment and hospitalization. Many people we met indicated that fear of Valley Fever kept them from exercising outdoors or encouraging their children to play outdoors. That, coupled with extreme heat in the summer and an overall lack of accessible and affordable indoor spaces for exercise, are significant barriers to ensuring people get enough physical activity in their daily lives. Climate change may make Valley Fever worse, and agricultural workers are especially hard hit by the disease.[66]

How much physical activity do we need?

While no clear recommendations exist on how much exercise girls and women need to specifically reduce breast cancer risk, the new general guidelines from the U.S. Department of Health and Human Services (updated in 2018)[60] serve as a sensible guide for all Californians:

- **Children age 3 to 5**: Daily general physical activity (a minimum of 3 hours of activity) at all intensities.
- **Children age 6 to 17**: A minimum of 60 minutes per day in moderate to vigorous activity (mostly aerobic complimented with strength and bone building activity).
- **Adults**: Sit less; a weekly minimum of 150–300 minutes moderate intensity OR 75-150 minutes vigorous OR a combination of both; strength training twice per week.
- **Older Adults**: Follow the Adult recommendations within one's own relative fitness level and within the recommendation for any chronic conditions (see following); practice balance and strength training.
- **Adults with Chronic Conditions**: Avoid inactivity; consult with a health care professional regarding appropriate exercise mode, duration, intensity, and frequency.

INTERVENTIONS

Overarching Goal: Encourage and support regular physical activity throughout the life course by addressing personal, cultural, and systemic barriers.

Intervention Goal 1

Develop strong habits in children and adolescents to support a life-long practice of physical activity.

Objective 1: Enhance physical activity and education requirements in schools.

- **Strategy 1:** Increase physical education standards, including both actual physical activity and education about its benefits, to match the Institute of Medicine's recommendation of 150 minutes per week for elementary school and 225 minutes per week for middle and high school.[67] Current California standards for duration of physical education are 100 minutes per week for elementary school[68] and 200 minutes per week for middle and high school.[69]
- **Strategy 2:** Increase high school graduation requirements to require 4 years of physical education, a significant step up from current requirement of only two courses.[70]
- **Strategy 3:** Ensure all schools have a sufficient number of physical education teachers who are adequately trained in physical education in addition to teacher credentials[70] and provide adequate funding for physical education throughout all years of public education.
- **Strategy 4:** Implement policies at the state, county, and school board levels to limit screen time in childcare centers and schools. Provide education on appropriate screen times, benefits of limiting screen time, and strategies to meet those limits to parents and children.[71,72]
- **Strategy 5:** Promote gender, economic, and racial equity in physical education and athletic opportunities, including intramural and interscholastic sports.

Objective 2: Support an integrated school curriculum and policies to include opportunities for physical activity.

- **Strategy 1:** Encourage 3-minute exercise breaks[73] and physical activity integrated curriculum[74] within the class lesson structure.[75]
- **Strategy 2:** Provide training for movement-based learning during teacher continuing education and trainings.[76]

Objective 3: Ensure school districts offer adequate daily recess.

- **Strategy 1:** Amend the education code to prohibit taking away recess as punishment. Current California Education Code section 44807.5 states that teacher authorization to discipline by withdrawing recess may be granted.[77]
- **Strategy 2:** Promote research to identify appropriate recess break durations and frequency by age group.

Objective 4: Promote walking and biking to school. The California Department of Education (CDE) reports that 42% of US students biked or walked to school in 1979 compared to 16% in 2009.[78]

- **Strategy 1:** Collaborate with the PTA chapters to coordinate neighborhood walk to school clubs, groups, and events, and assess safety for walking and biking in school neighborhoods.[79,80]

Intervention Goal 1 (continued)

Develop strong habits in children and adolescents to support a life-long practice of physical activity.

- **Strategy 2:** Promote teacher and administrator walk or bike to school participation to increase role models for active transportation.
- **Strategy 3:** Support community planning efforts that establish and sustain safe routes to school for walking, biking, and public transit.

Objective 5: Keep elementary school homework to a minimum to allow kids time to get physical activity.

- **Strategy 1:** Support accepted guidelines for homework volume: 10 to 20 minutes in first grade, adding 10 minutes for each successive grade.[81] A recent study suggests homework volume may be triple the recommendations.[82]
- **Strategy 2:** Encourage elementary schools to consider adopting a no-homework policy.[83]

Objective 6: Support physical activity outside of the school day.

- **Strategy 1:** Provide public access to schools during off hours for play space.
- **Strategy 2:** Provide gender and ethnic specific role modeling to encourage wide participation in athletic and physical activity programs,[84,85] such as girls' running clubs.
- **Strategy 3:** Collaborate with local organizations in providing after school physical activity programs (See CDE guidelines for after school physical activity programs78). Possible organizations for collaboration include YMCA/YWCA, CANFIT,[86] Boys and Girls Clubs of America,[87] and Bay Area Women's Sports Initiative,[84] among others.
- **Strategy 4:** Since parents significantly influence physical activity in youth,[88] collaborate with PTA for fun after school physical activity opportunities and family play time.

Intervention Goal 2

Design workplaces to support more physical activity and provide access and incentives for physical activity, particularly for sedentary jobs. Ensure all programs are designed in conjunction with workers.

Objective 1: Provide access to affordable fitness options in or near the workplace.

- **Strategy 1:** Encourage workplace onsite wellness programs. Benefits of workplace wellness programs include increased productivity, decreased absenteeism, and reduced healthcare costs.[89,90]
- **Strategy 2:** Develop physical activity programs promoting movement at work. Taking stairs, counting steps, walking/biking/mass transit modes of commute, and other activities may be encouraged through programs.
- **Strategy 3:** Encourage executive and management role models for workplace fitness participation.
- **Strategy 4:** Encourage "walking meetings"—outdoor meetings that happen as people walk rather than sitting at a table.
- **Strategy 5:** Incentivize health insurance coverage for primary prevention strategies such as fitness program costs.

Objective 2: Provide employer support for workforce participation in exercise programs and physical activity.

- **Strategy 1:** Provide employees incentives that encourage and support physical activity including subsidized memberships, paid time off to go to the gym, on-site yoga and/or other exercise classes, and ensure a workload to support this practice.

Intervention Goal 2 (continued)

Design workplaces to support more physical activity and provide access and incentives for physical activity, particularly for sedentary jobs. Ensure all programs are designed in conjunction with workers.

- **Strategy 2:** Prioritize equitable pay for women. In a study of working adults in Finland, higher income was associated with more physical activity in women, both self-reported activity and as measured by pedometer.[91]
- **Strategy 3:** Adopt flexible workplace policies to promote health-supportive employee commutes by encouraging mass transit use, flexible work schedules that accommodate transit schedules, and stipend programs for transit use and allowing remote work options. Longer commutes reduce time spent in physical activity.[92] Mass transit use correlates with increased physical activity.[93]

Intervention Goal 3

Support accessible, affordable and culturally relevant community opportunities for physical activity.

Objective 1: Ensure community centers and other meeting areas are able to offer affordable opportunities for physical activity.

- **Strategy 1:** Initiate mall-walking programs that target mid-life and older adults to increase their physical activity in safe, climate controlled environments as well as encouraging non-competitive social support. Refer to the mall-walking program recommendations provided by the University of Washington Health Promotion Resource Center and the CDC.[94]
- **Strategy 2:** Initiate zoo and amusement park off-hour availability for physical activity programs. San Jose's Happy Hollow Senior Safari[95] is one example where visitors over 50 can enter the park one hour before the general public for free and enjoy outdoor walking as well as other healthy activities.
- **Strategy 3:** Facilitate access to available and convenient mass transit routes and frequency of stops near physical activity program locations.
- **Strategy 4:** Develop local, county, and state partnerships with community-based organizations to promote physical activity and provide funding mechanisms to support community centers and other entities that offer physical activity for people at different life stages.

Objective 2: Improve dissemination of information and access to physical activity opportunities through collaborations between the medical system and fitness industry.

- **Strategy 1:** Encourage medical professionals to recommend physical activity, a practice that has been shown to increase patient physical activity.[96,97]
- **Strategy 2:** Encourage medical professionals to share options for affordable, accessible physical activity option. Silver Sneakers is an example of program that is available to people over 65 years old and who have many Medicare Advantage plans.[98]
- **Strategy 3:** Facilitate collaboration between medical professionals and qualified fitness industry professionals to promote participation in physical activity.

Objective 3: Provide adequate public space such as parks and walkways that are developed in close collaboration with the people who live in the area

- **Strategy 1:** Increase park access in underserved communities.[99] Determine where park deficient neighborhoods exist and focus the Office of Grants and Local Services (OGALS) resources on these areas.[100]

Intervention Goal 3 (continued)

Support accessible, affordable and culturally relevant community opportunities for physical activity.

- **Strategy 2:** Minimize eco-gentrification risks by collaborating with neighborhood residents in small-scale park design and by implementing plans gradually.[101,102]

Objective 4: Create community support that encourages participation in physical activity.

- **Strategy 1:** Increase free community physical activity options modeling existing examples such as Girl Trek (a walking program for Black girls and women),[103] or free, outdoor, public dance programs such as Zumba in the Park,[104] and Lindy in the Park.[105]
- **Strategy 2:** Streamline permit protocols for outdoor commercial physical activity classes and events.
- **Strategy 3:** Build capacity within neighborhoods and communities for physical activity leadership roles through scholarships for certification programs.
- **Strategy 4:** Design physical activity options that integrate community cultural factors such as language, norms, beliefs, and values.
- **Strategy 5:** Enlist corporations and local business to offer neighborhood health grant funding and/or offer equipment and athletic apparel donations and discounts. Examples of existing programs include Allina Health neighborhood connection grants,[106] Title Nine Bra Brigade program[107] and Soles for Souls shoe distributions.[108]

Intervention Goal 4

Conduct more research on the benefits of physical activity, including impacts on breast cancer risk, and effective interventions to increase physical education and activity in all populations.

Objective 1: Promote research on the effect of flexible schedules and remote work on physical activity, productivity, and healthcare costs.

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JOHN DEERE

Place-based Chemicals

Science Summary

Place-based chemical exposures refer to air pollutants, pesticides, water, and soil contamination and industrial pollutants, and many of those exposures have been linked to increased risk of breast cancer.

What the Foundational Documents Say

The World Health Organization (WHO) and the International Agency for Research on Cancer (IARC) estimated that 7-19% of cancers may be attributable to toxic environmental exposures.[1,2] The Endocrine Society states that endocrine-disrupting compounds (EDCs) can affect breast development and make breast tissue more susceptible to cancer,[3] and the Halifax project identifies that some chemical mixtures, including mixtures of EDCs, may have adverse effects beyond exposures to a single chemical. Yet, fewer than 2% of the chemicals registered with the Environmental Protection Agency have been tested to determine breast cancer risk.[4] The Interagency Breast Cancer and Environmental Research Coordinating Committee and CBCRP identify gaps in data about chemical exposures and call for more research into the effects on breast cancer risk.[5,6]

The Current State of the Evidence

Exposures to chemicals from industrial or contaminated sites have been shown to contribute to breast cancer risk.

A study of cancer incidence in National Priority Contaminated Sites in Italy, which are characterized by major industrial activities, found elevated risk of breast cancer among people living in eight of the 14 sites.[7]

One Canadian study found that women living in proximity to steel mills, thermal power plants, petroleum refiners, and pulp mills have an increased risk of breast cancer.[8] Women living near the Tittabawassee and Saginaw Rivers in Michigan, which are contaminated from industrial sources, were also at an increased risk for breast cancer.[9] Dioxin contamination of soil from industrial sites in Italy and Michigan has been associated with an increase in the incidence of breast cancer in regions with higher contamination. In Seveso, Italy, an industrial accident exposed

large portions of the population to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Women in areas with the highest contamination showed a significantly elevated risk of breast cancer after 15 years.[10] In another study of the Seveso population, an increase of all cancers was associated with an increase of serum TCDD, although the association was not found to be significant for breast cancer.[11] Researchers in Michigan found a statistically significant increase in breast cancer incidence in areas with soil contaminated with dioxins from a chemical plant in Midland.[12]

The incidence of breast cancer in Nigeria has shown a steep increase in recent years. Heavy metal contamination in the soil due to rapid industrialization and poorly regulated disposal of hazardous materials may be contributing to this increase. Newly diagnosed breast cancer patients were shown to have higher levels of lead in blood and hair samples.[13] Priolo, Italy has been designated as a contaminated site due to the large number of industrial facilities in the area. These sites may contribute to multiple pollution modalities—water, air, soil—and both male and female residents of this area have experienced increased incidence of breast cancer.[14]

Industrial accidents have led to numerous other exposures, increasing the risk for breast cancer. An industrial accident in Michigan in the 1970s led to the contamination of livestock feed with polybrominated biphenyls (PBB). Milk, meat and eggs were contaminated as a result, and the issue was not discovered for more than a year. Women who had higher levels of PBB in their blood may have had elevated risk of breast cancer. The study found more than double the risk, although the findings were not statistically significant.[15] Another accidental exposure occurred when oil spilled, contaminating a river in Sweden with polychlorinated biphenyls (PCBs). Women who consumed pike or perch more than twice a month had a significantly higher risk of breast cancer.[16]

After the World Trade Center collapsed in New York City on 9/11, citizens were exposed to hazardous substances in the dust and debris. These substances included polycyclic aromatic hydrocarbons (PAHs), heavy metals, and PCBs. Those not involved in rescue efforts but who were in the nearby vicinity, were found to have a significantly increased incidence of breast cancer, among other health issues.[17]

Air Pollution

PAHs are among the most common air contaminants. This class of chemicals is created when materials combust. Sources of exposure include active smoking, environmental tobacco smoke (ETS), indoor wood burning, vehicular traffic, and grilled and smoked meat consumption. In one study, exposure to vehicular traffic did not affect breast cancer risk, but total exposure from indoor sources of PAHs (active smoking, residential ETS, grilled foods, and fireplace use) was associated with 45% higher risk.[18] Studies specifically of indoor fireplaces and wood-burning stoves indicate increased risk with having an indoor fireplace in the home of longest adult residence. Risk increased with more frequent use.[19]

Pollution from traffic sources may be a substantial source of chemical exposure with potential links to breast cancer. Multiple studies have shown a positive association between breast cancer and nitrogen dioxide (NO_2) levels, formed by fossil fuel combustion and used as an indicator of air pollution.[20,21,22] Another study using nitrogen dioxides (NOx), found that areas with motor vehicle density greater than 13 vehicles per square mile had a significantly higher risk of breast cancer when compared with regions with lower density.[23] Long-term benzo[a]

pyrene exposure, a compound found in residential traffic-related air pollution, was associated with a modest increase in breast cancer incidence.[24] A 2019 study of women largely residing in Los Angeles found significantly increased risks of breast cancer among women living within 500m of major roads with NOx, NO_2, $PM_{2.5}$, or PM_{10} (airborne particulate matter of 2.5 or 10 micrometers or less in size). Stronger associations were seen for Black women and Japanese-American women.[25] However, the Danish Nurse Cohort Study did not find an association between breast cancer and $PM_{2.5}$ or PM_{10} or NO_2 in adult women.[26]

A California cohort study modeled exposures to 24 mammary gland carcinogens and found that estimated exposures to the air pollutants propylene oxide and vinyl chloride were significantly associated with breast cancer incidence.[27] In this same group, cadmium and inorganic arsenic, which are both EDCs and carcinogens present in ambient air pollution, were associated with an increase in hormone-receptor negative breast cancer.[28] A U.S.-wide cohort study found higher airborne levels of mercury, cadmium, and lead were associated with a higher risk of post-menopausal breast cancer.[29] Multiple studies showed that metropolitan areas with higher ambient air pollution were associated with a higher breast cancer incidence.[30,31]

Water Contamination

Studies conducted in Cape Cod, Massachusetts showed multiple examples of the link between drinking water contamination and breast cancer. Exposure to tetrachloroethylene (PCE or PERC), which was applied to water mains as a part of repair process, has been associated with an increased risk of breast cancer in those with the highest exposure levels, especially after latency periods of 9-13 years.[32] Water contaminated by landfills or wastewater showed a statistically significant association between exposure and risk for breast cancer.[33]

The drinking water supply at the Camp Lejeune U.S. Marine Corps base in North Carolina was contaminated with benzene, trichloroethylene (TCE), PCE, and vinyl chloride from the 1950's until 1985. A case-control study was conducted to evaluate the possible correlation between the contamination and male breast cancer. The study showed that marines stationed at Camp Lejeune at any time during this period had a 14% higher risk of breast cancer with an earlier age at onset than marines stationed elsewhere.[34] While this finding was not statistically significant, it has drawn attention to the possibility of a link between male breast cancer and water contamination.

A different consideration is water contamination from naturally occurring sources. In Iceland, water naturally heated by geothermal activity is used for heating, bathing, and washing. Geothermal sources also emit gases that may expose the population to potentially toxic gases and heavy metals like radon, sulphur dioxide, arsenic, lead, and mercury. A higher incidence of breast cancer was associated with geothermal activity (living in geothermal heating areas in Iceland). This incidence showed a positive dose-response relationship with number of years of residence and the level of geothermal activity.[35]

Exposures to Agricultural Pesticides

Chemicals used as pesticides in agriculture can impact breast cancer risk. As discussed in the section on consumer chemicals, Dichlorodiphenyltrichloroethane (DDT) is a persistent organic pollutant (POP) that was used widely as a pesticide before being banned in the U.S. in 1972 and has been associated with an increased risk of breast cancer. It is still used in other countries, particularly for mosquito control.

The Chinese agricultural industry used high levels of DDT until it was banned in China in 1983, but residue still persists in the soil. A case-control study showed that women with breast cancer living in the Zhejiang province, an agricultural region, had higher serum levels of p.p'-DDE, a metabolite of DDT. This study showed a relatively low population attributable fraction (PAF-the amount of disease that can attributed to the exposure) at 0.6% overall, but this increased significantly in dense agricultural areas.[36]

The Long Island Breast Cancer Study Project (LICSP) found that women with ER+/PR+ breast cancer were 44% more likely to have reported seeing a fogger truck, which was used to spray DDT.[37] DDT is explored in further depth in the "Chemicals in Consumer Products" section, particularly with regard to early-life/prenatal exposures and later-life breast cancer risk.[38,39]

Mixtures of organochlorine pesticides (OCPs) are also of concern. A study of women living in the Canary Islands of Spain found that the combination of the pesticides aldrin and DDT was found in 24.8% of breast cancer cases and the combination was not found in any healthy controls. The total level of serum OCPs in those with breast cancer was significantly higher than in the sample of healthy women.[40] Studies have also found that wives of agricultural workers who used the herbicide 2-(2,4,5-trichlorophenoxy) propionic acid (2,4,5-TP) and lived close to agricultural sites had a slightly elevated risk for breast cancer.[41] A more recent follow-up of the wives found associations between use of chlorpyrifos, an insecticide that is in use today, and the development of pre-menopausal breast cancer.[42]

While many of the pesticides mentioned have been banned or phased out in the U.S., including DDT, aldrin and 2,4,5-TP, concern about them remains due to the persistence of some of the chemicals and the long latency period of breast cancer. Additionally, many newer pesticides on the market today have either shown concern for breast cancer in laboratory studies, such as chlorpyrifos and atrazine, or have not been adequately studied for potential breast cancer impacts.

Nuances and Emerging Considerations

Disparities

Place-based chemical exposures disproportionately affect already over-burdened populations based on socio-economic status or race/ethnicity. The same communities that lack access to clean water, who live in intentionally food-deprived areas, or lack safe spaces for physical activity, are also likely to work or live in areas of potentially toxic industries. For example, it was found that despite an overall reduction in NO_2 concentrations in the U.S., non-Whites were still 2.5 times more likely to live in an area with an average NO_2 concentration that was above the WHO recommendation.[43]

Windows of Exposure

As discussed in several studies, there may be periods of exposure, such as prenatal development or puberty, during which breast tissue is more susceptible to the effects of chemicals. Research that explores early-life exposures to chemicals is vitally important for understanding the risk of breast cancer from exposures across the lifespan. For example, a study of perfluorooctanoic acid (PFOA) exposures in children aged 8-18 found that higher concentrations of PFOA in blood serum were associated with delayed puberty.[44] As described above, exposure to the pesticide DDT also shows the strongest effect on breast cancer risk during critical windows of breast development.[38,39]

UC Berkeley's Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study, a longitudinal birth-cohort study examining chemicals and other factors in the environment and children's health, enrolled pregnant women living in the Salinas Valley in 1999, with 536 children at birth and another 305 at age 9. These children are now young adults, whose exposures to pesticides and other chemicals have been measured every 1-2 years. The results of this study provide powerful data about the life course effects of chemicals. One study of the cohort found delayed menarche in girls with higher concentrations of polybrominated diphenyl ether (PBDE) flame retardants.[45]

Laboratory studies suggest that prenatal exposures to chemical mixtures from fossil fuel fracking may alter mammary gland development, potentially reducing lactational capacity and increasing risk of breast cancer.[46]

Place-Based Exposures and Other Risk Factors for Breast Cancer

Traffic-related air pollution can influence the onset of puberty and breast density, well-known risk factors for breast cancer. Girls living within 150 meters of a major road had an earlier onset of pubic hair development than those with less exposure.[47] Exposures to both $PM_{2.5}$ (particulate matter smaller than 2.5 μm) and ozone were associated with increased breast density.[48] However, an earlier Danish study found no association between traffic-related air pollution and breast density.[49]

Take-Home Message

- Exposures to chemicals in air, water, soil, agriculture, and industry have been linked to increased risk of breast cancer.
- While results vary by specific exposure, the overall data suggest that policies and other interventions that reduce these exposures at the community and regional level could reduce breast cancer risk.

Place-Based Chemical Exposures: Context for Interventions

California is the world's fifth largest economy[50] and home to a wide range of industries, including agriculture; oil extraction and refining; utilities; technology; manufacturing; shipping, truck and rail distribution; and many others. These industries contribute to our strong economy, but also often lead to numerous harmful chemical exposures. In general, communities of color are hardest hit, with race being a stronger predictor of chemical exposure than income levels.[51,52,53] Yet these higher exposures are no guarantee of increased employment or income from the polluting industries.[54]

Linking exposures from traffic, industries, and other sources to increased risk for breast cancer is not simple, particularly since the lag time between exposure and developing the disease can be decades. However, proactively creating neighborhoods and communities that support people's health, particularly prenatally and in early childhood, is a critical step in long-term disease prevention, including numerous cancers and health outcomes. Lessons can be learned from past exposures, such as the pesticide DDT, where studies have shown *in utero* exposure increased the odds of breast cancer fourfold,[38] and women exposed before age 14 had a fivefold increase in breast cancer risk.[39] This shows the importance of a precautionary approach to public health interventions with early action based on credible science.

According to the American Lung Association (ALA), California has some of the worst air quality in the country. In 2018, ALA found seven out of ten of the smoggiest and six out of ten of the sootiest cities in the country were in California.[55,56] The greater Los Angeles area remains one of the most polluted areas in the country.[57] In response to the high level of air pollution in California communities, the state legislature passed AB 617 (C. Garcia) to create the Community Air Protection Program (CAPP) within the California Air Resources Board (CARB). The first state law of its kind, AB 617 requires local air districts to focus on air quality specifically in overburdened communities and to develop community-led action plans to reduce those exposures. AB 617 also provides resources for the communities selected to create and implement those plans by directing a portion of the cap-and-trade carbon tax revenue to fund CAPP. Since 2017, the legislature has budgeted $495 million for the Program.[58]

Water availability and quality are deep and ongoing concerns in California. Recent droughts have exacerbated the tension among those that need and use water, from individual consumers to agriculture. In response to these concerns, California passed the Human Right to Water law (AB 685) in 2013, becoming the first state in the nation to legislatively recognize that "every human being has the right to safe, clean, affordable, and accessible water adequate for human consumption, cooking, and sanitary purposes." Implementing the law,[59] including improving the quality of drinking water (e.g. eliminating contaminants such as trichloroethylene (TCE), benzene, perchloroethylene (PCE), perchlorate, toluene, and cadmium), will help reduce breast cancer risk in the state.

In 2016, Pacific Environment[60] and the Environmental Justice Coalition for Water[61] led a community-driven research effort to understand how to address the impact of drought on low-income communities in the San Francisco Bay Area. Their report, Drought and Equity in the San Francisco Bay Area,[62] contains key recommendations from this effort, which can serve as a tool for both water managers and community members everywhere as they work to

develop more equitable and resilient communities for the climate of the future. While the focus of this effort was on drought in the San Francisco Bay Area, the approach and findings can be applied to urbanized areas everywhere.

Numerous industries in the state, such as agriculture, fossil fuel extraction and refining, and transportation infrastructure, all contribute to the place-based exposures in the state. In 2017, California produced almost $50 billion in agricultural products, including "over a third of the country's vegetables and two-thirds of the country's fruits and nuts."[63] With that production comes the use of an enormous amount of pesticides. According to the California Department of Pesticide Regulation, 205 million pounds of pesticides were applied over 104 million acres in 2017.[64] These pesticides impact not just workers, but the communities living around the fields. Interventions to address a select number of these industries are provided below.

For the purpose of clarity, this Plan separates place-based exposures and occupational exposures into two different sections. However, it is important to note that people work at all of these polluting industries. When people are exposed to pesticide drift at school or at home, workers in the fields are also being exposed. Someone who works at a port and also lives nearby is exposed to the associated pollution on a nearly 24-hour a day basis. In other words, these place-based exposures are frequently occupational exposures for some portion of the local population. Scientific literature often separates these different realms of exposure, but in reality, there may be little or no distinction for many people. All proposals for reforms in place-based exposures must be linked to significant commitment to ensuring ongoing employment for workers, including providing new safe jobs and job training where necessary.

Reducing air, water, and land-based pollution, and cleaning up legacy contaminated sites, especially in communities of color and Native-American tribal lands, is a critical step in reducing risk for breast cancer and many other diseases and disorders. Such deep, systemic change can also ward off the impending climate disaster and create a just transition to an economy that supports all people's rights without destroying the ecosystems we rely on to live.

Community Input on Place-Based Chemical Exposures

At both urban and rural community listening sessions across the state, participants expressed concerns about air and water pollution and soil contamination. People were worried about being exposed to pesticides without notice or protection if they lived in agricultural areas; cumulative exposures from living and working in or near polluting industries and heavy traffic areas; lack of water in general; and widespread concerns about contaminated water and air, especially from agricultural practices and fossil fuel extraction.

Concerns went beyond what was happening locally—the Central Valley and Sierra foothills, for example, are hard hit with air pollution blowing in from more urban locations like the Bay Area and Los Angeles. The very high elevation of the Sierra Nevada Mountains blocks wind, trapping pollution in these areas until the rains come. Despite the clear need to accurately document the level of air pollution, community members expressed widespread concern about the significant gaps in monitoring air quality and informing residents when air pollution hits dangerous levels.

In nearly all communities, participants described a deep and urgent concern about climate change. People of color and low-income communities are expected to experience some of the greatest impacts from climate change and but also lack the resources to invest in adaptation strategies.[65] There was a clear and consistent call for a just transition—a shift from an extractive economy to a regenerative economy where past harms are redressed and opportunities are shared equitably by *all* people.[66] Across the state, participants believed that their survival depends upon it.

Environmental Racism and Native Americans in California

The industrialization and urbanization of California continues to place significant burden on California's Native peoples. Trauma of past violence affects many people's lives today. Native American communities are working to preserve their language and culture and teach younger generations traditional ways, but environmental degradation makes that challenging.

For example, Sulphur Bank, an abandoned Gold Rush-era mine near Clear Lake, leaches mercury into the soil and water, destroying the Elem Colony Pomos tribe's access to their traditional fish diet.[67] Acorns, a staple of many California tribes' traditional diets and medicines, have been poisoned by pollution and are eaten less as a result.[68] Agricultural pesticides have contaminated reeds used in traditional basket weaving, which are often licked before being woven, thus exposing people directly to these chemicals.[68] The legalization of marijuana use has led to rapid expansion of cultivation, and with that numerous chemicals and pesticides that are polluting waterways.[68]

The state should address and redress the past violence committed against Native Californians and their traditional lands. One important step would be to ensure ecological-scaled protection and restoration of the life systems on which their traditions rely. A step this grand would benefit all Californians.

Climate Disasters, Wildfires, Air Quality, Preparedness, and Worker Safety

In recent years, California has been devastated by increased intensity and frequency of wildfires linked to climate change.[69,70] Hundreds of people have died, billions of dollars of economic loss has occurred,[71] and communities and wildlife habitat have been decimated. The environmental and health impacts[72] are both extensive and still not fully understood. Because of Butte County's Camp Fire in November 2018,[73] Northern California experienced the worst air quality in the world.[74]

With the burning of homes, businesses, vehicles, and many other items, the toxic exposure in the air, water, and soil can be extremely high.[75] Wildfires pose great risk to human and ecological health, not only to first responders (including CA prisoners[76]) fighting wildfires, but also to day laborers and domestic workers who face elevated toxic exposures during clean up and often lack protective gear. Greater education and protection are needed for people who do clean-up and reconstruction in burn areas. Additionally people who make a living working

outdoors, such as agricultural workers, need protection during fires, not pressure to work with the threat of losing their jobs if they do not.[77] In response to a petition filed by worker rights and safety organizations, CAL/OSHA issued an emergency regulation in July 2019 to help protect outdoor workers from wildfire smoke. The regulation requires employers to bring workers inside or provide workers with approved respirators, such as N95 masks.[78,79]

Addressing wildfires requires a multi-pronged approach. Enforcing California's climate change policies is a critical piece of the solution, as is improving the safety of electric transmission lines,[80] managing vegetation load using[81] controlled burns[82] and traditional Native-American burn practices,[83] reducing options for building residential areas in densely forested lands and other approaches. See 2018 Strategic Fire Plan for California[84] for further details.

As noted elsewhere, California is a global leader in policy efforts to reduce climate change. Through the multi-year process of developing guidelines and legislative mechanisms, a number of funding streams have been developed to support programs across the state to reach climate-related goals. California Climate Investments[85] is a statewide initiative that makes funds from the Cap-and-Trade program available. These funds could be used to help communities plan and train for emergency responses and cleanup. Emergency response plans must be culturally and linguistically appropriate. The website includes a database of funding sources available to individuals, organizations, governments, and institutions. Available here: https://fundingwizard.arb.ca.gov/search/cci

California's Mining Legacy

The discovery of gold in California in the 1840's brought rapid changes to the region. Great fortunes were made, waves of immigrants arrived from around the world, and the indigenous populations were both oppressed and decimated through the violent European expansion.

The impact of this time still shapes much of California today. Importantly, the legacy of environmental devastation continues. Abandoned mining sites remain in the Sierra Nevada Mountains, and the toxic legacy from the mining process lingers. Elevated levels of contaminants linked to breast cancer, including arsenic, cadmium, mercury, and others, can be found in the region's soil and water.[86] [87] This toxic legacy continues downstream as well, with measurable contamination in the San Francisco Bay and the fish populations.[88]

Clean-up of contamination is complex. Working with state agencies is complicated and many communities lack the experience to collaborate effectively with them. State agencies are also often unfamiliar with local community groups that they could reach out to for collaboration. Tracking down the responsible parties is required to pursue cleanup, but this can prove challenging. Homeowners can become responsible for clean-up on their property, leading to some people not wanting to know if their land is contaminated. Clean-up at the necessary scale is expensive. Significant work is needed to remediate the toxic legacy of California's mining past.

Sierra Streams Institute,[87] located in Nevada City, has been exploring the link between mining's legacy and breast cancer risk.[89] Their efforts are an exceptional model of building bridges between scientists, community advocates, and policy experts to solve regional ecological and health problems.

INTERVENTIONS

Overarching Goal: Reduce exposures to chemicals linked to breast cancer in air, water, food, and soil, especially focusing on disproportionately impacted communities.

Intervention Goal 1

Build capacity for people to win greater protection from chemical exposures linked to breast cancer.

Objective 1: Create training opportunities for community members to collect data for air, soil, and water quality monitoring (see AB 617 Community Air Monitoring[90] program as an example). Connect these monitoring efforts to state regulatory agencies monitoring efforts and treat data with equal validity if monitoring is conducted to appropriate quality-control standards.

Objective 2: Ensure community members have access to all air, soil, and water monitoring information in their area, whether government or industry data. Include where and when data is collected so community members can judge if the data is truly representative of their experience.

Objective 3: Build capacity for communities to advocate on their own behalf and compete for state and federal funding designated for pollution reduction. See the AB 617 Community Engagement Resources[91] and the text box on California's Climate Change Efforts and Community Funding for ideas of how to access funds for community improvements.

Objective 4: Increase capacity and acceptance of community-based participatory research (CBPR) at California university systems to ensure local communities are involved in the research design, data collection and interpretation, and communicating and disseminating findings. Educate Institutional Review Boards about the importance of advocate/community leadership in qualified research projects related breast cancer and environmental exposures and encourage approval of well-designed CBPR projects.

Intervention Goal 2

Strengthen California's institutions that can and should be protecting people from exposures linked to breast cancer and other diseases. (For more information on state agencies see the California Environmental Justice Alliance's Environmental Justice Agency Assessment 2018 report.[92])

Objective 1: Hold the California Environmental Protection Agency (CalEPA), and specifically the Department of Toxic Substance Control (DTSC), accountable to operate more effectively and in coordination with local communities.

- **Strategy 1:** Hold agencies and agency staff accountable, through legislative oversight and strong agency leadership respectively, for exercising their responsibility to reduce exposure to harmful chemicals and ensure clean-up of legacy contamination sites.
- **Strategy 2:** Create a DTSC governing board that includes representatives of impacted communities to ensure transparency and timeliness in decision-making on permitting and regulatory enforcement activity and ensure those decisions and actions prioritize the health of those most directly affected.
- **Strategy 3:** Reform enforcement laws and practices to include significant consequences that will serve as meaningful deterrents to industries violating environmental laws and regulations.

Intervention Goal 2 (continued)

Strengthen California's institutions that can and should be protecting people from exposures linked to breast cancer and other diseases. (For more information on state agencies see the California Environmental Justice Alliance's Environmental Justice Agency Assessment 2018 report.[92])

- **Strategy 4:** Fully fund and implement the various laws within CalEPA, for instance the Hazardous Waste Control Law and the Pollution Prevention & Green Technology program, which are designed to reduce or eliminate the use and release of hazardous chemicals and protect communities from harmful exposures.
- **Strategy 5:** Ensure the state water and air boards are accountable and responsive to local communities and effectively protecting public health, including fully implementing CA's Human Right to Water[59] and Community Air Protection Program (AB 617 – see above) programs.

Objective 2: Hold the Department of Pesticide Regulation (DPR) accountable to operate more effectively and exercise its responsibility to reduce exposure to harmful chemicals.

- **Strategy 1:** Require DPR to convene Scientific Review Panels to address the backlog of pesticides designated as Toxic Air Contaminants. Ensure the panel members do not have financial conflicts and are not predominately industry scientists.

Objective 3: Reform the Geologic Energy Management Division, formerly known as the state Division of Oil, Gas, and Geothermal Resources, to ensure the agency acts in the public's interest, not the interests of the oil and gas industry.

- **Strategy 1:** Fully implement reforms recently signed into law by Gov. Newsom, including AB 1057, which transforms the agency's mission to consider public health, safety, and environmental concerns.
- **Strategy 2:** Institute a strong conflict-of-interest policy that applies to all agency staff.

Objective 4: Support the Biomonitoring California program,[93] specifically providing adequate and stable funding to conduct statewide biomonitoring studies, biomonitor potentially highly exposed populations, identify inequities based upon race/ethnicity and socioeconomic status, and assess the efficacy of interventions.

Objective 5: Align environmental and occupational legally permissible chemical exposure limits to ensure that workers are protected.

- **Strategy 1:** Require DTSC, DPR and Cal/OSHA to more systematically assess the risks and recommend protections for people with occupational exposures to chemicals[94] in recognition of the exceptional exposures many workers are subject to on a regular basis. This is particularly an issue for working women of child-bearing age.
- **Strategy 2:** Require the Office of Environmental Health Hazard Assessment (OEHHA) and DTSC to consistently consider workers as a 'vulnerable population' for protection during their risk analysis and regulatory decisions.

Objective 6: Provide outreach, education and training to ensure community groups know how to effectively engage with, and advocate within, government agencies.

Intervention Goal 3

In accordance with California's recognition of the human right to water, expand the State's capacity to ensure safe (free from chemicals linked to breast cancer), adequate, and affordable water for all California residents, regardless of whether they live in cities, towns, or unincorporated areas.

Objective 1: Improve access to clean, adequate, affordable drinking water, especially for the most marginalized communities, including unincorporated areas.

- **Strategy 1:** Call on the State and Regional Water Boards to expand the list of contaminants to be tracked and regulated to include a broader list of chemicals linked to breast cancer.
- **Strategy 2:** Improve water quality monitoring to ensure people are not exposed to harmful chemicals and contaminants, including incorporating the results of high-quality community scientists' monitoring data in regulatory decision-making.
- **Strategy 3:** Support local and regional efforts to promote residential, municipal, and industrial water conservation and protection.
- **Strategy 4:** In areas where drinking water is not safe, ensure adequate funding so water can be either filtered or brought to schools and other central community meeting areas in adequate supply to meet people's needs without passing on additional expenses and minimizing other environmental concerns, such as plastic water bottle pollution.
- **Strategy 5:** Invest in infrastructure to support water delivery to all California residents, including ensuring designated funding from water bonds to support water access in traditionally disadvantaged communities, such as unincorporated areas, and that water allocation does not degrade ecosystems that Native Californians and others depend on.
- **Strategy 6:** Develop funding mechanisms to ensure septic tanks are properly maintained.
- **Strategy 7:** Remove barriers and provide financial assistance to individuals and businesses that want to set up rainwater catchment systems and provide education on how to maintain and operate them.
- **Strategy 8:** Adequately fund groundwater monitoring and soil clean-up, especially in areas where people rely on wells for their water source.
- **Strategy 9:** Fund the monitoring and, if needed, replacement of pipes and other equipment to ensure water is not contaminated in transit.

Objective 2: Increase regulations of California's industries that use and/or pollute existing water supplies, including surface and ground water, and set enforceable goals for water conservation and reductions in pollution discharge.

- **Strategy 1:** Identify industry-specific best practices for water conservation, modeled, in part, after successful energy efficiency efforts and provide technical, and where appropriate financial, assistance for adopting those practices. Address critical issues such as incentivizing water conservation and adopting better pricing policies for water and wastewater. [96]
- **Strategy 2:** Adopt aggressive measures to reduce industrial water pollution.
- **Strategy 3:** Ban the use of contaminated water to irrigate agricultural crops, especially water that has been used to extract fossil fuels.[97]

Objective 3: Protect and restore ecological and hydrological systems.

- **Strategy 1:** Develop and support forward-thinking land use planning and promote large-scale ecological restoration that protects critical water supplies.
- **Strategy 2:** Clean up legacy soil contamination by industrial practices, including Superfund sites, radioactive waste, and site-specific contamination (see text box on California's Mining Legacy as an example). Where possible, ensure that the responsible polluter pays for the cleanup.

Intervention Goal 4

Improve air quality and air quality protections to reduce exposures to air pollutants linked to breast cancer.[98] (Also see "Social and Built Environment" section of this Plan for additional interventions linked to air quality).

Objective 1: Enhance air quality monitoring and measurement, particularly in low-income neighborhoods and communities of color.

- **Strategy 1:** Amend air quality standards to include regulation of substances linked to breast cancer, including endocrine-disrupting compounds.
- **Strategy 2:** Ensure adequate and functioning air monitoring stations near major industrial and traffic sources, as well as in residential neighborhoods, to provide an accurate assessment of air pollutant exposures by neighborhood.[99] Include data captured by community air monitoring efforts, such as the IVAN Air Monitoring program in Imperial Valley.[100] Also include monitoring ambient air for outdoor workers, such as construction and agricultural workers, or open-air warehouses.
- **Strategy 3:** Support equitable enforcement of the California Air Resources Board's Community Air Protection Program (AB 617),[101] which provides funding to reduce air pollution exposures in highly impacted communities. The program includes community air monitoring and community emissions reduction programs and greater transparency and availability of air quality and emissions data. Ensure resources from AB 617 support capacity building in communities so the funding supports the economic, as well as ecological, health of the community.
- **Strategy 4:** Develop regional approaches to addressing air quality. Many affected communities suffer poor air quality that is generated elsewhere. For example, California's topography traps air pollution from major urban areas like Los Angeles and the Bay Area in the Central Valley and Sierra foothills.

Objective 2: Enhance air quality by taking actions to reduce diesel exhaust, exposure to combustion products, particulate matter, and other air contaminants linked to breast cancer.

- **Strategy 1:** Develop, expand, and/or publicize incentives for individuals to use efficient/hybrid/electric cars. See the California Air Resources Board Drive Clean Program for existing incentives.[102] Also develop incentives and/or requirements for cities and counties to offer more electric car charging stations and expand carpooling benefits.
- **Strategy 2:** Adopt local measures that can mitigate potential harmful exposures. For example, improve street-cleaning methods in high-traffic and urban areas to reduce exposures to particulate matter.[103]
- **Strategy 3:** The State of California currently has an idling regulation[104] for commercial heavy-duty diesel vehicles and school buses,[105] but lacks idling regulations for passenger vehicles. Existing idling regulations should be strengthened and better enforced, and passenger vehicle idling should be regulated, especially near schools and other areas near children. See Idle-Free California[106] for more details.
- **Strategy 4:** Facilitate, through requirements and incentives, faster transition to cleaner diesel engine technologies, including in trucking, shipping, port operations, and trains. Ensure the financial burden for transitioning diesel truck technologies falls on employers and provide state financial support for individual truck drivers that are categorized, sometimes erroneously, as independent contractors.

Intervention Goal 4 (continued)

Improve air quality and air quality protections to reduce exposures to air pollutants linked to breast cancer.[98] (Also see "Social and Built Environment" section of this Plan for additional interventions linked to air quality).

- **Strategy 5:** Continually strengthen and fully enforce The California Air Resources Board's (CARB) Vapor Recovery Program,[107] which controls vapor emissions from gasoline marketing operations (gasoline dispensing facilities or service stations, tanker trucks (cargo tanks), bulk plants, and terminals), where gasoline vapor is a precursor to the formation of ozone and contains benzene, a breast carcinogen.
- **Strategy 6:** Limit wood-fire burning to reduce indoor and outdoor exposure to breast carcinogens.[19] Consider limiting or banning fireplaces and wood-burning stoves in new buildings.

Intervention Goal 5

Reduce exposure to harmful chemicals and pesticides in public areas.

Objective 1: Eliminate the use of harmful chemicals in schools and on public property.

- **Strategy 1**: Go beyond the requirements of California's Healthy Schools Act,[108] which regulates agricultural pesticide use in and around schools, to adopt district and county-level policies that use integrated pest management and other less toxic forms of pest control. See Beyond Pesticides[109] for a list of local school pesticide programs.
- **Strategy 2**: Eliminate use of cleaning products containing hazardous chemicals in schools and day care centers to reduce exposures to children and workers.
- **Strategy 3**: Develop municipal ordinances to restrict or eliminate pesticide use in parks, recreation fields, public property, and grounds.[110] See examples from across the country and a toolkit by Midwest Pesticide Action Center[111] for ideas to get started.
- **Strategy 4**: Eliminate use of cleaning products containing hazardous chemicals in public buildings to reduce exposures to workers and the public.
- **Strategy 5**: Ensure workers have adequate training to implement new protocols and practices.

Intervention Goal 6

Support public planning processes that strengthen long-term development with a health and equity lens by using the newly revised California General Plan Guidelines[112] as a foundational document for local and regional planning decisions

See "Social and Built Environment" section for more detail.

Intervention Goal 7 Support research to identify harmful chemicals linked to breast cancer, and design intrinsically safer chemicals through green chemistry.	**Objective 1:** Provide additional funding for research on primary prevention and chemical contributions to breast cancer risk by expanding the tobacco tax that funds the CA Breast Cancer Research Program to include all tobacco products, not just cigarettes. **Objective 2:** Increase funding and staffing for the Office of Environmental Health Hazard Assessment (OEHHA) to build capacity to develop a list of known and suspected endocrine disruptors, including those linked to breast cancer, which will allow advocates to push for their removal. **Objective 3:** Create and fund Green Chemistry programs at the University of California and California State University campuses. Require that chemistry classes included green chemistry concepts and practices in the curriculum, and support cross-disciplinary training in toxicology for chemists.

Recommendations for Specific Industries

California is fortunate to have a strong economy based on a wide range of industries. Unfortunately, many of these industries can expose workers and surrounding communities to numerous breast cancer risk factors. While it is beyond the scope of this Plan to suggest a full agenda of how to reform all of California's industries, below are some short and long-term recommendations to address concerns specific to breast cancer risk in a few key industries.

Industries represented here reflect the primary areas of concern discussed during the community outreach phase of the Plan's development: agriculture, fossil fuel extraction and refining, and ports. There is still a great deal of research needed to fully understand women's breast cancer risk from working in and living near specific industries, but no doubt there are many more industries to be concerned about. Exploring Chemical Exposures for California's Women Workers[113] is a project led by the Public Health Institute, California Department of Public Health, and University of California San Francisco that has begun tracking potential occupational exposures in more than 160 occupations women hold in California.

Key to all efforts to reduce breast cancer risk in the workplace includes the ability to hold industries accountable for their impact. All companies must be required to take proactive steps to prevent exposures to breast cancer risk factors as well as be held accountable and financially responsible for any clean up and redress for injured or harmed workers or community members.

Agriculture

Specific Breast Cancer Risks Related to the Industry:

- Pesticide exposure.
- Contaminated drinking water.
- Lack of worker exposure protection and decontamination.

Short-Term Goals:

- Identify and ban all pesticides that are known or suspected breast carcinogens or endocrine disruptors.
- Minimize the impact of pesticide exposure by giving advance notice to nearby residents, educators, and workers before pesticide applications and establishing and enforcing[114] wider buffer zones between agricultural fields and residential areas, schools, health clinics, and other key sites.
- Ensure adequate worker protection, livable wages, collective bargaining power, and freedom from sexual violence and fear of deportation.
- Prohibit the use of wastewater from fossil fuel extraction to irrigate crops.[115]
- Charge large agricultural companies' community-impact fees for water clean-up efforts, community evacuations in case of pesticide accidents, and other emergencies.
- Expand research on the link between pesticide-based farming practices and breast cancer risk.

Long-Term Goals:

- Convert to sustainable agriculture, including promoting pesticide-free organic and permaculture approaches to farming, using integrated pest management techniques, and eliminating water-intensive crops that are not appropriate for California's climate (growing water-intensive crops depletes ground water supplies and results in concentrated exposure to pollutants—potentially breast carcinogens—in drinking water for residents in agricultural areas).

Organizations Leading the Way in California: Pesticide Action Network,[117] United Farm Workers,[116] Californians for Pesticide Reform,[117] California Rural Legal Assistance, Inc.,[118] and others.

Fossil Fuel Extraction and Refining

Specific Breast Cancer Risks Related to the Industry:

- Air and water pollution and soil contamination related to extraction, refining, and combustion of fossil fuels.
- Accelerated climate change.
- Light-at-night and ambient noise from extraction operations.

Short-Term Goals:

- Identify and ban all chemicals used in the extraction or refining process that are known or suspected breast carcinogens or endocrine disruptors.
- Fully implement recent reforms of the Geologic Energy Management Division, formerly known as the state Division of Oil, Gas and Geothermal Resources, and ensure no agency staff have conflicts of interest.[119]
- Enact regulations around extraction times to reduce light and noise pollution.
- Expand the implementation and enforcement[120] of California Accidental Release Prevention Program,[121] Process Safety Management of Petroleum Refineries (focused on protecting worker safety and inherently safer practices),[122] [123] and The Community Air Protection Program (AB 617).[124]
- Create action standards for CARB's Study of Neighborhood Air Near Petroleum Sources (SNPA) program, which monitors air quality in communities. Community air monitoring is important; however, the agency should establish at what level action will be taken.
- Reduce fossil fuel demand by offering incentives for residential, municipal, and industrial buildings to use renewable energy and increasing the percentage of hybrid or electric vehicles.
- Monitor workplace and nearby community exposures to harmful or potentially harmful chemicals near refineries, including biomonitoring people who live and work near the refineries, to understand the long-term benefits from enacting and enforcing more stringent protections.
- Engage community and labor organizations across California to develop a just transition plan to ban new fossil fuel extraction operations and phase out existing operations.
- Provide adequate training for workers transitioning from jobs in fossil fuel extraction and refining to renewable energy. Guarantee new safe jobs are created for low-income communities and communities of color while ensuring that existing communities are not displaced.
- Expand research on the link between fossil fuel production and use and breast cancer risk.

Long-Term Goals:

Transition California's economy out of fossil fuel extraction to a fully renewable energy portfolio that provides safe, high-paying jobs for the local community.

Organizations Leading the Way in California: Communities for a Better Environment,[125] Center for Environmental Health,[126] Center on Race Poverty & the Environment,[127] Earthworks,[128] Pacoima Beautiful,[129] Physicians for Social Responsibility - Los Angeles,[130] Breast Cancer Action,[131] and others.

Ports

Specific Breast Cancer Risks Related to the Industry:

- Air and water pollution from ships, trucks, and operating equipment.
- Light at night and ambient noise.

Short-Term Goals:

- Expand and enforce bans on all truck idling in and around ports, upgrade trucks to cleaner burning diesel engines, and ultimately shift all trucks to electric vehicles or other clean technologies.
- Continue to upgrade ships and piers at both public and private ports to support a requirement that ships shut down their engines while in port and plug into shore-based electricity.
- Reduce or eliminate water pollution by ensuring improved pollution source control from ships.
- Transition port equipment, specifically cranes and forklifts, from diesel to electric.
- Ensure that lighting is positioned and timed so that nearby residents are not exposed to excessive levels of light at night.

Long-Term Goals:

- Transition ships from diesel and into greener fuel sources.
- Implement comprehensive plans to address all air and water pollution at California's 11 major ports. See the San Pedro Bay Ports Clean Air Action Plan 2017[132] as an important model that addresses many important health impacts.

Organizations Leading the Way in California: Natural Resources Defense Council,[133] West Oakland Environmental Indicators Project,[134] Coalition for a Safe Environment,[135] Communities for a Better Environment,[128] and others.

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Pregnancy-Related Factors

Science Summary

Giving birth and having children at a younger age is protective against ER+ breast cancer but not against other subtypes. There is a suggestion of increased risk of triple-negative breast cancer with parity, although breastfeeding is protective against this risk. No well-established association exists between miscarriages or abortions and breast cancer.

What the Foundational Documents Say

As stated in the IOM report, having a first child at an older age or never having children are generally accepted as increasing women's risk of breast cancer.[1]

The AICR Continuous Update Project report specifically states that not bearing children, and first full-term pregnancy over the age of 30, increase lifetime exposure to estrogen and ultimately risk of breast cancer.[2]

The Current State of the Evidence

Recent research confirms the established pregnancy risk factors for breast cancer in global populations and reveals variation by breast cancer subtypes, especially hormone receptor status. Many studies of developing countries are concluding that at least part of the rise in breast cancer in those populations can be explained by later age at first birth and lower total parity of women in more recent generations.[3]

Parity

Parity is the number of pregnancies carried to a viable gestational age. A woman who has never given birth is nulliparous.

Childbearing has been known to influence breast cancer risk for centuries. After a short-term increase in risk during and immediately after pregnancy and, depending on a woman's age at her first live birth, parity provides protection against breast cancer for the rest of the woman's life.[4]

The current consensus is that the first full-term pregnancy irreversibly changes breast tissue to make it less susceptible to cancer.[5,6] Mechanisms are still being elucidated, and may include the influence of pregnancy hormones such as human chorionic gonadotropin (hCG).[5,7]

Studies since 2012 have further confirmed that nulliparous women have a higher risk of both pre- and post-menopausal breast cancer compared to parous women.[4,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25] This has been seen with all categories of age at first live birth and number of pregnancies[26] and with both lobular and ductal cancers.[27] However, a case control analysis of the U.S. Two Sister Study (women with a sister with breast cancer) found no significant association of parity with early onset breast cancer in these women[28] and another study in China found no significant risk associated with nulliparity.[29] Researchers are beginning to look at variations by hormone receptor subtype (discussed below).

Breast cancer risk further decreases with an increase in parity especially with five or more children compared with one or none.[4,6,8,9,16,17,18,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44] One study found an 8% decrease in breast cancer risk for each full-term pregnancy independent of other risk factors and lasting for decades after a woman's last full-term pregnancy.[44]

Studies of twin births suggest that twin pregnancy does not significantly decrease the maternal risk of breast cancer.[45]

Age at First Live Birth

Of all reproduction-associated risk factors, early age at first birth is associated with one of the largest risk reductions and each subsequent pregnancy confers an additional though smaller benefit.[46] It has been speculated that a full-term pregnancy at an early age may reduce the likelihood of tumor initiation whereas a full-term pregnancy at a later age may promote the growth of existing tumor cells.[6]

Older age at first live birth (usually defined as over 25 or 35 years old but sometimes as young as 21 in developing country studies) results in a higher breast cancer risk in both pre- and post-menopausal women across the globe.[8,9,10,11,12,14,23,25,28,30,31,32,41,47,48,49,50,51,52,53,54,55] Risk is increased for both lobular and ductal carcinomas,[27,56,57,58] and in both urban and rural women.[59]

Variation by Hormone-Receptor Subtypes

Since 2012, a number of studies have evaluated the relationship between parity and specific subtypes of breast cancer.

The association between parity and breast cancer differs appreciably for ER+ and triple-negative breast cancers.[60] Most studies have shown that compared with nulliparous women, parous women have a reduced risk for ER+ or luminal breast cancer, but that there is no association for ER- cancers, HER2 overexpressing cancers, or triple-negative cancers (ER-, PR- and HER2-).[40,61,62,63,64,65,66,67,68,69,70,71] This has been seen in both U.S. White and Black women.[72,73]

In some studies, the risk of triple-negative breast cancer has been shown to increase with parity.[74] A 2018 meta-analysis of nine cohort studies found parous women had a lower risk of luminal A-like (ER+ or PR+/HER2-) and luminal B-like (ER+ or PR+/HER2-) breast cancers but a higher risk for triple-negative disease.[75]

Multiparity (3 or more births) is associated with lower risk of ER+ breast cancer in both White and Black women,[76] but in one study of Black women, higher parity was associated with an increased risk of ER-/PR- breast cancer. Higher parity was associated with a reduced risk of ER+/PR+ cancer in these women.[77]

Late age of first birth (after 30 or 35 in most studies) has been consistently associated with higher odds of ER+ breast cancer, but not ER- breast cancer (including triple-negative) or HER2+ breast cancers.[61,63,64,65,66,67,68,71,75] This has been seen in both U.S. White and Black women.[72,78] However, one study found similar results for ER+ and ER- breast cancer with increased risk with first live birth (FLB) at 25 to 29 and no association observed for FLB at age 30 years or older.[79] And a large study of East Asian women found later age at first live birth (after 25) increased risk of all breast cancer subtypes.[73]

Pregnancy risk factors may explain some of the racial disparities in ER-/PR- breast cancer discussed throughout this Plan. A cohort study of White, Black and Latina women in Chicago found that ethnic disparity in ER/PR-negative breast cancer was reduced by approximately 60% after control for socioeconomic status and reproductive factors (parity and age at first birth combined into a single factor).[80]

Reproductive Intervals

A reproductive interval is the length of time between reproductive events such as age at menarche (first period) and age at first live birth or intervals between births.

Studies looking at intervals from age of menarche until first birth have produced mixed results. A number have found that increased intervals increased the risk of breast cancer overall[30,50,81] and of ER+ breast cancer.[79,82] However, a study of Black women found those with a first live birth within 15 years of menarche had increased risk of ER- disease, with no significant associations for White women.[83] On the other hand, a study of U.S. nurses found no significant effect of this interval on either ER-/PR- or ER+/PR+ breast cancer.[84]

Intervals between births may affect breast cancer risk differently depending on age at first birth. Looking at intervals between first and second births, a study in Finland found that overall, a short interval between first and second births (<1.5 years versus +3 years) was associated with significantly decreased risk of breast cancer. However, when disaggregated by age at first birth, in women with the first birth at age 30+, a short interval was associated with a 5.8-fold increased risk of developing breast cancer before 50 years of age and a moderate birth interval (1-5-2.99 years) was associated with a 3.5-fold increased risk when compared to women with a long (3+ years) birth interval. Among women with a first birth before age 30 and breast cancer diagnosed after age 50, a short interval was associated with significantly decreased risk.[85]

Pregnancy-Associated Breast Cancer

Pregnancy-associated breast cancer (PABC) is breast cancer diagnosed during pregnancy and up to two years after pregnancy has ended (in some studies up to five years). There is a transient increased risk in the odds of breast cancer after first birth compared to nulliparous women.[86] Risk decreases as the number of years since the birth increases.[87] Prospective mothers with multiple births and a family history of breast cancer may have an elevated risk of breast cancer during their immediate postpartum period.[88] Older first-time mothers (over 35) are more prone to developing PABC than younger women.[89,90]

However, a Swedish study found that, compared to nulliparous women, risk of breast cancer was decreased during pregnancy and the first year after birth, but increased during the second year post-delivery. This pattern was similar in women with or without a family history of breast cancer. The peak in risk was observed 5-6 years following first birth regardless of family history. No peak was observed after a second birth except in women with a family history of breast cancer.[91]

Abortions (Induced and Spontaneous)

In the scientific literature, miscarriages are often referred to as spontaneous abortions. Data on abortion (induced or spontaneous) and breast cancer is varied and often conflicting.[6] Some of these conflicts may be due to methodological differences—with some studies taking into account subsequent parity and others not, and with differences in conclusions from case-control, cohort, retrospective, and prospective studies.

A 2013 meta-analysis found a significant increase in risk of breast cancer with induced abortions[92] and some retrospective studies and small case-control studies have found positive associations between breast cancer and a history of induced abortion.[22,30,48,93]

However, two more recent meta-analyses have found no association with induced or spontaneous abortions.[94,95] The 2018 study also found no significant effect of induced abortion on breast cancer in nulliparous women. In addition, a Danish prospective cohort of over 25 thousand women separated into three groups (had a child but never had an abortion, gave birth and had an abortion for a later pregnancy, had an abortion first then gave birth) found no association between breast cancer risk and induced abortion, regardless of whether abortion was before or after first birth.[96]

There have also been mixed results from studies of spontaneous abortions (miscarriages). A study of Israeli women with recurrent pregnancy loss (two or more consecutive spontaneous pregnancy losses) had a significantly increased risk of breast cancer.[97] However, a meta-analysis of 15 global studies found no significant association of breast cancer risk for either induced or spontaneous abortion.[94]

A study of Serbian women found that breast cancer risk was reduced among parous women who had a history of any abortion (induced or spontaneous), suggesting that even short pregnancies ending in abortion add to the protection against breast cancer.[98]

Risk associated with abortions and miscarriages may be affected by genetic factors and menopausal status of the breast cancer. A study of Chinese women found an increased risk of post-menopausal, but not pre-menopausal, breast cancer with a history of spontaneous abortion.[93] A French study of BRCA1 and BRCA2 carriers found a doubling of risk of breast cancer for at least three incomplete pregnancies compared to women with zero incomplete pregnancies. This increased risk was limited to incomplete pregnancies before the first full-term birth.[99]

Nuances and Emerging Considerations

Hormone Mechanisms

Researchers have begun to look at how hormone levels during pregnancy may impact later breast cancer risk. Studies in humans have revealed complex relationships that vary with breast cancer subtype and menopausal status at diagnosis. Studies have found that variations in early pregnancy steroid hormones can affect risk of breast cancer, with effects varying with menopausal and hormone receptor status.[100,101]

Studies looking at specific estrogens during pregnancy have found differing effects of Estrone (E1), Estradiol (E2) and Estriol (E3), with a doubling of E1 and E2 associated with a 70% greater risk while a doubling of E3 or the E3/E1+E2 ratio associated with 30% decrease in risk.[102] Excess E2 during pregnancy has also been seen to contribute to mammary gland tumor development in animal studies.[103]

Genetic Interactions

Recent research is looking at genetic variants and effects on pregnancy risk factors with varied, sometimes conflicting, results. More detailed studies may be needed focusing on specific genetic variants and the position of mutations within genes.

Two studies looking at BRCA1 and BRCA2 mutation carriers found that increasing number of full-term pregnancies is protective against breast cancer.[99,104] However, location of the BRCA1 mutation was important: Parity was associated with significantly decreased risk only among women with a mutation in the central region of BRCA1.[99] A meta-analysis of 10 studies on women with BRCA1 or BRCA2 mutations found no association between parity and breast cancer risk.[105]

One study found that young age at first birth protects against early-onset breast cancer in BRCA1 and BRCA2 carriers.[106] However, a pair of earlier meta-analyses found decreased risk of breast cancer in BRCA1 and BRCA2 mutation carriers with older age at first birth.[105,107] Yet another study found little influence of age at first birth on BRCA1 or BRCA2 breast cancer risk.[108]

One study found that though the number of deliveries had a dose-response protective effect on breast cancer; women carrying a specific variant in rs2229712 did not benefit from this protective effect.[109]

Preeclampsia and Pregnancy Induced Hypertension

There is some evidence that women who experience preeclampsia or hypertension during pregnancy have a 10-20% reduced risk of subsequent breast cancer.[110,111,112,113] This association is strongest for women with hypertension in pregnancy who delivered at or post-term.[110]

Obesity

Very few studies have looked at both pregnancy risk factors and risk from being overweight or obese, but those that do indicate some interaction. One study found that nulliparity and being overweight in adulthood may amplify each other's effect on breast cancer risk among women after 70 years,[114] while another found that the adverse effects of later age at first birth were stronger in obese than normal weight women in lobular but not ductal breast cancers.[56]

Interaction with Breastfeeding

Breastfeeding has been shown to have a profound protective effect on breast cancer risk and on the effects of pregnancy risk factors especially on hormone receptor negative cancers.

A number of studies have shown that high parity without breastfeeding is positively associated with ER-/PR- and triple-negative tumors and that breastfeeding ameliorates this increased risk.[115,116,117] This has been seen in Black women, and it has been suggested that the higher incidence of ER/PR- and triple- negative breast cancer in Black women may be explained in part by their higher parity and lower prevalence of breastfeeding relative to White women.[70,77,118] See the section on "Breastfeeding" for more.

Take-Home Message

- Giving birth at any age and having children at a younger age are protective against ER+ breast cancer but not against other subtypes.
- There is a suggestion of increased risk of triple-negative breast cancer with parity. Breastfeeding is protective against this risk.
- There is no convincing association between miscarriages or abortions and breast cancer.

Pregnancy-Related Factors: Context for Interventions

Though the science outlined above shows that early childbirth is protective against ER+ breast cancers, we celebrate that many women today in the U.S. have the freedom and opportunity to choose whether and when to start a family. That freedom has led to an unprecedented and invaluable increase in educational and occupational opportunities for women.

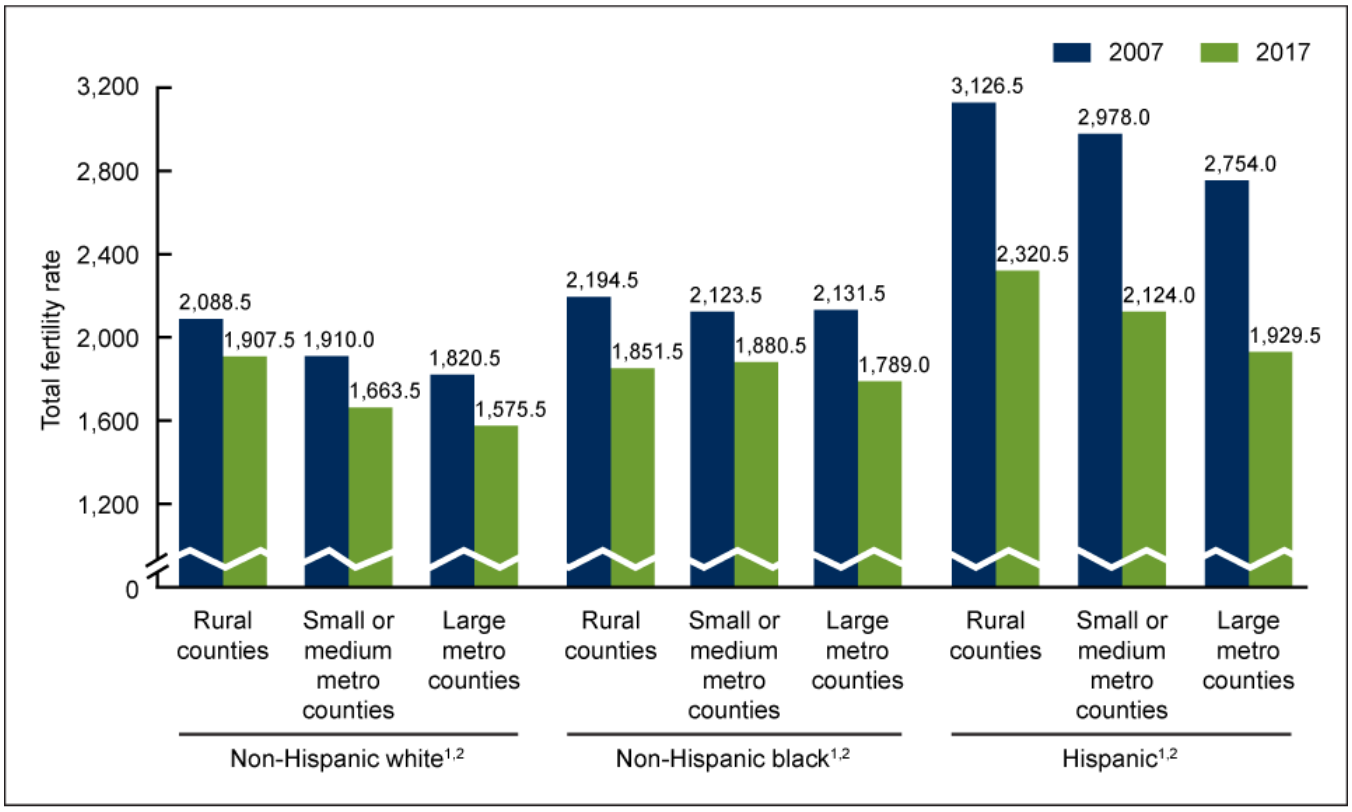
Many very personal decisions and factors contribute to whether and when women give birth. Some women do not give birth, which may be by choice or may be medically determined. Some women wish to have children earlier, but feel unable to do so for social, economic, or career reasons. No woman should be shamed for the reproductive decisions that she makes. The interventions suggested below are aimed at ensuring that women who wish to start a family do not face systemic barriers.

The average age at first birth has been increasing in the U.S. for decades. In 2016, the CDC reported that the average age of first-time mothers increased by 1.4 years from 2000 to 2014, with most of the increase occurring from 2009 to 2014. They also showed that in that time the average age at first birth has increased in all states, with California (along with D.C., Oregon and Utah) having the highest rise of 1.9 years or more. The CDC report concluded that the decrease in the proportion of first births to women under age 20 had the largest impact on this change, while increases in first births among mothers aged 30 and over also contributed to the increase in mean age.

This increase is occurring across racial and geographical groups. The most recent CDC figures show the average age at first birth for women living in large metro areas in the U.S. in 2017 was 29 years for White women, 25.6 for Black women and 25.4 for Latinas. Average ages were lower for each group in smaller metro areas and still lower in rural areas. All of these had significantly increased since 2007.[119]

While personal choice is the major reason for the increase in average age at first birth, systemic barriers to earlier childbirth also have an impact, including a lack of guaranteed parental leave from their jobs, especially paid leave, for both partners (if there are two); the lack of affordable high-quality child care; and the lack, especially during early careers, of flexible work and childcare schedules that take account of family responsibilities.[120]

Figure 10. Mean age at first birth, by race and Hispanic origin and urbanization level: United States, 2007 and 2017 (source: CDC[119])



Parental Leave

In the U.S., the Federal Family and Medical Leave Act (FMLA) entitles eligible employees of covered employers (50 or more employees) to take 12 work weeks of unpaid, job-protected leave in a 12-month period for the birth of a child and to care for the newborn child within one year of birth.[121]

In California, the follow forms of leave are also available:

- **Pregnancy Disability Leave (PDL):** part of the Short-term Disability Insurance (SDI) program—which provides for up to four months off for disability due to pregnancy and childbirth. For a normal pregnancy, the usual period of disability is from four weeks before birth to six weeks after delivery. Employees collect benefits under the SDI during this time and employers are required to allow employees to take this leave while guaranteeing their job.
- **California Family Rights Act (CFRA):** entitles an employee to 12 weeks of leave within one year of the child's birth. This leave runs after PDL and may run after FMLA. It is unpaid unless the employee uses paid vacation time.[122]
- **Paid Family Leave (PFL):**[123] available to new parents who need time to bond with a new child. They are eligible for up to six weeks of PFL benefits (60-70% of normal income up to a cap) within a 12-month period. In 2019, California passed SB 83, which will extend PFL benefits from six weeks to eight weeks for claims starting on or after July 1, 2020.[124]

Some California counties have further supplemented PFL. For example, the San Francisco Paid Parental Leave Ordinance requires employers in the City and County of San Francisco to pay "supplemental compensation" for the full period that a covered employee receives PFL to bond with a child. During the leave period, employers are required to provide supplemental compensation in an amount such that the PFL wage replacement plus the supplemental compensation equals 100% of the employee's gross weekly wage, subject to a cap. The 2019 PPLO Cap is $2,087 per week.[125]

All of this compares unfavorably with other developed countries' policies on paid maternity leave. The Organisation for Economic Co-operation and Development (OECD) data for 2018 (the latest available) reports that while the U.S. had no paid maternity leave at the federal level, Mexico (the next lowest) had 12 weeks of total paid leave, the UK 39 weeks, Germany 58 weeks, and Finland 161 weeks.[126]

Child Care

In 2017 California was the least-affordable state for center-based infant care in the U.S., with an annual cost of $16,542 (60% of a single parent family median income and 18.6% of a married couple family median income).[127] For family childcare for infants, California ranked as the 3rd least-affordable state, with an annual cost of $10,609 (48% of the median income of a single parent family and 12% of a married couple family). The California Department of Education claims to have the most comprehensive system in the nation of childcare and development programs to support low-income families. Funding for fiscal year 2015-16 was $2.4 billion projected to provide childcare to some 450,000 children.[128] Currently under the CalWORKS Childcare Program, to receive subsidized childcare a family cannot earn more than 85% of the state median income. For a family of three in 2018, that amount is $5,467 per month.[129]

INTERVENTIONS

Overarching Goal: Minimize the effect of pregnancy-related breast cancer risk by providing support and removing barriers to women's choices around childbearing.

Intervention Goal 1

Remove systemic barriers to having children for women who wish to do so.

Objective 1: Extend paid family leave in California.

- **Strategy 1:** Extend the duration of paid family leave in California beyond the eight weeks that will take effect in 2020. Examine data from other countries' policies to determine an ideal duration.
- **Strategy 2:** Extend paid family leave to all workers including contract workers and employees of small businesses. Use state funds to avoid a burden on small employers.

Objective 2: Increase provision of affordable childcare to families in California.

- **Strategy 1:** Implement Governor Newsom's goal to make preschool available to every 3 and 4-year-old in California.
- **Strategy 2:** Increase the income eligibility for subsidized childcare, including infant care, to enable more working families to benefit.
- **Strategy 3:** Expand after school care on site for low-income families.

Objective 3: Enable women to continue to work and study after giving birth.

- **Strategy 1:** Extend policies to prevent workplace discrimination against workers to include those with parental responsibilities. Federal Government Employment non-discrimination rules were extended to include parental status by Executive Order 11478.[130]
- **Strategy 2:** Encourage the establishment of childcare facilities in or near workplaces.
- **Strategy 3:** Support flexible school schedules that account for the needs of students with children and provide childcare at schools (high school, college, and post-graduate).
- **Strategy 4:** Support flexible work schedules, telecommuting and other ways of ensuring parents have the ability to be active participants in their children's lives.

Intervention Goal 2

Encourage women to breastfeed their babies for as long as they are able.

See "Breastfeeding" section for more detail.

Intervention Goal 3

Expand research into pregnancy-related breast cancer risk, stratifying by race, ethnicity, and hormone receptor status.

More research needed.

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Tobacco

Science Summary

Tobacco smoke contains a multitude of chemicals that have been linked with increased risk of breast cancer. In addition, evidence suggests both active smoking and passive smoking may lead to increased breast cancer risk.

Foundational Documents

Tobacco smoke contains many different chemical carcinogens and endocrine disruptors.[1] Most of our foundational documents concluded that active smoking is a risk factor for breast cancer. Risk was found to be highest with women who started smoking early on and/or before their first full-term pregnancy.[2,3] A few foundational documents also found evidence to indicate that passive smoking or exposure to environmental tobacco smoke (ETS) increases breast cancer risk,[4] especially in younger, primarily pre-menopausal women.[3]

The Current State of the Evidence

Tobacco smoke contains a host of chemicals that have been found to have carcinogenic and endocrine-disrupting effects, some of which cause mammary tumors in rodents or affect carcinogenic pathways in human breast cells.[5] Smokers have been shown to retain these chemicals in their bodies, with aromatic amines, polycyclic aromatic hydrocarbons (PAHs), and nitrosamines being found in the breast tissue and fluid of smokers.[6] Exposure to the harmful chemicals from smoking is not limited to those who smoke or have a history of smoking. Tobacco exposure is categorized as "Active" for current or former smokers and as "Passive" for individuals who are exposed to second- or third-hand smoke regularly in the home or workplace. The Surgeon General's 2014 report "The Health Consequences of Smoking—50 Years of Progress"[7] concluded that there was sufficient evidence for mechanisms by which cigarette smoking may cause breast cancer and suggestive evidence for a link between tobacco smoke, active smoking, and exposure to secondhand tobacco smoke and breast cancer.

Active Smoking

Risk of breast cancer has generally been shown to increase with increased duration and intensity of smoking. Women who initiate smoking at a young age, before menarche, or their first live birth,[8,9,10,11] are the most vulnerable to the harmful effects of tobacco smoke.[12,13,14,15] Increased risk has also been found for women who start smoking before menopause compared with those who do not.[16] One study found that starting to smoke before menarche, or after menarche but 11 or more years before first birth, were the strongest windows of susceptibility.[14]

Alcohol use has been correlated with cigarette smoking status. Since alcohol is, itself, causally linked to breast cancer risk, it is a common confounding variable for the associations between active smoking and breast cancer risk.[17] Several studies, especially those which focused on breast cancer risk in young, pre-menopausal, or non-parous women, found a relationship between active smoking and breast cancer persisted after adjustment for alcohol consumption.[8,10,11,14,16,18] Other studies found null results for active smoking and breast cancer risk after adjusting for alcohol consumption,[17] with one study finding null results for active smoking overall, but positive associations between active smoking and breast cancer risk when specifically looking at women who started smoking at an early age.[18]

One study on estrogen receptor positive (ER+) breast cancer noted that the chemicals in tobacco smoke have both estrogenic and anti-estrogenic effects. For pre-menopausal women however, it is unlikely that the anti-estrogenic effects overcome the body's high natural estrogen levels during that period. Active smoking was found to increase risk for ER+ breast cancer, particularly for those with long-term, more recent smoking.[6] Despite the anti-estrogenic effects of smoking, one study found that post-menopausal smoking was not a protective factor for breast cancer.[8]

Passive Smoking

The relationship between passive smoking exposure and breast cancer risk is less clear than with active smoking. Even though there is biological plausibility for the harmful effects of ETS, it is much harder to track a woman's lifetime exposure to passive smoking, also referred to as environmental tobacco smoke (ETS); thus, the results from epidemiological studies are less consistent.[19] In general exposure to ETS has been found to be modestly associated with breast cancer with the strongest associations being found in studies of young and pre-menopausal women.[16,17,20,21,22,23,24,25] One study with participants that reported a family history of smoking found that ETS exposure (defined as both household and maternal smoking) during prenatal development, childhood, and adolescence had the strongest effects on later life breast cancer risk.[17]

Nicotine-derived nitrosamine ketone (NNK), which is found in secondhand smoke, can persist in the environment and be absorbed and build up in household items like furniture and carpet. This build up is referred to as "third-hand smoke"[26] and can lead to continuing exposure even without being around active smoking. NNK has been found to potentially cause mammary tumors in animals and in studies with human cells, increase tumor cell proliferation and the transformation of healthy breast epithelial cells into cancer cells.[27,28,29,30]

Nuances and Emerging Considerations

Power and Inequities

A few studies looked at the potential interactions between social inequities and the risk of breast cancer associated with smoking. One study found that ethnic differences were mostly limited to women from Mexico when compared to Whites and U.S. Latinas and Native-American women.[31] Another study that looked at geographic patterns of tobacco purchasing and breast cancer in Black and White women found that even though there was not a significant interaction between tobacco spending and social class or race, there is still evidence to suggest tobacco addiction might result in worse breast cancer outcomes in low-resource and vulnerable populations.[32] Another study demonstrated that there is an association between smoking and luminal breast cancer risk, especially for Black women and women with longer histories of smoking.[33]

Genetic Susceptibility

There has been emerging concern for active smokers with slow NAT2 acetylation genotypes and the potential increased risk of breast cancer. NAT2 is involved in the metabolism and detoxification of aromatic amines, some of which are found in tobacco smoke and have carcinogenic effects.[5] Multiple studies have found that active smoking of higher intensity and longer duration has been associated with increased risk of breast cancer in women with slow NAT2 acetylation genotypes.[5,13,34]

Emerging evidence suggests that nicotine disrupts key regulatory processes in cell division through interactions with the CDC25A gene—a human cell division gene. In response to DNA damage, CDC25A is degraded, which prevents cell division of mutated and abnormal cells. A study using human cells found that when exposed to nicotine, CDC25A has shown increased expression in breast cancer cells, which has implications for disease progression through increased cell division.

Electronic Cigarette Usage

Research into the harmful effects of electronic cigarettes (e-cigs) has only just begun to emerge. E-cigs are thought to carry less risk of harmful side effects because they deliver nicotine through the heating and vaporizing of a liquid instead of burning. However, nicotine is still a carcinogen. In addition to nicotine, e-cig vapors contain undisclosed chemical flavorings and other additives that can interact with the user's body and ultimately cause harm.[35]

Take-Home Message

- Evidence suggests that smoking and environmental tobacco smoke exposures are associated with increased risk of breast cancer due to the carcinogenic and endocrine-disrupting effects of chemicals found in tobacco smoke.
- The persistence of these chemicals in the body and environment raises particular concern for those exposed at high levels, early on in life, and/or for long periods of time.

Tobacco: Context for Interventions

California has a long history of being a leader in efforts to reduce tobacco use. In 1990, San Luis Obispo was the first city in the country to ban indoor smoking in public places.[36] The state followed by becoming the first in the country to ban smoking in the workplace and other indoor public spaces in 1995.[37] In 1998 the ban expanded to include bars, taverns, and gaming clubs.[38] Numerous other laws ban or restrict a wide range of other tobacco-related practices that pertain to advertising, limits on exposures or sales to youth, tobacco-free campuses,[39] and others.[40,41,42]

These restrictions have made a significant impact. In California, the adult cigarette smoking rate declined by 57.4% between 1988 and 2017,[43] with a current rate of 10.1% or about 2.8 million adults.[44] Across the state, adult tobacco smoking is:

- Highest in Native Americans (19.1%), followed by Blacks (17.0%), Whites (11.8%), Hispanic or Latinos (10.2%), and Asian, Native Hawaiian, and Pacific Islanders (7.4%);
- Higher in LGBTQ people (17.4%) than non-LGBTQ (12.4%);
- Higher in men (14.4%) than women (7.8%); and
- Higher in rural areas (14.9%) than urban (10.6%).[44]

One in eight (12.7%) high-school aged youth uses tobacco products, with youth who do not identify as male or female having the highest rates (21.8%). LGBTQ youth use tobacco at higher rates (15.0%) than non-LGBTQ youth (12.0%). Tobacco use trends by race are different in youth than adults, with Native American youth having the highest rates (19.7%), followed by White (18.2%), Pacific Islander (17.1%), Hispanic or Latino (10.3%), African American or Black (9.9%) and Asian (7.0%). Tobacco products come in many forms. While cigarettes remain the preferred tobacco product for adults in California, for high-school aged youth in California, electronic smoking devices are more than five times more popular than cigarettes (10.9% to 2.0%).[44]

In 2016, California raised the legal age for tobacco purchases from 18 to 21 (active military are excluded). The Institutes of Medicine predicts that if all states raised the tobacco age to 21, the number of teen and young adult smokers would drop by 12%.[45] Initial evaluation indicates that this restriction is having some success in reducing tobacco use in young people.[46]

Yet, widespread use of tobacco products by youth remains, generally through illegal sales or from adults providing the product to underage users. This is especially concerning as nearly 9 out of 10 smokers start before the age of 18 and almost all start smoking by age 26.[47] People, and females in particular, who initiate tobacco use between the ages of 10 and 20 have the greatest dependence in adulthood, with initiation at age 10 leading to the highest dependence rates.[48]

Overall, it is more effective to prevent people from starting to smoke than it is to help people stop smoking.[49] The National Institutes of Health estimates that 75-80% of smokers who try to quit relapse within six months.[50] Preventing girls from starting tobacco use at a young age is especially critical as it relates to later life breast cancer risk,[8,9,10,11] and as a result, interventions focused on young girls should be prioritized. Research indicates that school-based interventions focused on preventing children from starting to smoke, especially if they are sustained for more than a year, have real potential.[49] On the flip side, smoking cessation is very difficult in young people.[51] Authors of a major review of interventions found "we cannot currently identify a program for helping adolescents to stop smoking that is more successful than trying to stop unaided."[52]

Flavored tobacco products are especially popular in younger smokers;[44] 80% of young people who have ever used tobacco started with a flavored tobacco product.[53,54] The California Department of Public Health reports that "the FDA has banned the sale of flavored cigarettes (other than menthol) because they appeal to youth." But flavored e-cigarettes, e-liquid, cigars, hookah, and chewing tobacco continue to be sold. Prohibiting the sale of all flavored tobacco products is a critical step to preventing another generation of young people from living with a lifetime of addiction."[44] A bill was introduced in the California Legislature in 2019 to ban the sale of flavored tobacco products, but the bill died before it was approved.[55]

Several different policy approaches to restricting tobacco use enjoy widespread support in California, including smoke-free policies, bans on flavored and menthol tobacco products, and restrictions on retail practices. Even a gradual ban on the sale of cigarettes is supported by 57% of Californians.[44] Despite this, great barriers to creating a tobacco-free state remain. The tobacco industry still dominates policy making on this issue. The industry spent: over $64 million on political activities in the state between 2007-2013;[56] $71 million on fighting Prop 56, CA Healthcare, Research and Prevention Tobacco Tax Act of 2016,[57] which increased the excise tax by $2.00 on cigarettes and other tobacco products; and $11.5 million, from the e-cig company Juul, supporting San Francisco Prop C, which would repeal a ban on the sale of e-cigarettes in the city.[58,59] Additionally, new tobacco products can be introduced that do not fall under existing tobacco restrictions,[57] making it difficult to stay ahead of the problem. In the wake of these barriers, local governments have taken the lead in developing tobacco-cessation policies, such as restrictions on flavored tobacco products, limiting licenses to sell tobacco products near schools, and increased taxes on tobacco sales.[42,61]

California spends less than 75% of what the Centers for Disease Control and Prevention recommends on tobacco prevention and cessation programs.[60,61] The CDC estimates that for every dollar spent on tobacco prevention, states can reduce tobacco-related health care expenditures and hospitalizations by up to $55.[47] Increased taxes on tobacco products, if allocated to tobacco prevention and cessation programs, could not only be a deterrent, it could make up that gap and help continue to reduce tobacco use across the state.

Reducing financial barriers to treatment is a critical piece of helping people to stop smoking.[62] California offers California Smokers' Helpline, which is free for everyone to use. Additionally, California Medicaid covers a full range of tobacco cessation supports, including many pharmaceuticals. State employees' coverage is not as comprehensive, and private insurance companies are not required to cover cessation treatments.[63]

The CDC recommends focusing interventions on 1) preventing initiation of tobacco use, especially among youth and young adults; 2) promoting cessation and assisting tobacco users to quit; and 3) protecting people from secondhand smoke.[64] Recommended priority areas for interventions include establishing smoke-free policies, increasing the price of tobacco products, and launching significant mass-media communication efforts to confront tobacco use.[64]

By Spring 2019, 92 (63%) of public colleges and universities in California are now 100% smoke or tobacco-free,39 an approach that effectively reduces student smoking.[65,66]

A systematic review by CDC's Community Preventive Services Task Force found that a 20% increase in tobacco unit price would be expected to:

- Reduce adult tobacco use by 7.4%,
- Reduce tobacco use by young people by 14.8%, and
- Reduce initiation of tobacco use by young people by 8.6%.[67]

Tobacco Use Doesn't Stand in Isolation

Tobacco use cannot be addressed as a stand-alone issue. Other factors and habits influence people's tobacco use. For example, one longitudinal study found that former smokers who use cannabis are also more likely to relapse, and current smokers who use cannabis are less likely to quit.[68] Another study found that cigarette smokers are five times more likely to be daily marijuana users, and 12 to 17 year olds who smoke cigarettes are 50 times more likely to be daily cannabis users than non-cigarette smokers.[69] Alcohol can also impact people's tobacco use: people who smoke are more likely to drink, and people who drink are more likely to smoke.[70,71,72,73] While most laws are focused on controlling individual substances, the larger implementation and public education efforts should look to ways to address the connection between tobacco, alcohol, and marijuana as interdependent habits.

Additionally, quitting smoking can lead to weight gain and new onset of obesity and diabetes.[74,75,76] While this is not a reason not to quit smoking, it may be helpful to provide a range of support services as people make the transition.

California and its Cities Leading Efforts to Reduce Tobacco Use

California has long been a global leader in efforts to reduce tobacco use. It was the first state to ban smoking in public places. Since then many cities across the state have led efforts to prevent or stop tobacco use, implement restrictions on the number of permits to sell tobacco, prohibit or limit the sale of flavored tobacco products, ban pharmacies from selling tobacco products, and other policies. The Truth Initiative has an extensive list of these initiatives.[42]

Community Input on Tobacco

People in several communities made similar comments: Don't tell me not to smoke, help me figure out how to end the stressors that lead me to smoke. As discussed in other sections, there are many sources of stress for women in California, including access to healthy, affordable food; safe neighborhoods; wages high enough for women to make ends meet working only one job; and time to take care of themselves and their families. Many women understood what drives them to smoke and had made multiple attempts to stop smoking, with limited success. They wanted systemic change to reduce stress rather than being shamed for smoking.

Additionally, there was widespread interest in participants to better understand what the risks might be related to smoking marijuana. With its recent legalization in California, participants felt like they wanted more research done to understand the risk to themselves, and especially their children. They also wanted to better understand the risks of vaping.

Don't tell me
not to smoke,
help me figure
out how to end
the stressors that
lead me to smoke.

Overarching Goal: End tobacco use in California, with an accelerated commitment to prevent children and young adults from starting to use tobacco.

Intervention Goal 1

Reduce the number of people who use tobacco products.

Objective 1: Develop aggressive programs to prevent children, youth, and young adults from initiating tobacco use. (*Note: There is a lot of overlap in what interventions work to prevent youth from initiating tobacco use and to help all people who use tobacco to stop. Strategies in Objective 2 can support efforts to prevent youth tobacco use, and strategies in this objective can help support all people's efforts to stop tobacco use. They have been separated here to reflect the critical nature of addressing early-life tobacco use and its prevention.*)

- **Strategy 1:** Support local and county-level bans[110] on flavored tobacco (including menthol) as the state builds toward a complete ban. Bans should include flavored cigarettes, e-cigarettes, e-liquid, cigars, hookah, and chewing tobacco. According to the California Department of Public Health, "Prohibiting the sale of all flavored tobacco products is a critical step to preventing another generation of young people from living with a lifetime of addiction."[55]
- **Strategy 2:** Increase tax on all tobacco products. California ranks 11th in state tobacco taxes in the U.S.[77] Currently each pack of cigarettes is taxed at $2.87.[78] For comparison, Connecticut, New York, Rhode Island, and Washington D.C. all tax more than $4.00 per cigarette pack.[79] Taxation on tobacco is a potentially effective deterrent, especially for targeting youth.[70,77]
- **Strategy 3:** Restrict permitting for tobacco retail,[80] with an emphasis on prohibiting retail sales of tobacco near residential areas[81] and schools.[82,83] Prohibiting sales of tobacco within 1,000 feet of schools has been shown to be effective,[80] and may be especially beneficial for reducing socio-economic and racial disparities in tobacco use.[84]
- **Strategy 4:** Ban advertising of any form of tobacco product to youth. Advertising tobacco to youth significantly increases the likelihood that they will use tobacco products,[85,86,87] so stricter regulations may contribute to reducing tobacco use among youth.[86]
- **Strategy 5:** Invest in school-based tobacco education and prevention programs that consider intersections between race/ethnicity, sexual identity, and biological sex[88] and are sustained for a year or longer.[89]
- **Strategy 6:** Sponsor sustained[90] mass media campaigns to reduce tobacco use in youth, with special emphasis on messages that reach different racial and ethnic populations and at-risk groups.[91,92,93]
- **Strategy 7:** Revise the *Health Education Curriculum Framework for California Public Schools, Transitional Kindergarten Through Grade Twelve* to include the connection between tobacco use and breast cancer risk.[94]

Intervention Goal 1 (continued)

Reduce the number of people who use tobacco products.

Objective 2: Provide widely available, culturally appropriate, affordable resources and implement policies to help people stop tobacco use.

- **Strategy 1:** Limit tobacco sales permits in cities.[95,96] In California, retailers are required to have permits to sell tobacco products.[78] ChangeLab Solutions provides guidance on how to implement these restrictions.[97]
- **Strategy 2:** Ban the sale of tobacco products at pharmacies.[98] In 2008, San Francisco became the first jurisdiction to ban the sale of tobacco products in pharmacies.[99] In 2019, Massachusetts became the first state to ban tobacco sales in pharmacies.[100] California should adopt a similar state-wide ban.[101,102]
- **Strategy 3:** Implement a state mandate requiring private health insurers to provide comprehensive cessation coverage.[48,66]
- **Strategy 4:** Ensure ongoing, adequate funding for the California Smokers' Helpline, which offers free telephone counseling, self-help materials, and online help in six languages.[103] Quitlines, telephone helplines that offer treatment for addiction, play an important role in supporting individuals to end tobacco use.[104] California was the first state to offer a tobacco helpline.
- **Strategy 5:** Sponsor sustained,[95] mass media campaigns to end tobacco use, with special emphasis on messages that reach different racial and ethnic populations.[94,105,106,107] These efforts can be combined to enhance other interventions. For example, the Community Preventive Services Task Force reports that "mass-reach communication interventions that combine cessation messages with a quit line number and that are disseminated through multiple channels have been shown to increase call volume by a median of 132%."[62]

Intervention Goal 2

Protect people from secondhand smoke. Smoke-free policies can reduce people's exposure to secondhand smoke by 50%, reduce indoor air pollution by 88%, and reduce tobacco use overall.[108]

Objective 1: Establish smoking bans on multi-unit housing. In 2018, a U.S. ban on smoking in all public housing was established, affecting two million public housing residents across the country.[109] However, statewide, people in private residential areas such as apartments and condominiums are allowed to smoke in their homes. Several cities in California require all residential multi-unit housing to be 100% smoke free. This policy should be expanded in other cities, and ultimately implemented state-wide.[110]

Objective 2: Expand tobacco-free campuses. All University of California campuses and California State Universities have adopted 100% tobacco-free campus policies, including e-cigarettes.[111] All community colleges and private colleges in California should adopt similar policies.

Objective 3: Fully enforce all bans on smoking.

Intervention Goal 3

Expand research into the link between breast cancer risk and tobacco use and marijuana use.

Objective 1: Expand the 2c per pack cigarette excise tax to include all other tobacco products in order to increase the California Breast Cancer Fund. Half of this money goes to the California Breast Cancer Research Program to fund innovative research on breast cancer in California. The other half goes to Every Woman Counts to provide breast and cervical cancer screening to low-income women.

Objective 2: Expand research on effective interventions to prevent or stop tobacco use, including vaping. Specific focus should be paid to the effectiveness in specific racial and cultural groups, as well as any at-risk groups. Ensure a focus on Native-American populations, including Native-American youth, as they tend to be the heaviest smokers and very limited data on effective interventions exists.[112,113]

Objective 3: Expand research to understand the specific relationship between marijuana use in youth and its potential impact on initiation, perpetuating, relapsing, or increasing of tobacco use.

Objective 4: Expand research to better understand if there is any connection between marijuana smoking and breast cancer risk.

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SECTION 3

RISK FACTORS WHICH REQUIRE ADDITIONAL RESEARCH TO BETTER UNDERSTAND THEIR CONNECTION TO BREAST CANCER AND EFFECTIVE INTERVENTIONS

3

Ambient Noise

Science Summary

Evidence of the impact of ambient noise on breast cancer incidence is inconsistent and more research is needed.

What the Foundational Documents Say

There is no mention of ambient noise specifically in the foundational documents.

The Current State of the Evidence

There have been a few innovative recent studies of the impact of ambient noise on breast cancer risk, but the results have been inconsistent.

- One study in Germany found that exposure to aircraft, road, and railway noise caused significant increase in risk of ER- breast cancer, but not ER+, with a 4.9% increased risk of ER- for each 10dB increase in aircraft noise.[1]
- Another study of exposure to road traffic and railway noise in Denmark found no overall effect for all breast cancer subtypes combined, but saw an increased risk of ER- breast cancer with each 10dB increase in railway noise.[2]

Ambient noise can affect or co-occur with other breast cancer risk factors including: sleep disturbances, stress, light at night, and chemical exposure.

- However, a study of a Danish nurse cohort looking at road traffic noise modeled at nurses' residences between 1970 and 2013 found 17% increase in total breast cancer for each 10dB increase in 24 year mean noise levels at a residence. Unlike the other studies, this one found statistically significant increased risk of ER+ breast cancer with noise levels but not ER- breast cancers. There was a stronger association with PR+ breast cancers but no significant association with PR- cancers. Interestingly, associations between noise and ER+ breast cancer were statistically significantly stronger in nurses working night shifts than in those not working at night.[3]
- Possible mechanisms of action that have been suggested include the effect of sleep disruption, lowered melatonin levels, and stress-related activation of the HPA axis (hypothalamic-pituitary-adrenal axis) in response to noise.[1]
- There is concern that studies to date have been inconsistent in measuring the type of noise exposure and that results have not been adjusted for common co-occurring factors, such as exposure to traffic exhaust and light at night.[4]

Take-Home Message

- Current evidence for the effect of ambient noise on breast cancer incidence is limited, with inconsistent data.
- Further research is needed, including studies that directly measure noise exposure and that take into account other exposures that co-occur with noise, such as light at night, shift work, and chemical exposures.

Ambient Noise: Context for Interventions

Ambient noise, sometimes also called environmental noise, does not have a definitive relationship to breast cancer risk, but does affect other risk factors such as sleep disturbances and stress. California is the site of numerous sources of ambient noise, including a growing construction and development industry;[5,6] 11 major ports, including three of the top 10 ports in the U.S.[7]; 145 airports,[8] including two of the top 10 airports in the country (LAX being second and SFO seventh)[9]; numerous industries and fossil fuel extraction sites; and many others. There is some evidence that communities of color and lower-income communities are disproportionately impacted by noise[10] and we heard concerns about ambient noise from community members at several listening sessions. Wherever possible, precautionary measures to reduce ambient noise are recommended.

In California, ambient noise restrictions are addressed through city general plans and regulations issued by California's Department of Transportation.[11] Cities such as San Francisco[12] and Los Angeles[13] have incorporated noise ordinances into their general plans, which may be helpful models for other cities to consider.

Ambient Noise and Other Breast Cancer Risk Factors

While the link between ambient noise and breast cancer risk is not well established, ambient noise can affect or co-occur with other breast cancer risk factors, including:

- Sleep disturbances;
- Stress;
- Light at night (from night work);
- Chemical exposure (if ambient noise is related to industrial activity or traffic).

As a precautionary measure, cities can reduce noise exposure by establishing and fully enforcing noise ordinances. Workplaces should set and enforce maximum noise standards while also innovating ways to further reduce noise from machinery and equipment in work environments and surrounding communities.

INTERVENTIONS

Overarching Goal: Expand research on the link between ambient noise and breast cancer risk.

Intervention Goal 1

Increase worker awareness of these issues. Develop workplace policies, with worker involvement, to reduce, eliminate, or mitigate unnecessary exposures to light at night.

Objective 1: Support research on the relationship between breast cancer risk and ambient noise.

Objective 2: Support research that investigates the role of ambient noise in relation to related breast cancer risk factors, including sleep and hormone disruption, stress, light at night, chemical exposures, and others.

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Body Weight

Science Summary

The breast cancer risk association with body fat, as measured by Body Mass Index (BMI), differs by menopausal status. Higher BMI after menopause increases breast cancer risk, while higher BMI in youth, adolescence, and young adulthood may reduce breast cancer risk. Risks may be further influenced by distribution of body fat, hormone replacement therapy use, breast cancer subtypes, and race and ethnicity.

What the Foundational Documents Say

The Institutes of Medicine (IOM), Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC), World Cancer Research Fund (WCRF), and American Institute for Cancer Research (AICR) concur that while excess body fat after menopause increases risk of breast cancer, excess body fat prior to menopause may be protective against breast cancer.[1,2,3]

In addition to age and menopausal status, hormone therapy use may influence weight-related risk of breast cancer. Higher body weight is associated with increased risk of estrogen- and progesterone-positive breast cancers.[1,2] The association between body weight and post-menopausal breast cancer is stronger for those who do not use hormone therapy.[2]

The Current State of the Evidence

BMI is calculated as a ratio of body weight relative to height (squared) to describe the general mass of the body. Standard BMI categories described by the World Health Organization (WHO) are: underweight (<18.5kg/m^2); normal weight (18.5kg/m^2 – 24.9kg/m^2); over-weight (25kg/m^2 – 29.9kg/m^2); and obese (>30kg/m^2).[4] While it may be a useful health risk and research tool, BMI alone may not adequately describe body composition and fat distribution.[5,6,7] When combined with other measurements such as waist circumference or waist to hip ratio, BMI becomes a more accurately predictive value to assess where body fat is stored, a factor associated with a number of health outcomes.[5]

Aromatase is an enzyme secreted from fat cells that is involved in non-ovarian estrogen synthesis,[8,9,10] through converting androgens into estrogen. Increased levels of body fat create increased levels of aromatase. Chronic inflammation is a characteristic of obesity.[11,12] Inflammatory cyclooxygenase-2 (COX2) enzyme levels are positively associated with obesity[13] and indirectly result in higher aromatase expression.

Obesity is associated with higher leptin and lower adiponectin levels,[14,15] both of which are produced primarily within fat cells. While leptin's primary function is regulation of energy balance,[16] it can also can increase aromatase synthesis and expression.[12] Adiponectin functions to improve insulin sensitivity and glucose metabolism,[10] and is involved in inhibiting aromatase synthesis.[12] While there is some suggestion of a positive association between leptin and breast cancer,[14,17] inconsistencies in this association exist in the literature.[18,19] Adiponectin and breast cancer are inversely associated,[8,18,19] but the association may be dependent on menopausal status.[20]

Menopausal Status

While research suggests that a BMI in the overweight and obese categories increases risk of breast cancer, this risk varies by menopausal status. In addition to menopausal status, fat distribution patterns, breast cancer subtype, and hormone therapy use may influence the association in both pre- and post-menopausal women.

Post-Menopause

BMI and Body Fat Distribution: Post-menopausal BMI is positively associated with breast cancer risk.[6,7,21,22,23,24,25,26] Research reports a 3.4% to 6%[27,28,29] increase in post-menopausal breast cancer risk with each unit increase in BMI. In a study of women who had never used hormone replacement therapy (HRT), each 5-unit increase in BMI increased risk 18%.[30] This risk may be reduced in obese post-menopausal women who use hormone replacement therapy.[5,27,31,32,33,34] The positive association between BMI and post-menopausal breast cancer risk[34,35,36] is strengthened with the duration of post-menopausal status.[37,38] Some research suggests increased risk of post-menopausal breast cancer with a central body fat distribution,[39,40] while other research shows no post-menopausal association with fat distribution.[41,42]

BMI and Subtype: While exploring the association between body mass and breast cancer subtypes, research shows a positive association between BMI and risk of receptor-positive breast cancer in post-menopausal women.[26,43,44] The association of post-menopausal BMI and risk of hormone receptor-negative breast cancer, including a triple-negative subtype, is less clear, with inconsistent evidence showing both inverse associations with BMI[41,45] or no significant association.[26,32,46]

BMI and Race/Ethnicity: A BMI value between 25kg/m^2 and 29.9kg/m^2 is considered overweight and a BMI value of 30kg/m^2 or greater is considered obese. There is some suggestion that associations between breast cancer and these BMI categories may differ among racial and ethnic groups.[31,47,48] While markers for a central fat distribution may better inform risk in Black women,[47,48] increased risk in post-menopausal Asian, Native-Hawaiian, and Pacific-Islander (ANHPI) women may occur at lower BMI values.[31,48]

Possible Biological Mechanisms: It is hypothesized that the lower risk associated with elevated pre-menopausal BMI versus the higher risk with post-menopausal BMI is explained by elevated estrogen production via aromatase.[9,49] Before menopause, the ovaries are the primary source of endogenous estrogen and aromatase activity does not provide a significant contribution. After menopause, the ovaries are no longer producing estrogen and therefore the estrogen produced by aromatase activity elevates estrogen levels which subsequently increase post-menopausal breast cancer risk in women with higher BMIs. Other possible mechanisms by which higher BMI may increase risk include through related pathways such as insulin resistance, inflammation and effects on immune function.[2]

Pre-Menopause

BMI and Body Fat Distribution: In contrast to the positive association between post-menopausal BMI and breast cancer risk, research suggests an inverse association between pre-menopausal BMI and risk.[8,13,21,33,39,50,51,52,53] The inverse association between body mass and pre-menopausal risk is especially apparent in youth.[19,26,42,54,55,56,57] Research also suggests an inverse association with young adult BMI,[56,57,58] although results are inconsistent and some studies suggest no association with young adult BMI and breast cancer risk.[7,42,59,60]

While pre-menopausal BMI is associated with reduced breast cancer risk, greater central body fat distribution (as measured by waist circumference or waist-to-hip ratio) in pre-menopause is associated with increased breast cancer risk.[37,39,40,55,61,62]

BMI and Subtype: In contrast to post-menopausal status, increased BMI appears to be positively associated with receptor-negative subtypes in pre-menopause,[44,45,49] although no association was detected in pre-menopausal women (age 20-44) in one study.[63] Triple-negative/basal-like breast cancer risk has been associated with elevated BMI in pre-menopausal women[49,64,65,66] and with a change in weight after 18 years of age.[63] However, the association of BMI with breast cancer subtypes is not completely understood due to inconsistent findings, and more research is needed.[26]

BMI and Race/Ethnicity: Differences in BMI associations with breast cancer among racial and ethnic groups in pre-menopause are mixed. One meta-analysis found an inverse association between BMI and breast cancer in Black women and White women, but a positive association in ANHPI women.[51] However, in another meta-analysis, an inverse association was seen in European pre-menopausal women while no association was found for ANHPI and U.S. pre-menopausal women.[27]

Possible Biological Mechanisms: In pre-menopause, aromatase-derived elevated estrogen levels interfere with ovarian estrogen production, resulting in reduced gonadal estrogen and progesterone secretions and an anovulatory state (eggs no longer released during menstrual cycle). The anovulatory state is thought to reduce risk due to lower contributions from reproductive hormones.[9,24,67]

Nuances and Emerging Considerations

Early menarche is a risk for breast cancer,[1,3] and body fat in youth is linked to earlier age at menarche.[1] Though this suggests that higher body weight in youth indirectly increases risk of breast cancer, the current body of literature suggests that higher body fat in youth actually is protective against breast cancer risk. Future research to investigate the relationship between youth body fat, menarche age, and breast cancer risk is needed.

The increased risk of pre-menopausal breast cancer with higher waist circumference appears to contradict the pre-menopausal BMI inverse association with breast cancer. Additionally, while anovulation resulting from obesity may explain the inverse association with pre-menopausal breast cancer, it does not explain why non-ovulating post-menopausal women do not share the same inverse association. BMI is an imperfect measure of body fatness. It may mask differences between lean and adipose tissue, or fat distribution, which carries across individuals, ethnicities, and stage in the lifespan.[68] It is important to remember that BMI does not assess lean muscle composition, so two people with the same BMI may have different proportions of lean and fat tissue. While assessing BMI in relation to central adiposity measures attempts to resolve this, the muscle contributions to BMI in young adult women compared to post-menopausal women in association with breast cancer risk has yet to be explored.

Take-Home Message

- The impact of body weight on breast cancer risk differs by menopausal status. Higher BMI after menopause increases breast cancer risk, while higher BMI in youth, adolescence, and young adulthood may reduce breast cancer risk.
- In pre-menopause, a higher waist circumference may increase breast cancer risk.
- The association with BMI differs by breast cancer subtype: BMI in post-menopause is associated with risk of receptor-positive breast cancer, whereas the association is not well understood for hormone receptor-negative breast cancer.
- Associations between breast cancer and BMI may differ among racial and ethnic groups.
- Obesity may increase risk through several related pathways that lead to hormonal and metabolic disruption. For instance, adipokines, such as leptin and adiponectin, and inflammatory proteins, such as COX-2, may influence estrogen levels through their effects on aromatase.

Body Weight: Context for Interventions

Body weight can be influenced by many factors over a woman's lifetime: physical activity levels, eating (both quantity and quality), chemical exposures, sleep disturbances and others.[69,70,71] All these factors can be modified through changes in individual behavior and/or through systemic changes as discussed in other sections of this Plan. Genetics can also play a role in people's body weight, and external factors, such as exposures to an obesogenic environment (including chemical exposures and the built environment), can influence how genes affect body weight.[71]

While the evidence connecting body weight and breast cancer risk is complex and much more research is needed, the positive impact of many of the factors impacting body weight are undeniable for breast cancer as well as numerous other health impacts. Data showing that physical exercise at any stage of life reduces breast cancer risk is clear and consistent. While the evidence of the impact of diet and nutrition on breast cancer risk is more nuanced, generally a healthy diet potentially reduces breast cancer risk, and provides other health benefits. Interventions that impact these factors, and therefore body weight, can be found in the "Social and Built Environment," "Diet and Nutrition," and "Physical Activity" sections of this Plan.

Understanding Weight in a Complex World

Body weight is often discussed in terms of Body Mass Index (BMI). The medical community relies heavily on BMI to assess people's weight and recommend goals for the ideal weight range. But not all body weight is the same. For example, BMI does not distinguish fat from mass such as muscle and bone.[72] Additionally, many feel it is too limited in how it considers health. There is growing awareness of the limitations of BMI and interest in other measures that provide more meaningful information for individuals.[72,73,74,75]

However, even better measures may have limited impact on helping people understand their weight or in motivating them to change behavior. In fact, "[s]hame, self-criticism, and perceptions of inferiority may play a significant role in self-regulation of eating behaviour in overweight people trying to manage their weight."[76] The stigma of being overweight in our society can actually lead to behaviors that may increase weight, such as binge eating and reduced physical activity, especially in children.[77]

There are movements to simultaneously encourage healthy behavior while de-stigmatizing weight and reducing shame, which can inhibit healthy habits. Health at Every Size[78] is one approach that seeks to help people celebrate body diversity while adopting healthy behaviors. This approach has had some success helping people be more receptive to interventions, however more empirical data is needed on how effective this approach is in helping individuals to adopt healthy behavior.[79]

INTERVENTIONS

Overarching Goal: Expand research to better understand the link between body weight and breast cancer risk at various life stages and the most effective interventions to reduce risk.

Intervention Goal 1

Support research on the relationship between body weight and breast cancer risk at various life stages.

Objective 1: Support research to better understand the relationship of body weight in youth and future breast cancer risk, specifically considering how youth body fat affects menarche age and growth and its ultimate effect on breast cancer risk over the lifetime.

Objective 2: Support research to better understand the relationship between pre-menopausal and post-menopausal body weight and breast cancer risk, including the impact of hormone replacement therapy.

Objective 3: Support research on the relationship to different aspects of body weight other than BMI and breast cancer risk—for example, body composition or central adiposity.

Objective 4: Support research to better understand the specific nuances of how race/ethnicity affects the relationship between body weight and breast cancer risk at different stages of life and by subtype.

Intervention Goal 2

Expand empirical research on the efficacy of interventions to reduce breast cancer risk as it relates to body weight.

Objective 1: Support research on the effectiveness of systemic interventions that help women maintain a healthy body weight.

Objective 2: Support research that explores the specific emotional or psychological barriers to girls and women of a wide range of weights adopting healthier habits.

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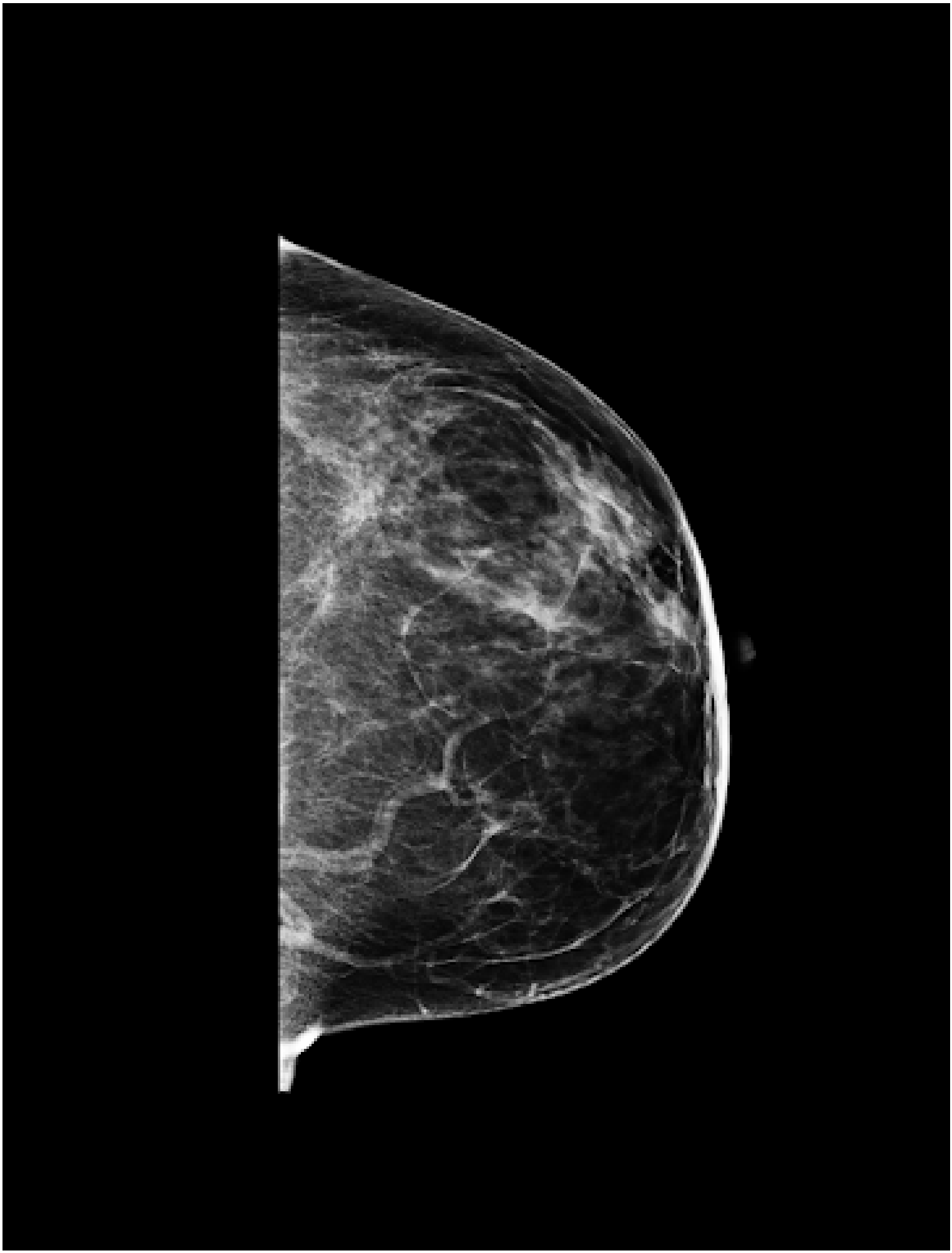


Breast Density

Science Summary

Increased breast density is considered one of the strongest risk factors for breast cancer after female sex, age, family history, and/or specific gene mutations. Various factors can influence breast density, either increasing or reducing density, including ionizing radiation, pharmaceutical hormones, parity, menopause, air pollution, smoking, and body weight. However, more research is needed on these factors and the role of genetics.

What the Foundational Documents Say

The EDC-2, IBCERCC, and IOM reports all state that there is increased risk of breast cancer associated with increased breast density.[1,2,3] The IBCERCC report states that studies even report a more than four-fold increased risk of breast cancer among women with very dense breasts compared to women with no mammographic dense tissue.[2] However, as the reports also state, the mechanistic basis for this association is still unknown,[2,3] though many hypotheses have been proposed.

The IOM review proposes that the link between breast density and breast cancer arises from the extracellular matrix (ECM) composition associated with higher mammographic density.[3] The hypothesis suggests that changes in ECM composition may play a role in tumorigenesis; thus, women with higher breast density are more likely to develop breast cancer.[3]

Meanwhile, the IBCERCC report proposes that the number and proliferative state of epithelial cells—the cells that make up the ducts and lobules of the breasts—may affect breast density and the likelihood of genetic damage that leads to cancer.[2] However, the report also states that breast density can also be altered by Body Mass Index (BMI), parity, age, and menopausal status, and may act as a mediator between some of these factors and breast cancer risk. The question remains whether innate breast density or the interaction between environmental factors and breast density contributes more to the association between breast density and breast cancer.

The Current State of the Evidence

What is Breast Density?

Breasts are composed of fibroglandular tissue (also known as dense tissue) and fatty tissue. In a mammographic image, fibroglandular tissue appears as white matter, while fatty tissue appears translucent. Breast density refers to the amount of fibroglandular tissue, or white matter, that appears in a mammogram.

There are various ways to measure the fibroglandular tissue in a mammogram. The most popular measurements include absolute dense area (the total area of white matter on a mammogram) and percent density (the area of white matter as a percentage of the whole breast). Additional methods of measurement include absolute dense volume, which similarly measures fibroglandular tissue but in cm^3 rather than cm^2, and non-dense area, which is the area of fatty tissue in a mammogram. One of the most increasingly popular and more generalized methods to measure breast density is a Breast Imaging, Reporting & Data System (BI-RADS) score. A BI-RADS score of 1 indicates that breasts are less than 25% dense and are considered almost entirely fatty. A score of 2 (25-50% dense) is also called scattered, a score of 3 (50-75% dense) is called heterogeneously dense, and a score of 4 (more than 75% dense) are called extremely dense.[161]

A study with a sample size of over one million women reported that 43.3% of women in the United States aged 40 to 74 years had BI-RADS scores of 3 or 4 (mostly 3), indicating a strong prevalence of high breast density in the nation.[4] Variations among ethnic and geographic groups are discussed below.

Breast Density Linked to Breast Cancer

Science has consistently found a positive association between breast density and breast cancer risk for pre-, peri-, and post-menopausal women.[5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34] Studies report that women with high density (BI-RADS score of 4) have four to six times higher risk of breast cancer than women with low density (BIRADS score of 1).[5,11,22,24] When measured quantitatively, studies have found a 3% increase in risk of breast cancer per 10 cm^3 dense tissue, and a 14% risk per 10 cm^2.[11,16] However, one study found no significant association between breast density and breast cancer in pre-menopausal women except for those with large tumors (≥ 2cm).[35]

While the evidence is clear that breast cancer risk increases with the density of a woman's breast, the combination of factors that contribute to increasing or decreasing breast density is far more complex and are explored below. Most of these factors are address in other sections of this Plan, where potential interventions are provided.

Reproductive/Hormonal Factors

Menstrual Onset and Duration: The current evidence evaluating the association between breast density and menstrual onset and duration is inconclusive. Two studies found a positive association between older age at menarche (initial menstruation) and breast density, but one of the studies found the association to be insignificant after adjustment for childhood adiposity.[36,6,37] Meanwhile, two additional studies found no association between age at menarche and breast density.[38,39]

Menopausal status, unlike age at menarche, has a clear association with breast density; the mean breast density of pre-menopausal women was found to be significantly higher than peri- and post-menopausal women.[36,40]

Parity: Parity, or number of pregnancies carried to a viable gestational age, is inversely associated with breast density, and the generally consensus is that increased parity can be protective against breast cancer.[14,36,41,42,43,44,45,46,47,48,49,50,51] Studies report the probability of having high mammographic breast density decreases from 4-16% per new birth.[44,47] Additionally, nulliparous women (women who have never carried a pregnancy to term) were reported to be 70% more likely to have dense breasts (BI-RADS score 3 or 4).[46] Therefore, the increased risk of breast cancer associated nulliparity may be mediated (partially explained) by increased breast density. Additionally, age at first birth is positively associated with breast density, with a significantly higher prevalence of high mammographic density in mothers of an advanced age at first birth.[47,49,50,52]

Breastfeeding: The current state of the evidence regarding the relationship between breast density and breastfeeding is conflicting. Two of the four studies evaluated found a negative association between history and duration of breastfeeding and breast density (longer breastfeeding associated with lower breast density); one study found the association among all women and another among only post-menopausal women.[36,49]

However, a 2016 study found a positive association only among pre-menopausal women between breastfeeding and both absolute dense and non-dense area; thus, no overall change in percent density.[51] Additionally, a 2012 study found a higher prevalence of high mammographic density in mothers who breastfed for a longer duration.[47] As a result of the conflicting evidence, no conclusion regarding the relationship between breastfeeding and breast density, nor breast density's role as a mediator, can be reached.

Hormonal Contraceptive Use (history, start of use, duration): When measured by history of use (ever or never), current evidence suggests no association between hormonal contraceptives and breast density.[36,53] However, when measured by age of initiation and duration of use, significant associations arose. A 2013 study found that density, as measured by mean percent dense breast volume, was lower in women who began taking hormonal contraceptives at the age of 22-28 compared with women who began at 12-17 years of age (14.7% vs. 21.7% respectively). Therefore, a significant inverse association between age at start of use and breast density was found. The study also found a significant positive association between duration of hormonal contraceptive use and breast density.[43]

Hormone Replacement Therapy (HRT): The current state of the evidence regarding the association between menopausal hormone replacement therapy use and breast density is mixed with most finding a positive association.

Two studies found no association between current use or history of use of hormone therapy and breast density.[36,28] Meanwhile, a 2017 study and a review found a positive association between mammographic density and specifically combined estrogen plus progestin hormone therapy use.[13,44] According to the study, among women who used estrogen plus progestin hormone therapy, each 1% positive change in percent mammographic density increased breast cancer risk 3%, and women in the highest quintile of percent density change (> 19.3% increase) were 3.6 times more likely to develop breast cancer. The study also concluded that all increased risk of breast cancer associated with estrogen plus progestin therapy use was mediated by increase in breast density.[13] Additionally, estrogen plus progestin therapy users had a smaller decline in mammographic density with age compared to non-users.[44]

Endogenous Sex Hormones: There is conflicting evidence among studies regarding an association between circulating endogenous hormone levels and breast density. The endogenous hormones evaluated include progesterone, estrogens, testosterone and androstenedione. While some studies report a positive association between hormone levels and breast density,[54,55] others report no association.[56,57] Thus, more research is needed to further evaluate an association and whether breast density acts as a mediator.

Metabolic Factors

Body Weight Over Lifespan

Body Mass Index (BMI): There is a significant negative association between BMI and breast density, measured by percent density, dense area, BI-RADS scores, percent dense volume and absolute dense volume, with studies reporting up to a 17% decrease in percent breast density in women in the obese category compared to normal category of BMI scale.[6,41,58,54,42,59,15,40,60,61,62,63,64,65,66,67,24,4,68,69,70] Studies have also reported that women with a BMI less than 25 kg/m^2 (or 0.036 lbs/in^2) are four times more likely to be classified as having dense breasts.[41] Consistent with previous findings, there is a positive association between non-dense area as well as total breast area and BMI.[60,68] The association can be explained by an accumulation of fat in the breasts rather than an alteration of dense breast (fibroglandular) tissue after weight gain.[68] One study reported a positive association between exclusively dense volume and BMI, contradicting the findings of most other studies.[64]

Early Childhood BMI: There is conflicting evidence regarding the relationship between birth weight and breast density. Two studies found a positive association,[71,67] while another found no association.[7]

One study found that childhood BMI is inversely associated with percent density but not with dense area,[72] and another reports no association at all.[73]

Multiple studies confirm an inverse association between infant, childhood and adolescent (ages 1-16) BMI and breast density, using all measurements, reporting up to a 24-38% lower dense breast volume per unit BMI increase in youth (ages 8-10).[58,7,74,37] One study looking at birth weight and weight gain during infancy and early childhood and midlife breast density found birth weight positively associated with dense breast area as was weight gain from 4-12 months of average birth weight babies. However, weight gains from 1-4 years were negatively associated with breast density.[75] More research is needed.

Weight Measurement Other Than BMI: When weight was measured by body fat percentage, total adipose area and waist to hip ratio, an inverse association with breast density remained.[54,76,77] However, one study found a positive association between adult weight gain and breast density, reporting that women who gained more than 24 kg (or about 52 pounds) had twice as high breast density.[77]

Diet

Here we focus only on studies that specifically looked at diet in terms of its impact on breast density. Studies assessed diet by participant recall using food frequency questionnaires at the time of the study rather than directly measuring diet, including earlier in life. Studies looking at other pathways or mechanisms through which diet may be linked to breast cancer are covered in the "Diet and Nutrition" section of this Plan.

Dairy: No significant association between breast density and rate of dairy consumption (when consuming zero to more than three servings of dairy products/day) has been found.[78] One study found a positive association between exclusively drinking whole milk and mammographic density, but it was not statistically significant.[79]

Fat and Fatty Acid Intake: Studies have found a significant positive association between animal fat and saturated fat intake and breast density.[80,81] One study found that those who were in the highest quartile of animal fat intake during adolescence had 3.9% higher mean breast density,[80] while another found up to a 5.1% increase in breast density among high saturated fat consumers.[81]

When evaluating both omega 3 and omega 6 polyunsaturated fatty acids, studies have found no association between omega 6 and breast density.[82,83] However, while two studies found no association between omega 3 fatty acid and breast density,[83,84] one reported an inverse association.[82]

Mediterranean Versus Western Dietary Patterns: The Mediterranean diet is characterized by low consumption of dairy, red meat, and processed foods; and high consumption of fish, poultry, fruit, unrefined grains, plant-based foods and olive oil. Meanwhile, the Western diet is characterized by high consumption of red and processed meat, refined grains, whole-fat dairy products and refined sugar. When the Mediterranean diet was studied in relation to breast density, there was either no association or a weak inverse association with breast density.[85,86] However, one study found that women with a higher adherence to a Western dietary pattern had increased breast density, with overweight/obese women showing up to 8% higher mammographic density.[85]

Additional studies evaluated the impact of high consumption of certain foods associated with a Western diet. A study that evaluated the impact of adolescent red meat intake found a weak and statistically nonsignificant positive association.[80] Also, sugar intake, measured by spoonfuls, glycemic index and glycemic load, was found to have weak positive to no associations with mammographic density.[87,88]

Coffee: Studies found a positive association between both regular and decaf coffee and breast density.[89,90] Drinking more than two cups of decaf coffee was found to be associated with up to a 2.6% increase in percent breast density in pre-menopausal women.[90] The same study found an inverse association among post-menopausal women for both regular and decaf coffee.

Soy: Inconclusive results were found regarding the relationship between soy and breast density. One study found no association between soy and mammographic density,[91] while another found that individuals with a specific gene (PPARy rs880663) had lower breast density, a finding that was significantly stronger in high-soy consumers than those with lower soy intake.[92]

Green Tea Extract: One randomized controlled trial found that women aged 50-55 taking green tea extracts had a 3.38% reduction in percent breast density compared to those who did not receive supplements; however, these associations could not be generalized to women of all ages.[93]

Insulin and Diabetes

There is conflicting data regarding an association between diabetes, diabetic factors, insulin resistance and breast density. One study reported that women taking insulin were more than twice as likely to have mixed or dense breasts[94] and was supported by an additional study which found that high blood glucose and insulin resistance were positively associated with breast density.[95] However, a conflicting study reported that pre-menopausal women with type 2 diabetes had much lower breast density than those without, but there was no difference among post-menopausal women.[96] More research is needed in this area.

Leptin Levels

Leptin is a hormone, primarily made by adipose cells, that helps to controls hunger. High leptin levels, which usually indicate obesity, were found to be significantly associated with lower breast density.[97] Women in the highest leptin quartile had 12.1% lower breast density than women in the lowest quartile. Thus, leptin levels may be one of the pathways through which body weight impacts breast density.

Vascular Endothelial Growth Factors (VEGF)

A study reported that dense breast tissue showed increased levels of 20 proteinogenic amino acids, 18 of which were significantly correlated with vascular endothelial growth factors (VEGF—proteins that stimulate the formation of blood vessels).[98] Thus, more research should be conducted to continue the evaluation of an association between VEGF and breast density.

Metabolic Syndrome

Studies indicate that having various metabolic syndromes is associated with lowered breast density.[95,99,100,101] Metabolic syndromes that influence high-density lipoprotein (HDL) levels were shown to have the greatest impact on breast density; low HDL levels were strongly associated with larger dense area and percent density.[99,100]

However, less data exists for metabolic syndromes that impact other mechanisms of the body and many of the studies conducted found statistically insignificant results; thus, more research is needed to properly evaluate the reported association.

Alcohol Consumption

The evidence regarding the relationship between alcohol consumption and breast density is inconclusive. Some studies found a positive association between alcohol consumption, measured by ever versus never use, and breast density.[42,102,103,104,105] Others found a positive association between high alcohol consumption (7 or more drinks per week) and breast density,[106,102,22,107,103,86] with one study reporting that women with high alcohol consumption have 12.3% higher breast density compared to nondrinkers after adjustment for confounding factors.[22] Additional studies either found a statistically insignificant association or no association at all.[108,109,110,111,112]

While the effects of alcohol consumption alone on breast density are inconclusive, studies looking at the effects of alcohol consumption among HRT users on breast density were more consistent. The hypothesized positive association between alcohol consumption and breast density is believed to be stronger in women currently using HRT or with a history of HRT use.[42,104]

One study reports an 8.3% increase in breast density among HRT users who consume high amounts of alcohol (7 or more drinks per week) compared to nondrinkers.[104] However, a 2018 study of cancer-free post-menopausal women found that associations of alcohol with breast density did not vary by hormone therapy status.[113]

Additionally, evidence is conflicting as to whether the age at initiation of drinking, frequency of consumption during various age intervals, or type of alcohol consumed (spirit, beer, or wine) have an impact on breast density.[114,22]

Physical Activity

No consensus exists among current researchers regarding an association between physical activity and breast density. While three studies and a review (which evaluated 20 relevant studies) agree that there is no significant association between physical activity and breast density,[78,42,115,116] two others found significant inverse associations limited to nonsmokers and overweight women (BMI 25.0-29.9).[106,117] One additional study found that both dense and non-dense volume decreased with increased physical activity (overall breast volume was reduced), resulting in no change in percent dense volume.[118]

Inflammation

NSAID Use: Research is conflicting regarding the association between nonsteroidal anti-inflammatory drug (NSAID) use and breast density. One study found a statistically significant inverse association between NSAID use, specifically aspirin, and mammographic density.[119] However, another study found no association between dense area and any NSAID use for any frequency or duration.[120] Thus, no conclusion regarding the relationship between breast density and NSAID use can be reached.

Inflammatory Markers and Proteins: Dense breasts, as measured by BI-RADS scores, contain higher levels of pro-inflammatory proteins and inflammatory cells compared to non-dense breasts, and higher expression levels of anti-inflammatory markers are associated with lower breast density.[121,122] Inflammatory markers have been linked to breast carcinogenesis, and based on the current evidence, this pathway may be mediated by increased breast density.

Vitamin D

Vitamin D Dietary Intake: There is conflicting evidence regarding the association between Vitamin D intake and breast density. Two studies found no significant association between Vitamin D consumption and breast density,[78,123] while two others found a significant inverse association limited to pre-menopausal women or women under the age of 55.[124,125] Additionally, a 2017 study and five out of nine studies evaluated in a review found a significant inverse association between Vitamin D intake and breast density.[126,127]

Vitamin D Serum Levels: The circulating levels of vitamin D in the body are measured by vitamin D serum levels. Three studies, as well as four separate studies in a review, found no association between vitamin D serum levels and breast density among the general population,[53,128,125,127] while one study found a significant inverse association.[126]

Interaction with Genetics

Genes: Three isolated single nucleotide polymorphisms (SNPs) that were previously only associated with breast density in women of European ancestry, were also found to be associated with both percent density and dense area in Malaysian and Chinese women.[129] Black women, however, were found to have different SNPs associated with breast density than White women,[130] thus increasing the need for more research on genetic links between breast density and breast cancer.

Genetic Link and Heritability: Early studies looking at monozygotic (identical) and dizygotic (non-identical) twins found heritability could account for 60% of variation of breast density among twins.[131] More recent studies have conflicting results on which genes are linked to density, their level of heritability, how they are expressed, to which quantitative measurement they correspond, and to which demographic(s) they apply.[132,133,60,92,134,135,136,129] Additionally, one study reports a 1.5% increase in breast density associated with a family history of breast cancer but did not evaluate the hereditary mechanisms. More research is needed to clarify the genetic basis for breast density.

BRCA 1/2: One study reported that breast density was significantly lower among BRCA 2 mutation carriers compared to non-carriers, but not among BRCA 1 mutation carriers.[137] More research is needed to evaluate extent to which breast density mediates the risk between BRCA 2 mutations and breast cancer, if at all.

Race and Social Factors

As with most issues, data on racial and ethnic differences in breast density is very limited and more research is needed. However, some studies (detailed below) have looked at difference by race and ethnicity and found significant results.

Asian women, specifically Chinese, Malay and Indian women (in studies from Malaysia and New Zealand), were found to have higher breast density than women of other ethnic groups.[138,139,140] Of those groups, Chinese women had the highest breast density when compared to Malay and Indian women, with a study reporting a 4.3% and 4.2% increase in percent density respectively.[141] Pacific Islander women, including Maori women, were also found to have increased breast density compared to White women, but not as high as Asian women.[138] A study of Korean women found a five-fold higher breast cancer risk for women with extremely dense breasts than for women with an entirely fatty breast. The prevalence of dense breasts was higher in younger women and the association between a denser breast and breast cancer was stronger in women in their 40s than women older than 70 years. The positive association remained irrespective of menopausal status but the effect of a dense breast on breast cancer risk was stronger in pre-menopausal women.[142]

Additionally, a study with a sample population consisting of U.S. Black, Latina and White women found that Latina women had the highest breast density followed by Black women.[66] Another study reported that for quantitative measures of breast density (percent density, absolute dense volume and percent dense volume), Black women had significantly greater odds of high density compared to White women for each measurement listed.[143] However, in the same study when density was measured using BI-RADS scores, there was no significant difference in density between White and Black women. Contributing to the inconclusiveness of evidence using BI-RADS scores, another study

observed an increased risk of breast cancer in the highest versus lowest BI-RADS categories, but with a much higher risk in White than Black women. More research is needed to further evaluate the impact of race on breast density.[27]

Urbanization: Women living in extremely urbanized areas had a higher percent breast density (21.4%) and were more frequently categorized as BI-RADS 3 or 4 than women living in non-urbanized areas (16.1%).[144]

Socio-economic Status: Studies conducted to evaluate the impact of socioeconomic status on breast density, using education level, family income level at birth, and parental education as proxies, found varying results. Two studies found significant and strong inverse associations between socioeconomic status and breast density, with one showing up to a 29% decrease in likelihood of having dense breasts among those with a high socioeconomic status.[145,146] One additional study, which evaluated the impact measured by family income level at time of birth and parental education, found an inverse association as well, but it became insignificant after adjustment for confounding variables.[147]

Air Pollution: A few studies have explored the relationship between air pollution—specifically particulate matter and ozone—and breast density. A study found a statistically borderline inverse association between long term exposure to air pollution and mammographic density.[148]

Particulate matter (PM) is defined as the sum of particles in the air including dust, pollen, soot, smoke and liquid droplets, many of which can be hazardous, and is often reported with the size of the particles being measured, so $PM_{2.5}$ measures the number of airborne particles equal to or greater than 2.5 micrometers in diameter. Studies have found varying results regarding the impact of particulate matter on breast density. One study found no association after adjustment for confounding variables,[144] while another found significant associations limited by region. Recent exposure to fine particulate matter, $PM_{2.5}$, in the northeast region of the U.S. was associated with a 3.4% increase in percent breast density among post-menopausal women, and recent exposure to coarse matter ($PM_{2.5-10}$) in the West showed a 2% decrease in percent breast density for post-menopausal women.[149]

Meanwhile, an additional study found evidence to suggest a positive association. Women with extremely dense breasts (BI-RADS 4) had higher mean $PM_{2.5}$ exposure than women with fatty breasts. This study also reported that a one unit increase in $PM_{2.5}$ concentration in the atmosphere was associated with up to a 4% increased chance of having dense breasts (BI-RADS 3) and 2% lowered chance of having fatty breasts.[150]

A study of ozone exposure found that women with BI-RADS 3 and 4 had lower ozone (O3) exposures than women with fatty breasts, and thus reported an inverse association between the two.[150]

Occupational Factors

Few studies have been conducted to evaluate the association between occupation and breast density, but current research found that nurses and secondary school teachers were the occupations with the highest average mammographic density.[151] While it is not known why secondary school teachers show increased mammographic density, research suggests that the high amount of exposure to ionizing radiation among nurses could explain their collective increased breast density.[152]

A 2018 study of female workers in Spanish breast cancer screening programs found that percentage of breast density increased 3% for each five years of occupational exposure to ionizing radiation after adjustment for confounding variables.[152]

Additionally, exposure to perchloroethylene and aliphatic/alicyclic hydrocarbon solvents, substances commonly used by launderers or pressers, are positively associated with breast density.[152] Thus, workers in those occupations may be more at risk of increased breast density.

Tobacco Use/Smoking

Of the four studies that evaluated the relationship between active smoking and breast density, three found a significant inverse association and one found no association.[36,42,106,114] The inverse association was found to be strongest among women who initiated smoking before the age of 16, smoked more than 15 cigarettes a day, smoked more than five pack-years (one pack a day for five years), smoked for more than 30 years and smoked for more than 11 years before first childbirth. However, former smoking was found to have no association with breast density.[114] A study of prenatal exposures to cigarette smoke found a significant decrease in mid-life density in women whose mothers smoked during pregnancy compared with those whose mothers did not smoke during pregnancy.[153]

Factors with No Identified Association

Studies have found no association with breast density for certain factors. While included here for completeness, we note that these conclusions are based on only one or two studies, so more research may be warranted.

- **Ambient Noise:** Current research suggests no association between mammographic density and ambient noise, as measured by road or railway noise.[154]
- **Consumer Products:** A 2018 study found that there is no association between childhood and ever use of hair products/hair oils (including in childhood) and breast density.[155]
- **Fiber:** There was no association found between total fiber intake during adolescence and breast density.[156]
- **Night Shift Work:** Studies suggest that night shift work is not associated with mammographic density.[157,158]

Nuances and Emerging Considerations

Subtypes

There is a slight suggestive stronger association between breast density and estrogen receptor-positive (ER+) breast cancer, but the current research is still inconclusive.[10,18,19,29,34,159] Additionally, one study found that the risk of specifically luminal A (ER and/or PR+ and HER2-) breast cancer increased among women with higher breast density.[29] Given the lack of strong and/or conclusive evidence regarding breast cancer risk by subtype linked to breast density, more researched is needed.

Take-Home Message

- Breast density is one of the strongest risk factors for breast cancer.
- While the data is clear that higher breast density is associated with a higher risk of breast cancer, the mechanism of that association is unknown.
- Extensive research has looked at numerous factors that can potentially impact breast density, with mixed results, perhaps due to different methodologies (measuring continuous density versus categorical BI-RADS) and studies in women who are being mammographically screened (mostly over 50 years old, so studies are skewed to older ages and are thus less able to assess risk factors and pre-menopausal breast density).
- It is still unknown whether intrinsic breast density or the impact of environmental and lifestyle factors on breast density contribute more to the association between breast density and breast cancer.

Breast Density: Context for Interventions

According to the National Cancer Institute: "Breasts contain glandular, connective, and fat tissue. Breast density is a term that describes the relative amount of these different types of breast tissue as seen on a mammogram. Dense breasts have relatively high amounts of glandular tissue and fibrous connective tissue and relatively low amounts of fatty breast tissue." (See the Text Box on the following page for more detail.)

In 2012, California began requiring women who had a screening mammogram be informed if they have dense breast tissue.[160] This allows women to discuss whether they should consider alternative screening technologies, as mammograms of women with dense breasts can be harder to read. Additionally, this information may help women have a sense of their inherent breast cancer risk related to breast density and decide if they want to change their personal habits to be more protective and preventative.

From a societal level, there are other considerations. While there is more to learn about what exactly influences breast density, ionizing radiation, pharmaceutical hormones, parity, menopause, and air pollution were all found to increase the likelihood of denser breasts (described above). These risk factors have direct impact on breast cancer risk, as well as the indirect risk of increasing breast density. See other sections in this Plan for intervention recommendations around these factors that can influence breast cancer risk, potentially at least partly by impacting breast density.

Looking at breast density through a racial lens, more research is needed to understand any distinct connection between race and breast density, the way other breast cancer risk factors influence breast density disproportionately due to race, and what interventions show potential for ensuring that women are not experiencing higher breast cancer risk due to higher breast density from external and environmental factors. For example, we know that communities of color are often exposed to higher levels of air pollution, making it a doubly critical risk factor to focus intervention resources on.

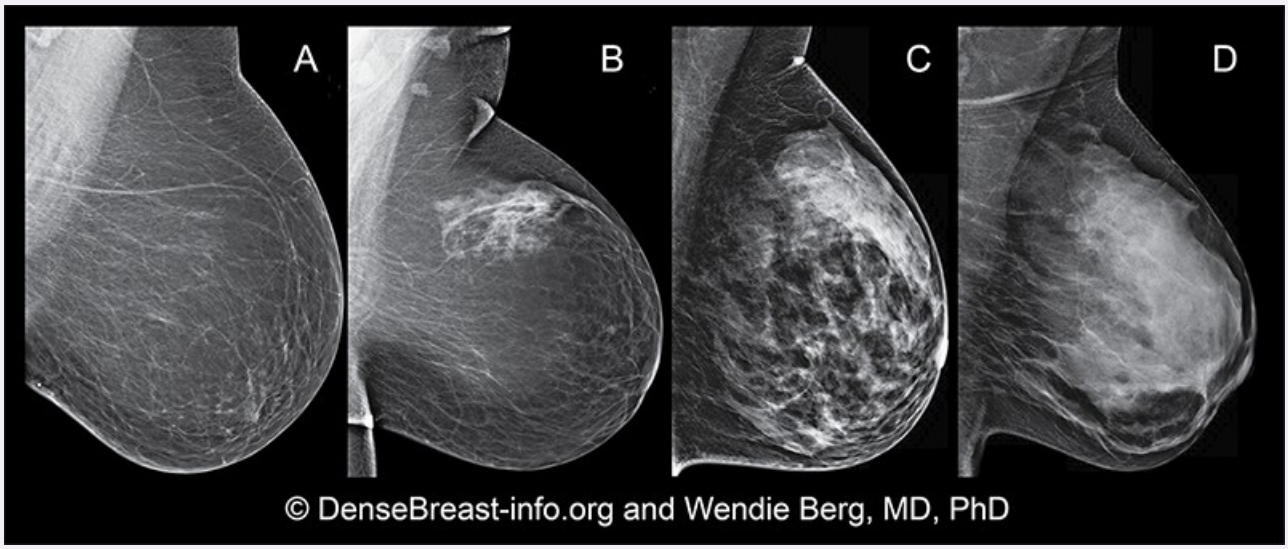
The interconnectedness of breast density and other risk factors demonstrates the need for a holistic and equitable approach to health protective policies across the state. It also requires some common sense. For example, heavy smoking at an early age may reduce breast density, but for many obvious reasons, it is not recommended that anything other than aggressively trying to prevent youth and young adults from starting to use tobacco products, and helping those who have started end their use, be pursued. (See more details in the "Tobacco" section of this Plan).

How is breast density categorized? (Source: National Cancer Institute website)[161]

Doctors use the Breast Imaging Reporting and Data System (BI-RADS) to group different types of breast density. This system, developed by the American College of Radiology, helps doctors to interpret and report back mammogram findings. BI-RADS classifies breast density into four categories, as follows:

- (**A**): Almost entirely fatty breast tissue, found in about 10% of women
- (**B**): Scattered areas of dense glandular tissue and fibrous connective tissue (scattered fibroglandular breast tissue) found in about 40% of women
- (**C**): Heterogeneously dense breast tissue with many areas of glandular tissue and fibrous connective tissue, found in about 40% of women
- (D): Extremely dense breast tissue, found in about 10% of women

Having dense breasts means that you have either "heterogeneously dense" (C) or "extremely dense" (D) breasts.



INTERVENTIONS

Overarching Goal: Improve research on understanding the role of breast density in breast cancer risk and the factors that impact breast density.

Intervention Goal 1

Expand research on understanding the breast density-breast cancer connection.

Objective 1: Support research to better understand the mechanism of how breast density impacts breast cancer risk.

Objective 2: Support research to more accurately assess breast density, including developing protocols for other technologies such as 3-D mammography, MRI, or ultrasound.[161]

Objective 3: Support research to improve and better interpret scans of dense breasts to identify breast cancer risk, for example, identifying if density patterns or areas of dense breast indicate risk,[161] or identifying biomarkers that predict breast cancer risk in women with dense breasts.[161]

Objective 4: Support research to better understand the link between breast density and other breast cancer risk factors, for example, diet, physical activity, or air pollution in relationship to genetics/heritability.

Objective 5: Support research to identify interventions that may help reduce breast density and/or mitigate changes in breast density due to other exposures and risk factors.

Objective 6: Support research to better understand breast density, breast density risk factors, and potential interventions to prevent increased breast density specific to different ethnic and racial groups.

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Inflammation

Science Summary

Inflammation plays a critical role in tumorigenesis (tumor formation). It is one of the mechanisms by which environmental factors may increase risk for breast cancer. Chronic inflammation should, where possible, be reduced and controlled. The promotion of less inflammatory diets and physical activity may contribute to breast cancer prevention. The use of anti-inflammatory drugs may be a potential intervention.

What the Foundational Documents Say

As highlighted in the Halifax Project paper, tumor-promoting inflammation is one of the Hallmarks of Cancer—helping cancer cells grow via the same growth signals normal cells provide to each other during wound healing and embryonic growth. Inflammation is an immediate and necessary host defense mechanism in response to infection or tissue injury. However, inflammation can play a critical role in all stages of tumorigenesis. It promotes an increase in cell proliferation and differentiation, generation of new blood vessels, and induction of epigenetic events while also inhibiting apoptosis (cell death) and disrupting antitumor immune surveillance mechanisms.

The other foundational documents list inflammation as one of the mechanisms by which environmental factors may increase cancer risk. Both the IOM report and the WCRF/AICR CUP 2017 report state that the amount of body and abdominal fat levels could influence cancer risk through several mechanisms, including the induction of a chronic state of low-grade inflammation. Compared with lean people, obese individuals commonly have elevated concentrations of common biomarkers of inflammation: circulating leptin, which can function as an inflammatory cytokine; tumor necrosis factor (TNF)-alpha; interleukin (IL)-6; and C-reactive protein.

The WCRF/AICR CUP 2017 report points to a reduction of inflammation as one of the potential mechanisms by which physical activity is protective of breast cancer—though it states that it is unclear whether physical activity that is not accompanied by weight loss has a significant impact on inflammation.

IBCERCC also pointed to animal models demonstrating inflammation as a possible mechanism involved in the association between obesity and mammary gland cancer. Looking specifically at inflammation, they cited studies showing that anti-inflammatory drugs may reduce the risk of both receptor-positive and receptor-negative breast cancer.

They also stated that some environmental exposures can increase inflammatory processes in the mammary gland, e.g. a diet high in saturated fat is known to promote mammary gland cancer in rats, and prenatal exposure to bisphenol A (BPA)—an endocrine disruptor—increased the expression of several pro-inflammatory cytokines and chemokines in rats.

The Current State of the Evidence

Recent studies have examined associations between inflammation and breast cancer through looking at levels of inflammatory biomarkers, the effect of pro and anti-inflammatory diets and the breast cancer preventive potential of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).

Inflammatory Biomarkers and Breast Cancer

Many studies conclude that inflammation may partially explain the elevated risk for breast cancer in post-menopausal women. These studies specifically explore inflammatory markers associated with obesity, post-menopausal weight gain, and adiposity and thus a potential target for preventive interventions.[1,2,3,4,5,6] Some have shown that inflammation can affect cancer risk independently of BMI.[7,8] The most common biomarker of inflammation used in studies is serum level of C-reactive protein (CRP) or high-sensitivity C-reactive protein (hs-CRP). Other biomarkers include leptin, tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6) and other less commonly used biomarkers.

CRP and hs-CRP: Most studies looking at populations across the world have indicated a positive association between serum CRP or hs-CRP and breast cancer risk varying from a 5% increase to more than doubling.[7,9,5,10,11,12,13,14,15] A few have found a suggestive but not significant association.[16,17,18]

Findings have been inconsistent with regard to the association of CRP and hs-CRP and menopausal status.[7,5,10,14] For instance, one study found post-menopausal women who did not use menopausal Hormone Replacement Therapy (HRT) and who had the highest levels of hs-CRP levels before diagnosis had a doubled risk of breast cancer compared to women with the lowest levels.[19] However, a prospective cohort study in China found higher hs-CRP levels were significantly associated with breast cancer risk, with a stronger association among younger women (under 50 years old).[12]

Conflicting interactions between CRP levels and obesity have been seen in post-menopausal women. One U.S. study found a significant positive association with breast cancer only in normal weight women ($BMI<25kg/m^2$)[20] while a French study showed higher breast cancer risk with higher CRP levels in overweight or obese women only ($BMI\geq25kg/m^2$).[21]

Looking at plasma CRP levels after diagnosis, a study of Italian women found that triple negative disease was significantly more frequent than luminal A in premenopausal women with high plasma CRP post-diagnosis. When the tumor stage at diagnosis was examined, the association between increasing CRP and triple negative tumors only occurred in early-stage tumors and not late stage tumors suggesting high CRP levels after diagnosis may be a consequence of the tumor growth.[22]

Other Inflammatory Biomarkers: Fewer studies have looked at other inflammatory biomarkers and results are more mixed. A study of Italian women found that in pre-menopausal women, divided by High, Medium, or Low tumor necrosis factor-alpha TNF-α, those with the highest levels of TNF-α had increased breast cancer risk compared with those with the lowest. The same study also showed high interleukin-6 (IL-6) was associated with increased risk with risk increasing per unit increase in IL-6.[14] A case-control study of Korean women found that plasma (blood) concentrations of IL-6 and IL-1β were significantly higher in women with breast cancer than control women.[23] A French study found that high levels of soluble intercellular adhesion molecule 1 (sICAM-1) was associated with an 86% increase in breast cancer risk.[24] In contrast, a U.S. study found that sICAM-1 was associated with a decreased risk of breast cancer.[25] This study also did not find an association with CRP though it did report a 25% increased risk with high levels of fibrinogen (a pro-inflammatory blood coagulation protein). A Swedish study looked at levels of inflammatory F2-isoprostane, prostaglandin F2α, pentraxin 3 and found no significant associations with breast cancer risk.[26]

Diet and Inflammation

Researchers have begun to look at the influence of pro- or anti-inflammatory diets on breast cancer risk. This work is supported by animal studies that have shown diet-mediated prevention of mammary carcinogenesis involving anti-inflammatory mechanisms.[27]

A study of nurses looking at adolescent and early-adulthood dietary patterns associated with inflammation (high intake of sugar sweetened and diet soft drinks, refined grains, red and processed meat, and margarine and low intake of green leafy vegetables, cruciferous vegetables, and coffee) found that such a pattern increased the incidence of pre- but not post-menopausal breast cancer.[28]

A growing body of research has used the Dietary Inflammatory Index (DII), which was developed to measure the inflammatory potential of diet and can be used in diverse populations to predict levels of inflammatory markers, including CRP, interelukin-6, and homocysteine. Studies have found that a pro-inflammatory diet with higher DII scores is associated with an increased risk of breast cancer overall,[29,30,31] with one study finding stronger associations in obese, post-menopausal women.[30] However, a study of the Women's' Health Initiative post-menopausal cohort found no association overall but a significant effect of DII on the ER-, PR-, Her2+ subtype.[32]

One study found that the timing of diet could affect inflammation levels. Eating more frequently, reducing evening energy intake, and fasting for longer nightly intervals was seen to decrease CRP levels, indicating lower systemic inflammation that may subsequently reduce breast cancer risk. More research is needed on timing of diet.[33]

Aspirin and Other NSAIDs

Lab studies have shown that inhibiting cyclooxygenase-2 (COX-2), an important part of the cyclooxygenase-prostaglandin inflammation pathway, inhibits mammary tumorigenesis in mice. Therefore, the consumption of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) that inhibit COX-2 is expected to help protect against cancer.[4] Researchers have examined whether regular use of aspirin and other NSAIDs have an effect on breast cancer risk.

Most studies since 2011 indicate that aspirin use is inversely associated with breast cancer incidence.[34,35,36,37,38,39] One study compared low-dose aspirin (81mg) with regular-dose aspirin (325mg) and only saw decreased breast cancer risk in those taking three or more low-dose aspirin tablets a week. The association was stronger in women with hormone receptor +/HER2- subtype. No association was seen with regular dose aspirin or other NSAIDs.[39] Two studies found no association with risk of breast cancer, though it is not clear what dose of aspirin was used by the women.[40,41]

Studies of other NSAIDs are more mixed with one study finding use of any NSAID decreasing risk of all subtypes but only among overweight women (BMI≥25 kg/m^2), not normal-weight women.[36] Another saw a decreased risk with any non-aspirin NSAID only for hormone + or Her2+ but not triple-negative breast cancers;[40] and two other studies found no association with breast cancer incidence.[37,41]

Nuances and Emerging Considerations

Diabetes

Researchers have begun to look at possible links between type 2 diabetes and breast cancer. Evidence points to a major role of the dysregulated glucose metabolism of diabetes causing a chronic pro-inflammatory condition, and an associated oxidative stress that promotes tumor initiation and progression.[42] Before menopause, type 2 diabetes—or perhaps the associated inflammation—may promote estrogen-independent (including triple-negative) breast cancer by mechanisms that may involve macrophage-secreted inflammatory cytokines, adipokines, and insulin.[43]

A study in China found that type 2 diabetes was associated with an increased risk of breast cancer and that these risks were further increased with specific polymorphisms in IL-6 and Heat shock protein 60 genes.[44]

Genetics

Research into polymorphisms in inflammation gene pathways has exploded recently. Connections to breast cancer risk are beginning to be identified.

Studies have shown that genetic variants, sometimes single nucleotide changes, in key inflammatory pathway genes are significantly associated with breast cancer risk in different populations of women.[45,46,47,48,49,50,51,52,53,54]

A research group looking at Latina and White women from the U.S. and Mexico found that post-menopausal women with higher indigenous ancestry had a reduced risk of breast cancer. They also found breast cancer risk associated with genetic variation in genes for 16 interleukins, TNF-? and toll-like receptors in these populations. Diet and lifestyle factors were also found to be important mediators of the breast cancer risk associated with these genes.[55,56,57,58]

More research is needed in this promising area of inflammation gene pathways.

Social Stress

Social stress has also been seen to increase the inflammatory status of individuals, which may influence breast cancer risk (See the section on "Stress"). A study of the Women's Health Initiative prospective cohort of post-menopausal women looked at CRP and social relationships. They found an association between social stress and CRP levels: larger social networks were associated with lower continuous CRP, and greater social strain associated with higher continuous CRP. However, they did not find any association between higher inflammation and invasive breast cancer.[59]

Take-Home Message

- Inflammation can play a critical role in tumorigenesis. It is one of the mechanisms by which environmental factors may increase risk for breast cancer.
- More research is needed to understand inflammation pathways and how these affect breast cancer risk.
- Chronic inflammation should, where possible, be decreased and controlled.
- The promotion of anti-inflammatory diets[33] and physical activity[60] are possible interventions that may contribute to breast cancer prevention.[61]
- The use of low-dose aspirin and other anti-inflammatory drugs for prevention should be further investigated.

Inflammation: Context for Interventions

As is the case for many of the breast cancer risk factors in this Breast Cancer Primary Prevention Plan, inflammation is complex and interconnected with numerous other factors. Based on the research described above, inflammation and inflammatory markers appear to be linked to breast cancer risk. More research is needed to understand the connection, as well as the best way to control chronic inflammation. In the meantime, the consumption of anti-inflammatory diets and healthy levels of physical activity should be encouraged—see the sections on "Diet and Nutrition" and "Physical Activity" for interventions to help achieve this.

On using low-dose aspirin and other anti-inflammatory drugs for primary prevention, it is important that the full risks and benefits are understood before any recommendations are made. In the field of cardiovascular disease, daily low-dose aspirin is a well-established treatment plan to reduce the risk of recurrence in patients who have had a heart attack or stroke.[62] However, recent research has shown that for healthy adults (with no previous heart attack or stroke), the risk of internal bleeding (hemorrhages) outweighs any primary prevention benefit. The American College of Cardiology's 2019 Guidelines recommend against the use of low-dose aspirin for primary prevention except for select high-risk patients.[63]

Chronic stress has also been linked to chronic inflammation. While more research is needed to elucidate this link, see the sections on: "Social and Built Environment;" "Race, Power, and Inequities;" and "Stress" for interventions that can be implemented now to reduce stressors.

INTERVENTIONS

Better understand the link between breast cancer and inflammation and identify effective options to control and reduce chronic inflammation.

Intervention Goal 1

Expand research on the connection between chronic inflammation and breast cancer risk.

Objective 1: Include testing for biomarkers of inflammation in ongoing and new prospective cohort studies of breast cancer.

Intervention Goal 2

Expand research on effective options to control and reduce chronic inflammation.

Objective 1: Research optimal diets to reduce chronic inflammation. (see the "Diet and Nutrition" section for interventions related to access to healthy and fresh foods).

Objective 2: Research optimal exercise regimens to reduce chronic inflammation (see the "Physical Activity" section for systems and built-environment interventions that support physical activity.)

Objective 3: Research benefits and especially risks of low-dose aspirin and other NSAIDs for primary prevention of breast cancer.

Objective 4: Research the link between chronic stress and chronic inflammation including interventions to reduce both.

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Menarche and Menopause

Science Summary

The timing of menarche and menopause, as well as the length of time between menarche and one's first full term pregnancy, have been shown to influence a woman's risk of developing breast cancer.

What the Foundational Documents Say

The AICR, IBCERCC, and IOM reports state that early menarche, late menopause, and late age at first birth are all risk factors for breast cancer.[1] Women are more vulnerable to environmental exposures during specific periods of time, like before menarche[2] and between menarche and menopause.[3]

More specifically the AICR report states that early menarche (before the age of 12), late natural menopause (after the age of 55), not bearing children, and first pregnancy over the age of 30 increase lifetime exposure to estrogen and ultimately risk of breast cancer (See "Pregnancy" section for more information).[4]

The Current State of the Evidence

Breast cancer risk is influenced by age at menarche (age at which a girl gets her first period – the end of the process of puberty), age at menopause, and the age at which first live birth occurs.

Several studies have found an inverse association between age at menarche and breast cancer risk i.e. early menarche—defined by AICR as being before the age of 12—increases overall risk of breast cancer and later menarche is thought to be protective.[5,6,7,8,9,10,11,12,13,14,15]

In addition, several studies found that a longer period between menarche and first live birth to be significantly associated with increased risk of breast cancer.[6,11,14,16,17,18,19,20,21] A number of studies showed stronger associations between risk and longer menarche to first birth interval for ER+/PR+ breast cancer;[6,18,19] while a longer interval between menarche and first birth was found to be protective for triple-negative breast cancer.[22,23]

Researchers suggest that early menopause or pre-menopausal hysterectomy reduces risk of breast cancer by reducing the circulation of sex hormones.[24] Early menarche, delayed menopause, fewer pregnancies were shown to have the opposite effect.[24,25,26] A Finnish study found that menarche before the age of 12 was associated with increased estradiol levels in adolescence and increased follicular estradiol levels in women age 20-31.[25]

Nuances and Emerging Considerations

Interactions

Chemical exposures and breastfeeding can each affect the relationship between menarche, menopause, pregnancy, and breast cancer.

- One study of the Multiethnic Cohort found that usage of hair products like oils, relaxers/perms, and hair dyes before age 13 was associated with decreased age at menarche.[27]
- A study of the interactions between bisphenol A and puberty found a suggestive trend that increasing levels of urinary BPA delayed menarche in adolescent girls. But the study also stated that BPA has been shown to be an obesogen and found that higher levels of BPA exposure are associated with higher BMI, which in turn increases risk for early puberty and menarche.[28]
- A study on proximity to traffic and exposure to traffic-related air pollution found that girls with higher exposure experienced the onset of puberty (pubic hair growth) several months earlier than girls exposed to lower amounts.[29]
- Several studies looking at breast cancer risk and the timing of menarche, menopause, and reproduction have highlighted breastfeeding as a protective factor.[10,20,22,30,31]

Take-Home Message

- Age of menarche, menopause, and the timing of one's first full-term pregnancy as well as the length of the intervals between these events all effect breast cancer risk.
- Women are more vulnerable to environmental exposures before menarche, around menopause, and before first pregnancy and such exposures can alter the timing of these milestones.
- This added vulnerability makes it even more important to promote systems-level change and work with communities and individuals to reduce controllable risk factors.

Menarche and Menopause: Context for Interventions

Natural Patterns of Menarche and Menopause

Early menarche and later menopause have both been associated with increased risk of breast cancer.[32] Along with other reproductive milestones (age at first pregnancy, number of live births, and breastfeeding), the number of menstrual cycles is associated with lifetime endogenous estrogen exposure—with higher exposure resulting in higher breast cancer risk.

Research on the natural trajectories of both female puberty and menarche and menopause is relatively new, with major research projects and collaborative projects emerging in the last 10-15 years.[33,34,35,36,37,38]

Collectively, the projects examining puberty demonstrate that the median age of pubertal onset has dropped in the past several decades,[38] and that the timing and chronology of pubertal events such as breast development (thelarche) and menarche have potentially shifted independently.[39,40] Historically, menarche has occurred, on average 2.3 years after thelarche. Recent studies document younger ages of thelarche and no change in the age of menarche, resulting in a longer period between thelarche and menarche and a potential decoupling of these markers of puberty.[41]

The onset of puberty varies by race and ethnicity. For instance, on average, breast development begins at age 8.8 among Black girls, 9.3 years in Latina girls and 9.7 years among Asian and Pacific Islander and White girls.[41] Furthermore, the age of menarche may be declining at different rates among girls around the globe. One study of three generations of women in Taiwan found that the age of menarche decreased by a year each generation.[42]

While impact on breast cancer risk is the focus of this Plan, it is important to note that earlier age at the onset of puberty carries with it a host of other potential harms. Research suggests that girls experiencing early menarche are more likely to initiate sex at an earlier age; engage in risky behaviors, such as smoking, drinking, drugs, crime and unprotected sex (resulting in more teen pregnancies); be physically and violently victimized; and are at higher risk of depression, anxiety, low self-esteem, and suicide.[43] Clearly the scope of this public health issue reaches far beyond breast cancer risk.

Research on the natural progression of menopause is only beginning to emerge. Historically, most research on menopause only studied White women, and often women in clinical settings.[44] This means we know less about the experiences of women of color and little about the patterns of menopause among women who do not seek medical intervention.

Research from a multi-ethnic cohort found that the median age at which the menopausal transition begins is age 47, and the earlier the transition begins, the longer it lasts.[45] Some studies suggest Black and Latina women begin menopause about 2 years before White women.[45] However, a 2018 study found no statistical difference in the age of onset of the menopausal transition between Black and White women, although the transition lasted longer among Black women.[46]

In 2012, a collaborative group sought to revise the staging criteria for reproductive markers. The Stages of Reproductive Aging Workshop (STRAW) identified 10 stages of the reproductive lifecycle, divided into the reproductive phase, the menopausal transition and post-menopause.[35] The group also identified key research needs, including a better understanding of hormonal changes through the post-menopausal stage.[35]

Externally Driven Changes in Patterns of Menarche and Menopause

Considerable attention has focused on decreases in the age of puberty and changes in the chronology of key pubertal events among girls. In addition, some data suggests that the age of menopause has increased over time.[45]

Higher body mass index is associated with both early menarche and later onset of menopause.[46,47] Studies have explored the impact of chemical exposures both prenatally[40] and postnatally.[40,48,49] These relationships are complex, depending on the timing of exposures and the type of chemicals, and they may interact with other factors that also affect pubertal timing, such as body mass index.[49,50]

A study of ethnically diverse girls born in California found that girls who were not breastfed had earlier onset of both breast development and pubic hair development, and this association was strongest for Black girls.[50]

Less research has examined factors that affect the age at which menopause begins. A 2012 review highlighted several factors associated with earlier age of menopause, including lower socioeconomic status, smoking, and some chemical exposures. Factors associated with later age of menopause included increasing parity (especially among women with higher socioeconomic status), oral contraceptive use, and adequate nutrition.[45]

Overall, research suggests that many of the other factors addressed in this Plan, including racial inequities, chemical exposures, body weight across the lifespan, and stress, may also affect the duration of a woman's reproductive years. While there are natural variations in the age at which puberty commences and when menopause begins, it is increasingly clear that external factors can also influence the timing and pattern of these natural processes. Efforts to reduce these external factors that are associated with changes in puberty, menopause, and breast cancer could have a profound effect on women's overall well-being and health.

INTERVENTIONS

Overarching Goal: Expand research into potential causes of early menarche and extended duration of menses, their impact on breast cancer risk, and interventions to mitigate those impacts.

Intervention Goal 1

Expand and extend research on early menarche and pubertal sequencing to better understand factors that affect breast development and breast cancer risk.

Objective 1: Conduct research on early menarche and breast cancer risk later in life.

- **Strategy 1**: Conduct research to identify and better understand the causes of intrinsic early puberty and early puberty resulting from external forces, both of which can increase breast cancer risk.
- **Strategy 2**: Expand research into the mechanisms by which pubertal timing, sequence, and phases affect breast cancer risk.
- **Strategy 3**: Conduct studies to understand whether body weight in early childhood and adolescence (a risk factor for early menarche) or early menarche itself is a concern for increased breast cancer risk, since the research in these areas may conflict.
- **Strategy 4**: Deepen our understanding of endocrine-disrupting compounds and pubertal timing and sequence, including prenatal exposures.
- **Strategy 5**: Provide resources to sustain prospective cohort studies already underway in California.

Objective 2: Implement policies that reduce chemical exposures linked to breast cancer and pubertal timing (See "Place-based Chemical Exposures" and "Chemicals in Consumer Products" sections of this Plan for more information).

Intervention Goal 2

Expand research on women's physiology and diverse experiences in peri-menopause and menopause.

Objective 1: Expand research on women's experiences of menopause, including experiences among otherwise healthy women, women going through induced menopause (including from breast cancer treatments), and across women of different racial, ethnic and economic backgrounds.

Objective 2: Explore whether extrinsic factors, such as stress, chemical exposures, and body weight, affect the timing, duration, and symptoms experienced in menopause.

Objective 3: Expand research on the overall duration of menses and breast cancer risk.

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Microbiome

Science Summary

Science is beginning to explore the health effects of the vast collection of microbes residing in and on the body, termed the microbiome. Across people, microbiome differences exist in breast tissue and the digestive tract, and these differences can influence levels of estrogen and other hormonally active agents, immune function, and inflammation. Microbial diversity in the breast may be protective against breast cancer, and a healthy gut microbiome may support immune function, which may help protect against breast cancer.

What the Foundational Documents Say

There is little published in the foundational documents on the microbiome. Goodson and colleagues mention a bacterial influence on inflammation which may impact metastatic processes.[1]

The Current State of the Evidence

NOTE: A microbiome describes a community of microorganisms: bacteria, fungi, and viruses of microscopic size. Taxonomy is the classification of organisms, typically starting from largest to more specific groupings. In this report, the microbiome's species is the smallest grouping. These species belong to a larger genus, and the genus belongs to a larger phylum.

Breast Microbiome

Researchers have found that breast tissue is normally host to communities of microorganisms.[2,3] It is not clear how these microbes get to the breast, although suggested routes include internal transfer from the gut microbiome and absorption though the skin, perhaps through the nipple. Though viral contributors to breast cancer have been hypothesized for a long time and continue to be considered,[4] most research has focused on the bacteria in these communities. Many studies have analyzed the composition of specific breast bacterial profiles associated with breast cancer and healthy tissue, but the specific bacteria identified differ between studies, and thus far no consistent species or community has been identified related to breast cancer risk.[5,6,7] Though identifying specific breast bacteria associated with healthy or diseased breast tissue remains elusive, evidence suggests that the profile of breast

bacteria differ in benign breast disease compared to cancerous breast tissue,[2] and between breast cancer patients compared to healthy controls.[5] Bacteria residing in healthy tissue adjacent to breast tumor sites are more similar to the bacteria found in the nearby tumors than to those found in healthy breast tissue. This was found both in benign and cancerous tumors. The authors note that some of the bacteria abundant in breast cancer patients had the ability to induce DNA double-stranded breaks, but that more research is needed to see if these differences are a cause or a consequence of the disease.[5]

In healthy breast tissue, bacterial diversity appears to be greater in breast tissue than in the breast skin, suggesting that the source of the breast tissue microbes may not be from nipple access alone.[2] Bacterial diversity found in nipple aspirate fluid (NAF) excreted from breast ductal tissue is similar to the respective nipple skin in both healthy ductal tissue and in ductal tissue of women with a breast cancer history.[8] However, when comparing healthy NAF to the NAF from women with a history of breast cancer, differences were seen in two classifications of microbes. The genus *Alistipes* was identified only in NAF of women with a history of breast cancer, and the genus *Sphingomonoadaceae* was identified only in NAF of healthy controls.[8]

One study suggests bacterial differences in breast cancer subtypes, finding more-diverse bacteria in ER+ tumors and less-diverse bacteria in triple-negative tumors.[6] While the bacterial makeup in triple-negative and triple-positive tumors were found to be unique in this study, ER+ and HER2+ tumors were similar in their signatures.[6] Another study found that total number of bacteria, termed bacterial load, was less in stage 3 breast tumors compared to stages 1 and 2, while the bacterial load found in healthy breast tissue of these same patients did not differ with stage of breast cancer.[7]

Though differences between healthy breast tissue bacterial composition and the composition found in breast cancer are not clearly understood, researchers have suggested that bacterial influence on breast cancer may be due to the synergy of a complex composition of breast microbes rather than due to a single species.[5]

Gut Microbiome

The composition of gut bacteria in women with post-menopausal breast cancer has been shown to differ compared to healthy women.[9,10] These gut-residing bacteria may affect breast cancer risk through several mechanisms: estrogen metabolism reversal,[11,12] altering immune function,[10,12,13] and mediating effects of diet (e.g. metabolites from dietary fiber).[12]

Though the ideal gut microbiome has yet to be determined, some bacteria produce an enzyme, B-glucuronidase, that is capable of reversing the metabolism (deconjugation) of estrogens (endogenous or ingested) previously earmarked for excretion.[11,12] By doing so, these estrogens are able to be re-absorbed into circulation, adding to total estrogen levels, which could in turn increase breast cancer risk.

This estrogen deconjugation by microbial B-glucuronidase may not be isolated in the digestive tract. B-glucuronidase enzymes were also seen in nipple aspirate fluid from the breast.[8] In addition, this enzyme may also be capable of reversing the metabolism of estrogenic chemicals such as BPA, which would normally be excreted, thus further adding to total estrogen levels.[14]

The gut microbiome can influence immune functions that protect against breast cancer.

Two literature reviews identify members of the Firmicutes phylum, such as *Ruminococcaceae*, and members of the Protobacteria phylum, such as *Escherichia coli*, as B-glucuronidase-producing bacteria.[12,14] In a third literature review, researchers suggest that while diets high in fat and protein may increase B-glucuronidase activity, vegetarian diets and diets high in fiber may reduce this activity.[15]

The gut microbiome may also affect breast cancer risk through its effect on immune function.[12,13] When immune system cells of the intestine (dendritic cells in the Peyer's Patches—important immune system organs in the gut) contact certain gut microbes, immune function may be influenced.[12] For example, CD8 T cells (immune cells capable of attacking breast tumor cells) mature when dendritic cells are exposed to the genus *Sphingomonas* within the intestinal lumen.[12,13] The species *Sphingomonas yanoikuyae* may be higher in normal breast tissue compared to breast cancer tissue.[7]

The process of recycling estrogen may also involve the immune system through secretory immunoglobulin A (s-IgA). This immune system protein, residing in the intestinal mucosa, binds to intestinal bacteria. One study found that the bacteria not bound to s-IgA were positively associated with circulating estrogens, and suggests that the unbound bacteria may be involved in estrogen recycling, preventing excretion and increasing total estrogen levels, which could increase risk for breast cancer.[10]

In addition to influencing endogenous estrogen levels, the gut bacteria may affect circulating levels of phytoestrogens such as enterolactone. Dietary fiber lignans (types of polyphenols) are metabolized by bacteria from both the Firmicutes and Bacteriodetes phyla into enterolactone and other phytoestrogens, which are absorbed into systemic circulation. According to one review of the literature, circulating enterolactone may be inversely associated with breast cancer risk. Soy and other legumes, seeds, fruit, vegetables, and whole grains provide dietary sources of lignans for this bacterial metabolism.[12]

Nuances and Emerging Considerations

In the human body, human cells are outnumbered by resident bacteria cells by a factor of 10, and these bacteria contribute up to 3% of the average person's weight.[16] The large numbers and types of bacteria residing in the human body create a challenge for identifying the optimal gut bacterial composition as well as investigating the relationship between breast cancer risk and the microbiome. Standardizing procedures and methodology for sampling the microbiome and DNA extraction (used to identify the bacterial species present) would assist analysis as microbiome research expands.

Further research investigating the interplay between the microbiome and the immune system, inflammation, carcinogenesis, metabolism, and disease is warranted to elucidate associations and mechanisms impacting breast cancer risk. Additionally, the interactions between the microbiome and other factors, such as exercise, diet, stress, and endocrine-disrupting compounds and other chemicals, would also help shed light on mechanisms involved in breast cancer risk. Research exploring the relationship between bacterial species, whether synergistic or antagonistic, may also shed light on how these relationships affect human health.

Take-Home Message

- A microbiome (community of microorganisms) exists in the breast tissue and is distinct from that of the outer skin of the breast.
- Microbial diversity in the breast may be protective against breast cancer.
- The bacterial composition of the microbiome in the gut can influence circulating estrogen levels.
- The gut microbiome can influence immune functions that protect against breast cancer.
- Through gut microbe metabolism, higher lignan intake from various sources of dietary fiber may reduce breast cancer risk.

Microbiome: Context for Interventions

Our bodies are inhabited by trillions of microorganisms—bacteria, fungi, viruses, and other organisms of microscopic size. This is known as the human microbiome. While many think of bacteria and viruses as making people sick, humans depend on the microbiome for basic functions, such as digesting our food. In fact, humans could not survive without many of these microbes. Though the microbiome has been known of for many years, it is only since the early 2000s that newer technologies have enabled researchers to make real strides in understanding the composition of the human microbiome and its relationship to overall health.

The vast majority of research to date has focused on the bacterial microbiome. In 2007, the National Institutes of Health (NIH) launched the Human Microbiome Project (HMP) to better understand the interactions between the microbiome and human health and disease.[17] Over the 10 years of the $215 million project (2007-2016), research exploded in the field. In addition to the HMP, NIH funded $728 million in extramural human microbiome research activities over fiscal years 2012–2016.[18] Though the HMP has ended, NIH still coordinates extramural microbiome research through the Trans-NIH Microbiome Working Group (TMWG).[19]

Over the last two decades, researchers have mapped the normal bacteria that live in and on the healthy human body and revealed that the microbial community makeup often varies from person to person, and the metabolic capabilities and immune-modulating effects of these communities can correlate with health and disease. Researchers are now exploring how changes in the microbiome are associated with—or even cause—illnesses. Studies are beginning to test new therapeutic approaches designed to manipulate the microbiome to treat disease, as well as to restore and support health.[20]

Below are some examples of other findings about the connection between health and the microbiome highlighted by the Human Microbiome Project. While these findings do not illuminate breast cancer risk, they do point to ways that researchers have only touched the tip of the iceberg on what the microbiome means for many aspects of health. The HMP states that the research findings include:

- Our diets, and in particular fat and fiber intake, can have immediate and dramatic impacts on the makeup of our microbiome—indicating that dietary interventions can have profound impact.

- The gut microbiome can metabolize a compound in red meat, resulting in the formation of a different compound, TMAO, which has a known role in promoting cardiovascular disease.
- Alterations in the gut microbiome can have a direct effect on colon cancer development.
- The gut microbiome also has its own circadian rhythm (a natural, internal process that regulates the sleep-wake cycle and repeats roughly every 24 hours), and a metabolite produced by these bacteria influences our own circadian rhythms. Furthermore, a high-fat diet can alter the microbiome circadian rhythm, suggesting a link between our diet, the gut microbiome, and our circadian clocks which could influence our sleep-wake cycle and metabolism more generally.
- Monitoring the gut microbiome can be used as an early detection of Crohn's disease and can also be used to monitor the effectiveness of various treatments for this disease.

Recent research has also confirmed that babies born by Cesarean section have dramatically different gut bacteria than those born vaginally.[21] Research is continuing into what health impacts these differences may have throughout a person's lifespan and whether there is a way of establishing a healthy microbiome at birth.

As stated above, the human microbiome mediates a number of other risk factors for breast cancer. We need to understand these interactions better. Once we understand those interactions and how to influence the microbiome, whether through dietary interventions or other means, enormous potential exists to optimize an individual's microbiome for health, including reducing breast cancer risk.

INTERVENTIONS

Overarching Goal: Improve research on understanding the role of the microbiome in breast cancer risk.

Intervention Goal 1

Expand research on understanding the microbiome-breast cancer connection.

Objective 1: Support research to more accurately assess the breast microbiome and its influence on breast cancer risk.

Objective 2: Support research to better understand the interactions between the gut microbiome and breast cancer risk.

Objective 3: Support research to better understand the link between the microbiome and other breast cancer risk factors, for example, diet, physical activity, and inflammation.

Objective 4: Support research to identify optimal microbiomes and how they might be achieved, whether through probiotics, transfer of microbiomes from healthy individuals, or other methods.

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Stress

Science Summary

Several studies have found associations between stress and breast cancer risk, but other studies find no relationship. Theoretical models propose that racial discrimination, economic deprivation, and other socio-environmental stressors may disrupt biological processes and lead to increased risk of breast cancer incidence.

What the Foundational Documents Say

Most of our foundational documents did not discuss stress or only offered brief mentions of oxidative stress as it relates to chemical exposures[1,2] and cellular stress.[2]

The Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC)[3] described research on the potential for extreme stress and caloric restriction to co-occur in extreme situations, such as wartime, and suggested that both may have different, independent effects on breast cancer risk. The report also included a section on psychosocial factors, including stress. They reported on data suggesting that stressful family environments have been linked to early puberty (a risk factor for later life breast cancer), and some data that suggests a relationship between stressful life events and breast cancer. Furthermore, the IBCERCC also referenced theoretic work that suggests that low-income communities of color may face unique stressors—such as overcrowding, racial discrimination and economic deprivation—that have the potential to affect health.

The Current State of the Evidence

"Stress" often describes the physical fight-or-flight response that helps organisms respond to threats or challenges. This response focuses all of the organism's energy on surviving the threat by engaging the HPA (hypothalamic-pituitary-adrenal) axis and increasing heart rate, muscular tension, and respiration, while shutting down digestion and other routine physiological processes. This response is very effective for short-term (acute) stressors. However, most modern-day stressors are either long-term (chronic) or recurring.[4] Chronic stressors include job stress, economic stress, family tensions, experiences of racism and

other social inequities, crowded living situations, and the experience of having multiple, competing demands. This long-term, sustained physiological response is associated with health outcomes ranging from heart disease to digestive issues, and including increased experiences of pain in those with chronic pain conditions.

While stress is often partly defined by how an individual experiences events and situations in their lives, researchers have attempted to quantify it in several ways.

Major Life Events

While individual studies may define life events differently, many include marital stress, death of a family member, serious financial difficulties, divorce, unemployment, and similarly disruptive major life events. A 2013 meta-analysis reviewed seven studies from the U.S., Australia, and Europe and they found that women with striking life events (such as the death of a spouse, child, or friend, or a change in financial status) had 50% higher risk of breast cancer, and those with the most severely stressful events had twice the risk of breast cancer.[5] One case-control study found that the experience of severe and moderate threats tripled breast cancer risk.[6] Another case-control found that experiencing a major life event stressor (e.g., unemployment, death of a loved one, relationship problems) within the last five years quadrupled risk, and that chronic stress increased risk by 44%.[7]

A systematic review of the literature found mixed results, with one-half of the studies reviewed showing a relationship between some definition of stress and breast cancer. The authors suggested that stress in childhood and adolescence may have a stronger effect on later breast cancer risk.[8] One study explored childhood stress specifically, and found that severe stressors in childhood were more common in breast cancer patients than those with benign breast disease or healthy controls, but that there was no difference in stressful life events in adolescence among these groups.[9]

Studies have found associations with some specific stressors including divorce (triple risk),[7] parental death (15% to 300% higher risk),[6,10] death of a close family member (2-8 times the risk),[6,11] personal illness or injury (more than doubled risk),[11] imprisonment or troubles with the law (almost tripled the risk),[11] retirement (50% higher risk),[11] financial difficulties (2-3 times the risk),[6,7] and son's military service (six times the risk).[6]

Despite these compelling findings, other meta-analyses[12] and prospective studies[13] have found no evidence that stress increases breast cancer risk, and while other research has found that stress relates to other breast cancer risk factors, such as alcohol use and obesity, but not directly to breast cancer.[14]

Humanitarian Violations and Extreme Stress

The extreme stressors and deprivations of wartime and humanitarian crises may also increase breast cancer risk among those who survive. Jewish women who lived in Europe during the Holocaust had a 20% higher risk of breast cancer.[15] Among women who were youngest during the latter years of World War II (those born between 1940-1945), breast cancer risk was more than doubled.[16] Another study of Jewish survivors found a linear association between war-related post-traumatic stress disorder (PTSD) and risk for developing breast cancer.

Those who reported PTSD had nearly tripled risk of breast cancer compared to those who did not report PTSD. Those who reported both severe hunger and PTSD had almost six times the breast cancer risk.[17] Another study that examined traumatic events among survivors of the war in Bosnia and Herzegovina found that those with breast cancer reported more traumatic wartime experiences.[18] The extreme stressors and deprivations illustrated in these situations share similarities with the disproportionate and often extreme neighborhood and environmental stressors experienced by racial and ethnic minorities in the United States.[19]

Risk Perception and Other Psychosocial Factors

In addition to stress, studies have found that depression[20,21] and anxiety[21] may also be linked to breast cancer. Avoidant coping approaches and a sense of inadequate social support each doubled or nearly doubled breast cancer risk in one study.[7]

Emerging research also suggests that the experience or perception of stress may have a stronger effect on risk than stressful events themselves. One study found that individuals whose life events were perceived as stressful had 63% higher breast cancer risk than individuals who did not perceive events as stressful. Previous personal illness affected breast cancer risk regardless of whether it was perceived as stressful.[22]

Work Stress

Several studies have looked specifically at work stress. A meta-analysis of 12 studies found no evidence of increased breast cancer based upon harmonizing the measure of work stress across all 12 studies.[23] However, a second study by the same researchers found that long work hours (more than 55 hours per week) were associated with a 60% increase in risk of breast cancer.[24] Another series of studies examined women who held higher status occupations in the 1970s. These studies found almost 60% increased breast cancer risk among women who had the authority to hire, fire, and influence pay in the 1970s.[25,26] The authors hypothesize that women who held higher status jobs may have experienced unique kinds of stressful interpersonal interactions due to resistance to women's authority in such jobs.

Stress, Racism, and Social Inequity

Researchers have also developed theoretical models, based on what we know about disparities in breast cancer; social, economic, and psychological stressors across the life course; and the social environment related to race. The concept of weathering describes the accelerated aging and biological wear and tear experienced by U.S. Blacks due to social and economic stressors, discrimination, and racism. These processes begin with prenatal and early childhood stressors that can dysregulate the biological stress pathways in ways that may predispose the body to later-life breast cancer.[27] Researchers in these areas call for research that addresses structural societal factors that shape and reinforce racial inequalities (both historically and presently) to understand the increased risk of aggressive triple-negative breast cancers among Black women,[28] and to develop prevention models[27] and interventions[28] that address the root of these inequities. Further research is needed to examine the effect of stress on breast cancer risk in other racial groups.

Nuances and Emerging Considerations

Mechanisms That Could Explain Links Between Stress and Breast Cancer

One study found that work stress, financial stress, and social stress were all associated with risk of benign breast disease, which is a risk for later-life breast cancer.[29] Several researchers have posited that the physiological disruptions that occur as a result of chronic stress (such as racism, deprivation, and neighborhood context) may disrupt the HPA axis, including the cortisol response, with the result being changes in the immune system, inflammatory response, and potential epigenetic changes.[28,30,31]

Laboratory research has examined the effects of social isolation in mice on mammary gland development and mammary gland tumors. One such study found that social isolation, which mimics the physiological effects of PTSD in humans, alters mammary gene expression, mammary gland development, and tumor formation.[32] Another found that obesity-inducing diets interacted with social isolation (which also promotes weight gain) to induce more mammary gland tumors than either factor alone.[33]

Oxidative Stress

Studies of oxidative stress at the cellular level may provide insights into the process of tumor formation. Oxidative stress can lead to changes in cells and tissues that set the stage for tumors to form,[34] grow, and metastasize.[35] Oxidative stress may partially explain the links between post-menopausal obesity and breast cancer and type 2 diabetes and breast cancer.[36,37,38] Researchers have also reported that genes that regulate the oxidant/antioxidant pathways may affect breast cancer risk.[39]

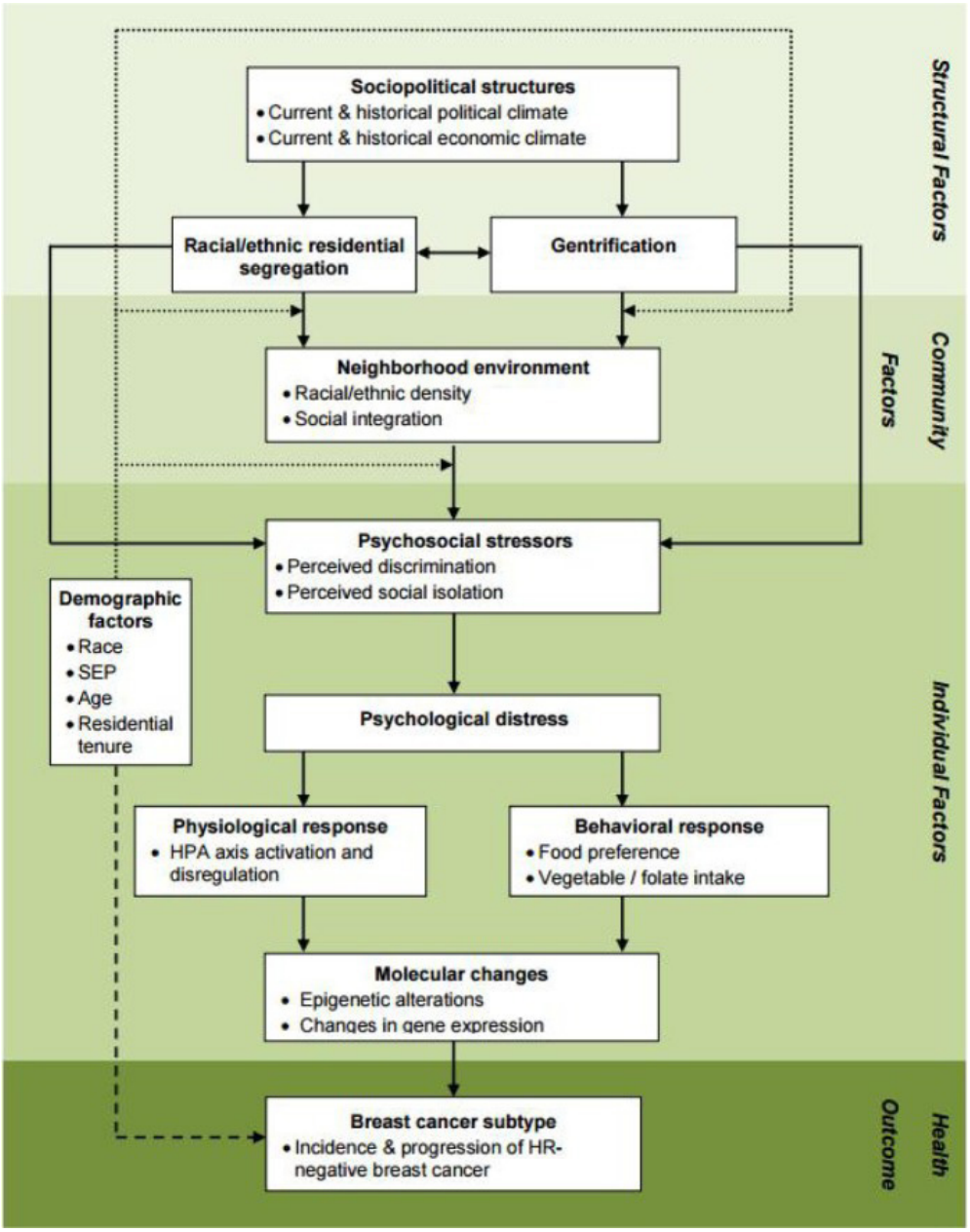
Take-Home Message

- Stress is defined and studied in many different ways, which may not capture what people colloquially mean when they talk about stress. Life events, chronic life stressors, physiological stress, and perceived stress all offer different meanings and insights into how stress is experienced and studied.
- Study findings are mixed, likely due to difference in definitions and data collection methods, but several studies suggest that both major life events and severe traumas are linked to breast cancer risk.
- Further research is needed to understand people's experience of stress, including the stresses of racism and economic deprivation, and the consequences of stress including biological changes and long-term health effects.

Stress: Context for Interventions

Stress is defined and studied in many different ways. As noted in the research review, findings are mixed, but several studies suggest that major life events and severe traumas are linked to breast cancer risk. The model below explores the relationship of social factors to stress and health outcomes, including the relationship of structural factors to stressors, the experience of stress, and physiological aspects.[28]

Figure 11.

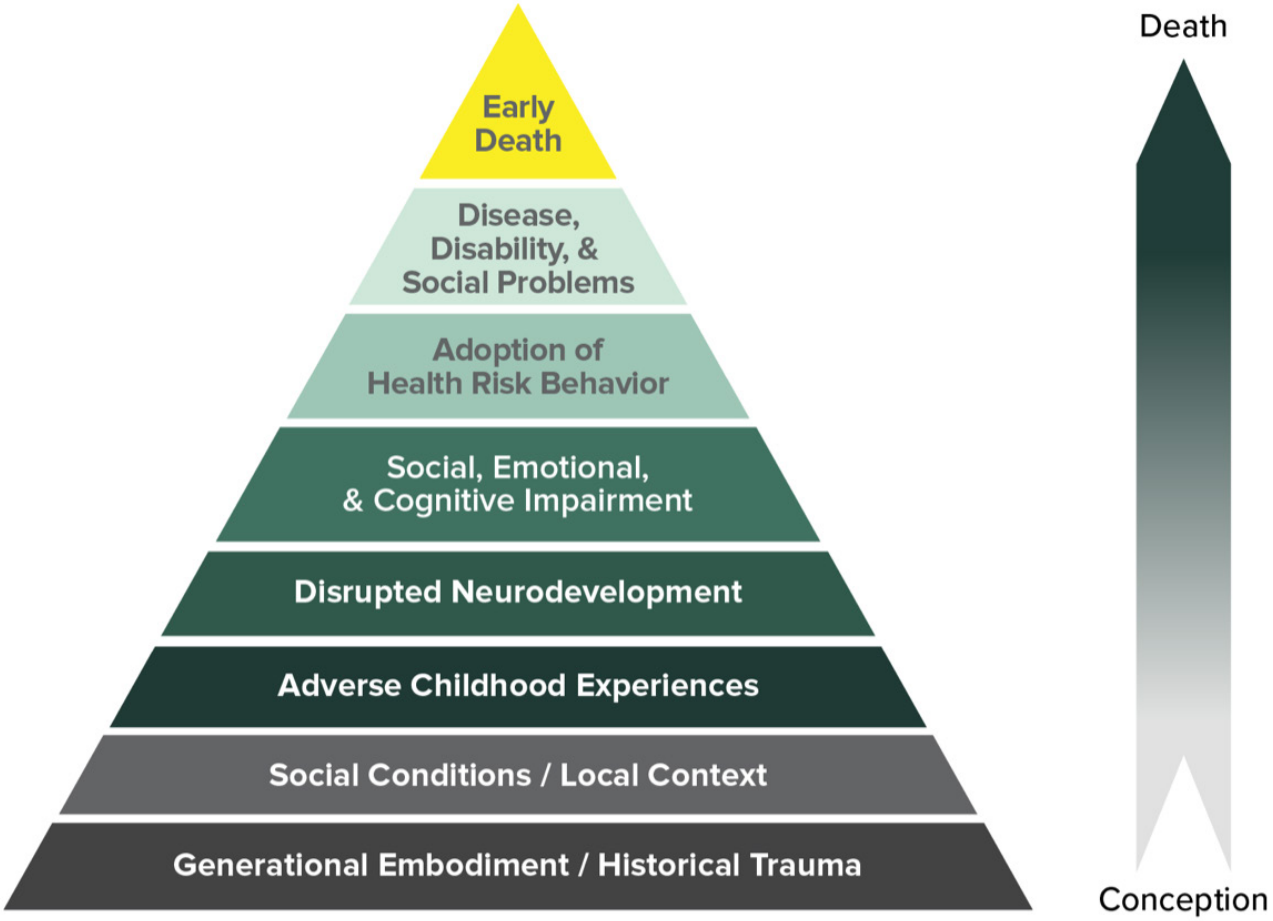

Structural Factors
Community Factors
Individual Factors
Health Outcome
Sociopolitical structures
• Current & historical political climate
• Current & historical economic climate
Racial/ethnic residential segregation
Gentrification
Neighborhood environment
• Racial/ethnic density
• Social integration
Psychosocial stressors
• Perceived discrimination
• Perceived social isolation
Demographic factors
• Race
• SEP
• Age
• Residential tenure
Psychological distress
Physiological response
• HPA axis activation and disregulation
Behavioral response
• Food preference
• Vegetable / folate intake
Molecular changes
• Epigenetic alterations
• Changes in gene expression
Breast cancer subtype
• Incidence & progression of HR-negative breast cancer

Data are less conclusive with regard to stressors induced by systemic racism, segregation, or economic disparities, as well as chronic stressors such as time constraints, financial challenges or ongoing workplace conflicts. Standard questionnaires may not capture what people colloquially mean when they talk about stress.[40] By one definition, perceived stress is the feeling when demands exceed an individual's personal and social resources. As such, it is a subjective experience shaped by context.

Emerging theories integrate research from multiple disciplines to understand how experiences of racism, isolation, and disparities affect the physiological stress response. The weathering hypothesis posits that the cumulative life experiences of Blacks contribute to the serious health disparities they experience regardless of socioeconomic status. Disparities in power, access, experiences of racism, and lifetime stress are captured by the concept of weathering.[27,28] Weathering characterizes a lifetime of cumulative adversity experiences by U.S. Blacks due to "historically structured differences by race in lived experience, exposure to stressors, and access to coping resources over the life-course."[41]

Stress experienced early in life may exert especially powerful effects on adult health.[42] Termed ACEs (adverse childhood experiences), these experiences are not distributed equitably in society. Kaiser Permanente and the CDC conducted the initial study of ACEs from 1995-1997, based upon data from 17,000 Southern California residents.[43] The conceptual model for the study outlined the mechanisms by which adverse experiences in early life, including historical trauma, contribute to adult disease and early mortality.

Figure 12. Referred to as the ACES pyramid, this figure illustrates how adverse childhood experiences, starting with historical trauma, have lifelong effects on well-being and health.[43]



In California, 61.7% of adults have experienced at least one adverse childhood experience (ACE), and 16.7% have experienced four or more ACEs, based upon the Center for Youth Wellness (CYW) analysis of the California Behavioral Risk Factor Surveillance System project.[44] In California, patterns of ACEs are associated with low income and parental education but are generally similar across racial and ethnic groups.[45] Exposure to four or more ACEs is associated with dramatically higher likelihoods of alcoholism, heart disease, stroke, and cancer.[46]

Post-traumatic stress injury (PTSI), previously termed post-traumatic stress disorder (PTSD), develops in some individuals who experience traumatic or dangerous events.[47] While PTSI is often associated with experiences in war, it is also associated with numerous other events, including experiencing, seeing, or learning about an event involving actual or threatened death, serious injury, or sexual violation.[48] Social support and coping strategies can affect both the likelihood of experiencing PTSI and recovery. Individuals in some occupations, such as military personnel and first responders, may be more likely to develop PTSI.[49,50] Research needs to explore the links between PTSI and health, especially among occupational groups with disproportionate exposures to severe stressors and trauma.

Interventions from the "Race, Power and Inequity" and "Social and Built Environment" sections can reduce disparities and social structures that induce stress. These should be implemented along with the specific stress interventions below.

Community Input on Stress

While stress was not formally presented at Community Listening Sessions, it was such a recurrent and consistent theme from so many of the people that we decided to highlight it as a separate topic. Community participants described stress as an overwhelming concern in their life that had a direct impact on many other breast cancer risk factors. For example, one participant said, "Don't tell me not to smoke, help me address the stressors in my life that lead me to smoke." Numerous challenges added to people's experience of stress, including overt acts of racism, micro-aggressions, economic uncertainty, and stress (e.g. not having a job or needing to work more than one job), food insecurity, living near sources of various forms of pollution, fear of violence, and fear of deportation. Our country's history of slavery, genocide, and ongoing racism was seen as the root cause of many of these sources of stress.

INTERVENTIONS

Overarching Goal: Understand and ameliorate the effects of stress, especially those that contribute to later-life adverse health outcomes including breast cancer.

Intervention Goal 1

Expand research to understand the links between prenatal and early childhood stress and breast cancer.

Objective 1: Conduct research on early-childhood adversity and breast cancer risk later in life, using strong prospective cohort studies already underway in California (for example, CHAMACOS[51] and the Child Health and Development Studies[52]).

- **Strategy 1:** Expand research on how people understand, define and experience stress, including the stresses of racism, economic deprivation, and other factors.
- **Strategy 2:** Expand research on stress to routinely include physiological measures such as cortisol levels and daily patterns of cortisol release. Develop and test models to understand the relationship of stressors, physiological responses to stress, sleep disruption, and other models to deepen understanding of how stress may affect breast cancer risk. For instance, discussions of the weathering hypothesis posit mechanisms ranging from the social to the molecular that will require sophisticated trans-disciplinary research methods to test and refine our understanding.[27,28]

Intervention Goal 2

Establish California's leadership in addressing adverse childhood experiences (ACEs) through work with the California surgeon general.

Objective 1: Support the California surgeon general's efforts to add screening for childhood trauma to routine pediatrician visits and ensure access to services to address identified stress and trauma.[53]

Objective 2: Implement the CDC's recommendations to reduce adverse childhood experiences, especially those that address social inequity. The recommendations below are drawn from the CDC's 2016 report Preventing Child Abuse and Neglect: A Technical Package for Policy, Norm, and Programmatic Activities.[54]

- **Strategy 1:** Strengthen economic supports to families. The CDC notes that policies that improve the socioeconomic conditions of families may have the largest impact on health.
- **Strategy 2:** Provide quality childcare and education early in life.

Intervention Goal 3

De-stigmatize use of mental health services and increase the availability of mental health services.

Objective 1: Expand mental health services for people living in challenging daily circumstances and at schools to support prenatal and early childhood stress reduction.

- **Strategy 1:** Provide free and widely available mental health services that are both culturally appropriate and that promote a client-focused model.
- **Strategy 2:** Provide training for providers to offer professional mental health services for diverse communities, including people of color, low-income individuals, and those living in rural areas.

Objective 2: Expand stress remediation programs in workplaces, especially workplaces that contribute to stress and trauma.

- **Strategy 1:** Develop culturally appropriate and occupationally relevant programs to address PTSI, such as the International Association of Fire Fighters recovery programs.[55]

Objective 3: Promote media messages, such as PSAs, to reduce the stigma currently associated with mental illness.

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Vitamin D

Science Summary

The literature linking Vitamin D status and breast cancer risk is complex and inconsistent, but overall provides some evidence to suggest that higher levels of Vitamin D may be protective for at least some women. Factors such as menopausal status, race/ethnicity, genetics and other risk factors may interact with Vitamin D. Since many women have lower-than-optimal levels of 25(OH)D (a metabolite of Vitamin D), supplementation may be warranted.

What the Foundational Documents Say

The Continuous Update Project found limited evidence regarding Vitamin D and breast cancer risk and considered the findings inconclusive.[1] Similarly, the CBCRP Gaps Project recognized that findings were mixed, although they concluded there is evidence that Vitamin D may be protective against pre-menopausal breast cancer. They called for more research on differences in Vitamin D levels based upon sunlight exposure and skin pigmentation.[2] The Endocrine Society noted research demonstrating that some endocrine-disrupting compounds (EDCs) disrupt Vitamin D receptor function[3] Finally, the President's Cancer Panel discussed the nuances of the need to protect against excessive sun exposure due to skin cancer risks, while at the same time recognizing that we need some UVB light for Vitamin D production. They note that there is some evidence that Vitamin D may protect against some cancers.[4]

The Current State of the Evidence

Vitamin D describes several different fat-soluble steroids that come in different forms from dietary plant and animal sources and from synthesis in the skin as a result ultraviolent B (UVB—ultraviolet radiation with wavelengths between 290 and 320nm) light exposure. The biologically active form of Vitamin D is 1,25(OH)2D, which is the form generated after metabolism of a precursor—25(OH)D—in the kidneys and other tissues. Vitamin D status is usually measured based upon serum 25(OH)D, an intermediate that best reflects overall Vitamin D stores.[5] Circulating levels of 25(OH)D vary based upon many factors, including seasonal light variations, skin pigmentation (darker skin blocks more UV light, which is needed for Vitamin D production from precursors in the skin), BMI, waist-hip ratio, tobacco use, alcohol consumption, physical activity, diet, and supplementation.[6]

Guidance regarding optimal levels of 25(0H)D varies, as discussed in the interventions section below. There is agreement that levels below 20 ng/ml are insufficient or deficient. Levels between 20-29.9 ng/ml are considered sufficient by some and insufficient by other professional communities.[7]

Several reviews indicate that meta-analyses report an inverse relationship between circulating 25(OH)D levels and breast cancer risk.[8] However, when the meta-analyses are conducted based upon study type, only case-control studies consistently show reduced risk (of 9 to 41%) in studies of both circulating 25(OH)D[8,9,10] and Vitamin D intake.[5] One meta-analysis found an inverse relationship only in case-control studies where 25(OH)D levels were measured close to the diagnosis, and not in cohort studies or in case-control studies with 25(OH)D levels measured years prior to diagnosis.[11] While breast cancer appears to be associated with lower 25(OH)D levels, most studies are case-control studies that cannot determine the causal direction of the association,[8,10,12] or whether consequences of a diagnosis, such as chemotherapy and low physical activity (common after a breast cancer diagnosis), are responsible for low circulating 25(OH)D levels.[10]

The inclusion of covariates that are closely associated with circulating 25(OH)D may contribute to mixed results. One nested study of Vitamin D supplementation in the Women's Health Initiative found increased risk of breast cancer among those with low circulating Vitamin D. However, once researchers controlled for BMI and physical activity—both of which are independent predictors of Vitamin D levels as well as breast cancer—this finding was no longer significant.[10] Other studies have found similar attenuations in the effect of Vitamin D with adjustment for known breast cancer risk factors.[12] Further research is needed to determine whether other risk factors alter the metabolism, absorption, or activity of 25(OH)D.

Researchers have looked at Vitamin D levels in two ways: 1) by measuring exposures that affect Vitamin D, such as dietary intake amounts or UV exposure, and 2) by directly measuring the level of 25(OH)D circulating in the body. Studies of pre-menopausal breast cancer risk demonstrate an inverse relationship for dietary intake,[5,9,10] but dose-response studies of circulating 25(OH)D show an inverse relationship between circulating levels and post-menopausal breast cancer.[5]

A review of Vitamin D deficiency and risk of triple-negative breast cancer among Black women suggests that Vitamin D deficiency is a plausible partial explanation for their higher rates of triple-negative breast cancer. The authors cite studies indicating lower levels of circulating 25(OH)D among pre-menopausal women with triple-negative breast cancer compared to those with luminal A breast cancer, along with data indicating that Vitamin D deficiency is 10 times more common among Black women than among White women.[13]

One review examined the Vitamin D literature to determine if the relationship of 25(OH)D levels and breast cancer risk met the Hill criteria (a set of criteria that assess whether a causal relationship can be posited between an exposure and disease). These authors made the case that a causal relationship is both supported by the literature and biologically plausible.[14]

Circulating Vitamin D

Cohort Studies: Two meta-analyses of prospective studies examining circulating 25(OH)D and breast cancer risk were published in 2013. The two projects overlapped considerably in the studies included in their data set, with eight overlapping studies out of nine for one analysis and out of 15 for the other.

Bauer and colleagues[15] found a borderline significant reduction in breast cancer risk for every increase of 5 ng/mL of circulating 25(OH)D. Menopausal status modified this effect, with a significant 12% reduced risk of breast cancer among post-menopausal women with circulating 25(OH)D levels between 27-35 ng/mL. Circulating 25(OH)D did not modify risk among pre-menopausal women.

Wang, et al[16] found 15% lower overall breast cancer risk among those in the highest quintile of 25(OH)D levels in a meta-analysis of prospective cohort and nested case-control studies. As with the other meta-analysis, when the results were analyzed by menopausal status, risk was reduced among post-menopausal women (25% lower risk) but there was no effect of circulating 25(OH)D among pre-menopausal women (as noted above, Vitamin D intake has been associated with lower risk of pre-menopausal breast cancer). This study found a dose-response association, with a 3.2% lower risk of breast cancer for each additional 10 ng/mL of serum 25(OH)D concentration.

Three cohort studies in Europe found no overall effect of Vitamin D status on breast cancer risk.[17,18,19] However, one of these studies, which included multiple cohorts from Europe, found that mid-range concentrations of circulating 25(OH)D (30-50 nmol/L) were associated with 33% lower risk compared to the highest levels of 25(OH)D.

In a cohort of 59,000 Black women, those with the lowest circulating 25(OH)D had 23% higher breast cancer risk overall. When analyses were conducted by breast cancer subtype, the effect on risk of ER+ breast cancer was similar to that of the full cohort, but there was no relationship for ER- breast cancer.[20]

In the Sister Study, a prospective cohort study of 50,884 women who have a sister with breast cancer, 25(OH)D levels over 38 ng/mL (highest quartile) were associated with 21% lower breast cancer risk within the next five years, compared to women in the lowest quartile of circulating 25(OH)D. Supplementation among this cohort was associated with 11% lower risk. Risk of breast cancer was 28% lower among post-menopausal women with over 38 ng/mL of circulating 25(OH)D, but there was no effect among pre-menopausal women.[21]

Case-Control Studies: The data from case-control studies varies and offers several areas for further investigation. Several case-control and nested case-control studies have found no association of circulating 25(OH)D levels on breast cancer risk,[22,23,24,25] while others, described below, have found associations that vary by population, breast cancer subtype and menopausal status.

In the multi-ethnic cohort, pre-diagnostic levels of both 25(OH)D and $25(OH)D_3$ were associated with 57-72% lower risk among White women, depending upon the measure. Vitamin D status was not associated with breast cancer risk among Black, Native Hawaiian, Japanese or Latina women in the cohort.[26]

A small case control study of primarily White women similarly found that women with suboptimal 25(OH) D levels (below 32 ng/mL) had more than doubled risk of ER- breast cancer and more than tripled risk for triple-negative breast cancer.[27]

A case-control study of Black and Latina women found 2.5 times higher risk among Black women and almost doubled risk among Latinas with circulating 25(OH)D_3 below 20 ng/mL. Risk of triple-negative breast cancer among Black women was especially striking among women with circulating 25(OH)D_3 below 20 ng/mL—risk was more than five times higher for this group.[28] A case-control study in Mexican women, found dose-response effects for reduced overall and post-menopausal breast cancer risk. Those with serum 25(OH)D levels of 30 ng/mL and above had 47% lower overall risk, 40% lower risk of pre-menopausal breast cancer and 53% lower risk of post-menopausal breast cancer.[29]

A study among women in Saudi Arabia found a dose response effect. Those with the lowest circulating 25(OH)D (<10 ng/mL) had six times higher risk of invasive breast cancer than those with the highest levels (>20 ng/mL), and those in the mid-range had four times higher risk than those with the highest level.[30]

A case control study nested within two prospective cohorts found no overall effect on breast cancer risk, but did find a 52% lower risk among women aged 45 or younger and 33% lower among pre-menopausal women with the highest quintile of circulating 25(OH)D.[31] A study of Vitamin D deficiency in Korea found 27% higher risk of breast cancer among Vitamin D deficient women, defined as levels of 25(OH)D lower than 30 ng/ml. The results did not vary significantly by menopausal status or subtype, although the association was slightly more pronounced in triple-negative breast cancer.[32] A Japanese study found 22% overall lower cancer risk with higher 25(OH)D levels, but no effect on breast cancer risk.[33]

A nested case-control study in a European prospective cohort found no overall effect of circulating 25(OH)D nor effects based upon tumor subtype. However, 25(OH)D was associated with 38% lower risk of breast cancer among those using HRT at the time of the blood draw, while no effect was found in those who were not using HRT.[34]

One study found a seasonal effect, with no overall impact on breast cancer risk, but a 34% lower risk among those with the highest quintile of summer (May-October) circulating 25(OH)D compared to the lowest quintile.[35]

A case-control study from a cohort in France found that the association between Vitamin D status and breast cancer risk was modified by BMI and alcohol. Among women with a BMI below the median of 22.4, those in the highest quartile of 25(OH)D had 54% lower risk compared to women with the lowest levels. For women with BMI above the median, higher 25(OH)D was associated with more than double the risk of breast cancer. Women with higher alcohol intake and sufficient 25(OH)D had 50% lower risk, while there was no association in those with lower alcohol consumption.[36]

Dietary Vitamin D Intake

Studies of dietary Vitamin D intake and breast cancer incidence have found mixed results. A study of dietary Vitamin D among women in Iran found a significant inverse relationship between Vitamin D consumption and breast cancer. Those in the highest quartile of dietary Vitamin D had 62% lower risk of breast cancer than women

in the lowest quartile, in a model adjusted for other dietary factors, BMI, menopausal status, education, use of exogenous hormones and duration of sun exposure.[37] However, another study found no effect of dietary Vitamin D on pre- or post-menopausal breast cancer risk.[38] In a prospective study of adolescent Vitamin D intake, dietary Vitamin D did not have an effect on benign breast disease among women in their 20's (at 12-14 years after they joined the study).[39]

Sun Exposure

Two studies explored the association of sun exposure and breast cancer. Neither study specifically measured Vitamin D levels, although a key premise of both articles was that sun exposure is inherently linked to increased Vitamin D levels. One study found a small decrease in breast cancer risk associated with routinely having at least one hour of sun exposure per day 10 years prior. When they examined risk by breast cancer subtype, they found that sun exposure reduced ER+ breast cancer by 30% and that there was no change in risk of ER- breast cancer.[40]

A second study compared breast cancer risk in two different regions of Turkey with different climates and different sunlight intensity over the year. They found significantly lower prevalence of triple-negative breast cancer in the area with less sunlight intensity.[41]

Supplementation

The literature on Vitamin D supplementation also offers mixed results. A 2013 meta-analysis examined the effects of Vitamin D supplements on breast cancer risk among post-menopausal women. The analysis pooled 5,372 post-menopausal women from two randomized trials and found no effect of supplementation on risk beginning three to four years after study initiation.[42] A large majority of participants in these two trials were supplemented with relatively modest daily doses of 800 IU Vitamin D.

A 2015 study examined Vitamin D supplementation in a prospective cohort of over 57,000 post-menopausal women. They found that current Vitamin D supplementation was associated with 18% lower breast cancer risk overall. When examined by tumor subtype, the results suggested 27% lower risk of ER+ breast cancer but no effect for ER- breast cancer. When the authors looked at the interaction of hormone therapy and Vitamin D supplements, they found 26% lower risk of breast cancer among those women who had ever taken menopausal hormone therapy and who were currently taking Vitamin D.[43]

Another study found similar results, with women who had three or more prescriptions for Vitamin D supplements showing 17% lower risk. However, when the analysis excluded women who started taking Vitamin D within a year of their diagnosis this effect disappeared. It is not possible to determine whether recent Vitamin D use is protective in post-menopausal women or whether women get prescribed Vitamin D more often when they go through tests to diagnose breast cancer.[44]

A study from Iran found 12% increased risk of pre-menopausal breast cancer among those who did not take Vitamin D supplements.[45]

Nuances and Emerging Considerations

Mechanisms

Several reviews articulate properties of Vitamin D that may limit the formation of tumors.[46,47,48] 1,25(OH)2D has anti-proliferative effects and supports cellular differentiation, both of which can suppress the fast growth of cancer cells. It also can induce apoptosis (cell death), whereby damaged cells are programmed to die. Further, 1,25(OH)2D may limit the ability of malignant cells to invade healthy tissues, as well as the ability for tumors to create a blood supply. Finally, it may reduce inflammatory pathways, which have been implicated in cancer formation. These actions of 1,25(OH)2D have been found in multiple types of cancer, including studies of breast cancer cell lines.[49] One study found that the anti-proliferative effects of 1,25(OH)2D were stronger in the presence of long-chain omega-3 fatty acids.[50] These effects need to be further assessed in human studies.[12,49]

Effects on Mammary Gland Development

Vitamin D plays a role in mammary gland development, as demonstrated by laboratory studies that suggest 1,25(OH)2D and the Vitamin D receptor has a role in limiting the branching and elongation of ducts and the responsiveness of breast tissue to hormones.[12,49] Other studies suggest 1,25(OH)2D may play an important role in the differentiation of mammary gland cells and in the maturation of the mammary gland during puberty.[51] Vitamin D receptor expression is disrupted in many breast tumors, relative to healthy tissue.[52] Vitamin D receptors are present in normal breast tissue of humans.[49]

Vitamin D Receptor Genes and Other Gene Polymorphisms

A growing body of research examines the effects on breast cancer risk of genetic polymorphisms and gene single nucleotide polymorphisms (SNPs; changes to a single nucleotide) in genes associated with Vitamin D. Polymorphisms of the Vitamin D Receptor gene (VDR) are the most thoroughly studied. This gene codes for the Vitamin D receptor protein; when Vitamin D binds to this protein it activates pathways involved in cellular growth and differentiation.

Meta-analyses of VDR polymorphisms have focused on six common polymorphisms: FokI, BsmI, TaqI, ApaI, Poly-A, and Cdx2. While many of these meta-analyses have found associations of specific genotypes in these polymorphisms and either increased or reduced breast cancer risk, the results are not consistent for any of the polymorphisms.[53,54,55,56,57] Individual studies have examined these same polymorphisms, with similar mixed results.[58,59,60,61,62]

Two meta-analytic studies have found interactions with specific polymorphism genotypes and race/ethnicity.[53,54] One study found that one genotype of FokI was associated with almost two-fold higher breast cancer risk among Blacks, but not Latinas.[63]

More recent studies have examined VDR SNPs and other genes associated with Vitamin D metabolism. These studies have found that some SNPs are associated with changes in circulating 25(OH)D and breast cancer risk.[64,65] One study of 82 SNPs on seven different Vitamin D related genes found that the interaction of circulating 25(OH)D and eight of the gene SNPs significantly affected breast cancer risk.[66]

One study found an association with breast cancer of a SNP on a gene that encodes enzymes involved in Vitamin D metabolism (CYP24A1) among Black women but not White women.[13] Another study examined the effects of multiple genes involved in Vitamin D metabolism among Black women. They found no effects on breast cancer for the full pathway, although 13 SNPs on eight different genes were associated with either increased or decreased breast cancer risk.[67] Similar studies of the Vitamin D pathway found no effect for the pathway-level analysis in Black[68] or German populations.[69] A study that created a multi-polymorphism score based upon the presence of four different SNPs also found no effect on breast cancer risk.[70]

One study found no evidence of direct effects on breast cancer risks for specific SNPs; however, they found interaction effects between SNPs and menopausal status among both European and East Asian women, that varied depending on the specific SNP.[71]

Effects on Breast Density

One review indicates that some studies have found inverse associations between Vitamin D and breast density.[47] A study of 25(OH)D3 levels among Mexican women found no overall association with mammographic density. Among women with BMI below the median, they found a significant inverse correlation between serum 25(OH) D3 and mammographic density.[72] In a study of Vitamin D supplementation, results suggested that doubling serum Vitamin D levels (25(OH)D and 1,25()H)2D) had no effect on mammographic density over the course of a year.[47] Studies have not assessed whether Vitamin D metabolites accumulate in breast tissue in ways that can affect breast density.

Take-Home Message

- The literature on Vitamin D status and breast cancer incidence is inconsistent with regard to effects on overall breast cancer risk although a number of studies report an association of higher risk with Vitamin D deficiency, which is fairly common in the U.S. general population.
- Studies of Vitamin D intake have been associated with reduced risk of pre-menopausal breast cancers, while studies of Vitamin D status—typically circulating levels of 25(OH)D—have found protective effects for post-menopausal breast cancer. Other studies have not found significant effects related to Vitamin D levels, regardless of menopausal status.
- Studies have varied findings related to breast cancer subtypes, although some studies of circulating 25(OH)D suggest a stronger relationship to triple-negative breast cancer.
- Many women have low levels of 25(OH)D, and this is more common in Black women. Supplementation may be warranted.
- Emerging studies suggest various properties of Vitamin D that may suppress tumor growth, and that have links to mammary gland development and to potential genetic factors that affect Vitamin D production and metabolism.

Vitamin D: Context for Interventions

In 2011, both the Endocrine Society[7] and the National Academy of Medicine (then the Institute of Medicine)[73] published guidance on optimal Vitamin D levels. These professional organizations concurred that circulating Vitamin D (25(OH)D) levels below 20 ng/mL were insufficient. The Endocrine Society further defined levels below 20 ng/mL as deficient and levels between 20-29.9 ng/mL as insufficient.[73]

Using these categories, many individuals are deficient in Vitamin D, with studies suggesting more than one-third of the U.S. population has insufficient levels of 25(OH)D and more than a quarter of the population is categorized as Vitamin D-deficient.[74,75]

Low Vitamin D status is more common in some populations than others, including:

- Individuals with metabolic syndrome[76]
- People with low sun exposure (based upon climate or activity)[6]
- People with darker skin[6]
- Individuals with lower levels of physical activity[6,75]
- Latina women in California can have lower levels compared to White women[77]

Nevertheless, debate exists about whether Vitamin D screening and supplementation is warranted for a range of health impacts, including cancer. The United States Preventive Services Task Force concluded in 2014 that the evidence is not sufficient to recommend screening for Vitamin D deficiency in asymptomatic adults.[78] In early 2019, they released a research plan to re-examine this conclusion.[78]

The American College of Obstetricians and Gynecologists evaluated the evidence on screening for Vitamin D deficiency among pregnant women and concluded that screening is not necessary. Supplementation through prenatal vitamins is common among pregnant women, although doses may be lower than necessary to reach optimal levels.[79] However, a 2019 review found that Vitamin D supplementation might reduce the risk of gestational diabetes but has little effect on other adverse birth outcomes.[80]

The National Institutes of Health Office of Dietary Supplements synthesizes the data on optimal Vitamin D levels (which they consider as levels of 25(OH)D above 20 ng/mL) and cites a review of the data indicating that both deficiency and higher levels may be linked to adverse health effects. They highlight that tests used to measure 25(OH)D levels are variable, and as a result, measures may not be consistent or reliable.[81]

INTERVENTIONS

Overarching Goal: Achieve optimal vitamin D status across the California population to reduce breast cancer risks potentially associated with vitamin D deficiency or insufficiency and to support other health outcomes.

Intervention Goal 1

Expand research to understand the links between vitamin D and breast cancer.

Objective 1: Conduct research to deepen understanding of the effects of circulating 25(OH)D on mammary gland development and timing of puberty.

Objective 2: Extend the follow-up period of existing longitudinal studies to better understand long-term effects of Vitamin D intake and levels. Measure 25(OH)D at multiple time-points to understand whether historical or proximal levels (or both) are of importance.

Objective 3: Conduct studies to assess both intake and circulating levels of Vitamin D to further understand associations with the risk for pre- and post-menopausal breast cancer, as well as different subtypes of the disease.

Objective 4: Examine Vitamin D intake and circulating levels among women of color and explore potential causes.

Intervention Goal 2

Refine and implement practice guidelines related to vitamin D, considering effects on breast cancer as well as other health outcomes.

Objective 1: Integrate assessment of circulating 25(OH)D into routine blood tests.

Objective 2: Among women prescribed Vitamin D supplements, monitor 25(OH)D levels to develop agreement around the dose and duration of supplementation required to attain optimal levels.

Objective 3: Ensure access to quality preventive health care for all Californians in order to provide adequate screening for Vitamin D deficiency.

Objective 4: Consider Vitamin D status across the lifespan in practice guidelines.[82]

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Conclusion

The complexity of reducing breast cancer risk rivals the complexity of the disease itself. As one of the biggest, most populous, and most diverse states in the country, California has a rich history of community leadership and advocacy, a world-class research community, and an innovative legislative body. Over the years, California has led by example, demonstrating ways states can address complex societal problems. We have led the nation in implementing policies on health, the environment, and human rights, such as establishing clean air standards and climate change initiatives;[1] becoming a sanctuary state for undocumented immigrants;[2] expanding planning requirements to include health and equity;[3] and many others. It is time to add reducing breast cancer risk to our state's list of leadership priorities.

Paths to Prevention would not have been possible without the generous time and energy of the many people we encountered throughout the process. We are especially grateful to the community members who gave their time, energy, and wisdom to help us understand the problems and opportunities across the state, and to see clearly the potential for unintended consequences of making recommendations that do not adequately incorporate community perspectives. We have made a concerted effort to reflect what we learned from the communities that helped us develop this historic Plan, and we invite ongoing conversation on how to partner in its full implementation.

At the end of the process of building *Paths to Prevention*, we stand even more firmly committed to the principles that guided its development, and believe that the principles can and should be adapted and applied to a wide range of environmental, health, and justice issues:

1. Breast cancer is a societal issue. Reducing risk requires systemic change.
2. To create a healthy society, we must address discrimination, racism, and inequities in power and access.
3. Community wisdom is a valuable source of information and often highlights areas that scientific research has not yet investigated.
4. Breast cancer risk is multi-factorial. Interventions to reduce risk should also be multi-factorial.
5. We do not need 100% certainty to act.

Paths to Prevention is the people's plan. It is a roadmap with a menu of options for how to address reducing breast cancer risk, support women's health generally, and confront a wide range of societal problems. Whether you are a community activist or health-care professional, city councilperson or county supervisor, worker or business owner, school board member or teacher, funder or state legislator; whether you are acting to improve conditions locally or statewide, there is a role for you in making this Plan a reality. Whether breast cancer is your primary issue, or you are bringing a breast cancer lens to a larger context, there is something for you in this Plan.

We invite Californians from across the state and from diverse backgrounds and interests to take part in bringing *Paths to Prevention* to life, making real change to reduce the incidence of breast cancer while impacting so many other societal challenges.

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Breast Cancer Prevention Partners (BCPP) is the leading science-based policy and advocacy organization working to prevent breast cancer by eliminating our exposure to toxic chemicals and radiation.

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