



## Special Research Initiatives

### Stakeholder Meeting Presentation April 2007

California Breast Cancer Research Program  
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## CBCRP- The Program

- ◆ Founded in 1993
- ◆ Funded by tobacco tax, line 55 CA Income Tax form 540, private donations
- ◆ Awarded more than \$164 million
  - for 672 research projects
  - at 73 institutions throughout the state
- ◆ Administered by the University of California, Office of the President

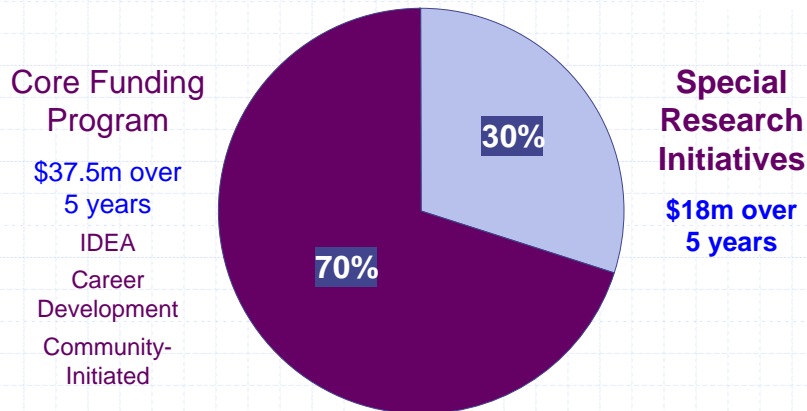


## SRI Strategic Planning 2001 - 2004

- ◆ Reviewed status of breast cancer research
- ◆ Reviewed program outcomes against program goals
- ◆ Reviewed status of breast cancer in California
- ◆ Heard expert presentations
- ◆ Commissioned position papers
- ◆ Held stakeholder meetings



## CBCRP: The Second Decade



## Special Research Initiatives

An \$18 million research effort to find answers to:

- What role does the environment play in breast cancer?
- Why do some groups of women bear a greater burden of disease?



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## Special Research Initiatives

### RATIONALE:

*California is uniquely positioned for large-scale research in these areas:*

- ◆ Extensive research infrastructure
- ◆ Established cancer registry and pesticide databases
- ◆ Regional and geographic diversity
- ◆ Racial, ethnic, and socioeconomic diversity



Photo Credits:

Ansel Adams   Geoffrey DeVerteuil  
Michael Dear

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## Vision and Goals

### VISION:

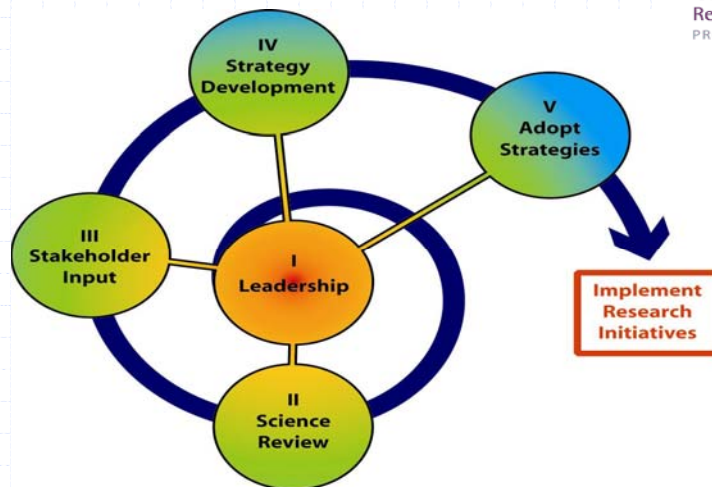
To identify and support research strategies that increase understanding of, and create solutions to, environmental links to breast cancer and disparities in breast cancer.

### GOALS:

- ◆ Support a coordinated statewide effort to explore innovative ideas and new theories.
- ◆ Leverage California's unique and diverse geographic and population resources.
- ◆ Undertake critical studies that significantly move these fields forward.



## The Five Phases of the SRI Strategy Development Plan





## Steering Committee

Julia G. Brody, PhD  
Silent Spring  
Institute



Susan M. Shinagawa  
Intercultural Cancer Council  
Asian and Pacific  
Islander National Cancer  
Survivors Network



Olufunmilayo I (Funmi)  
Olopade, MD  
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David R. Williams, PhD  
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Sandra Steingraber, PhD  
Ecologist, author, cancer  
survivor



Marion Kavanaugh-Lynch,  
MD, MPH  
California Breast Cancer  
Research Program



## Step III – Stakeholder Input

- ◆ Brainstorm ideas about the research topics and approaches that should be investigated to find solutions to the environmental causes and unequal burden of breast cancer.
- ◆ Rate the ideas based on their potential impact and feasibility at another time.

## Brainstorming

### ◆ Live stakeholder meetings throughout California:

- ◆ Ukiah
- ◆ Fresno
- ◆ Los Angeles
- ◆ San Francisco

### ◆ Teleconferences

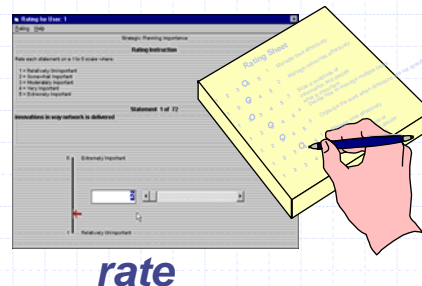
### ◆ Online brainstorming through April 19, 2007.



## Rating

### Those who have registered will:

- ◆ Be invited to rate the ideas based on their potential impact and feasibility.
- ◆ Invitations with details for completing the rating on the web will be emailed.





## Special Research Initiatives

### Identifying Gaps In Breast Cancer Research: Addressing Disparities and the Role of the Physical and Social Environment



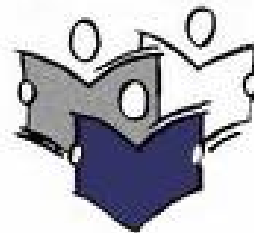
## Special Research Initiatives

### "Map of the Evidence"

- ◆ What is known
- ◆ What is missing
- ◆ What are current research needs

*Provide a common basis for decision-making*

- ◆ Process
  - Oversight by SRI Steering Committee
  - Commissioned papers
  - Adapted framework (Bigby and Holmes, 2005)
  - Extensive review process including over 25 additional scientists with expertise in the relevant fields



# Map of the Evidence

**Report Framework:  
An ecological vision  
connecting 3 inter-related  
sections**

- I. Individual Level  
Social Inequality
- II. Exposures from the  
Physical Environment
- III. Neighborhood Built and  
Social Environment



## I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

What is the relationship between individual level social inequalities and breast cancer?

- ◆ We know that breast cancer and its impacts are unequally distributed among different women. We know less about what characteristics underlie these disparities.
- ◆ To prevent breast cancer and provide equal access to a good outcome, we need to address individual level disparities.





I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Racial/Ethnic Disparities

◆ “Race/ethnicity” is an historical, politically constructed, complex mixture of characteristics. Vast diversity exists within categories of race/ethnicity.

“Asian American/Pacific Islander” includes many sub-populations each with its own distinct culture, beliefs and practices.

California’s more than 45 distinct Asian and Pacific Island ethnic groups speak 28 different languages and many more unique dialects.

◆ Important disparities may be hidden by the broad categories of race and ethnicity that have thus far dominated health research.

California’s Latino/Hispanic populations originate from more than 22 Spanish-speaking countries.



I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Racial/Ethnic Disparities

◆ Breast cancer occurs more often in non-Hispanic white women than in any other broad racial/ethnic group.

◆ But minority women who get breast cancer generally fare worse than white women.



Gaps: We do not know ...

◆ The underlying features that are responsible for racial/ethnic disparities.

◆ Whether differences in tumor biology may play a role in racial/ethnic disparities in breast cancer treatment, survival and mortality.

◆ About the relationship between racial/ethnic disparities, genes, and the environment.



Photo Credit: Ty Milford, Aurora Collection, Getty Images 18

I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Culture



Photo Credit: Sean Justice, Riser Collection, Getty Images

◆ A growing body of literature supports the influence of culture on breast cancer perceptions, screening, care, quality of life, and survival in a wide range of groups.

◆ Gaps: We do not know ...

◆ How to systematically define and collect quantitative data to assess the impact of culture on breast cancer.

I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Sexual Minority Women



Photo Credit: Girl Ray, The Image Bank Collection, Getty Images

◆ Sexual minority women (SMW) are at potentially increased risk of breast cancer, later stage at diagnosis, and worse prognosis.

◆ Gaps: We do not know ...

◆ Much at all about this disparity. Breast cancer among SMW has received little to no attention.

I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Disability

One in five women in the U.S. are disabled. Disabled women comprise a growing and economically disadvantaged segment of the population, at high risk for lack of physical activity, obesity, and smoking.



Gaps: We do not know ...

About the experience of disabled women with breast cancer. Understanding the relationships between disabilities and breast cancer is an essential component of disease control and prevention.



Photo Credit: Robert E Daemrich, Stone Collection, Getty Images

I. INDIVIDUAL LEVEL SOCIAL INEQUALITY

Insurance Status, Access to, and Quality of Care

Having health insurance plays a positive role in breast cancer outcomes. Many Californians lack health insurance, and some are more likely than others to be among the uninsured.



Gaps: We do not know ...

How to implement policies to reduce disparities in health care access.

Health Policy Research Brief

October 2006

One in Five Californians Were Uninsured in 2005 Despite Modest Gains in Coverage

Jean Yoon, E. Richard Brown, Shana Alex Lavarreda and Sungching Glenn

Six and one-half million Californians were uninsured for all or some of 2005, a number that is as large as the combined populations of nine other states. The number of uninsured represented one in five children and nonelderly adults, a rate that was slightly lower than in 2003 due to California's tight labor markets and expanding enrollment and retention in California's public coverage programs for children. These marginal improvements are unlikely to continue unabated given the instability of employment-based insurance coverage in the face

Source: Yoon J, Brown ER, Lavarreda SA, Glenn S. University of California Los Angeles Health Policy Research Brief. UCLA Center for Health Policy Research. October 2006

## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT


What is the relationship between exposures from the physical environment and breast cancer?

- ◆ We know that exposure to chemical and physical agents that do or may cause breast cancer is widespread, but we know much less about the impact of these exposures.
- ◆ To prevent breast cancer, we need to address the role of the physical environment.



## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Environmental Chemicals/Pollutants

- ◆ The U.S. EPA has registered approximately 85,000 synthetic chemicals for use.
- ◆ At least some evidence of increases in mammary tumors has been associated with more than 200 chemicals, mainly from animal studies.
- ◆  Gaps: We do not know ...
- ◆ The potential human health effects of approximately 90% of the synthetic chemicals registered by U.S. EPA.
- ◆ Much about human exposure to these chemicals, or health effects of chronic, low-level exposure to mixtures.



## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Pollutants of Concern

#### Solvents & industrial chemicals: PCBs

- ◆ Higher breast cancer risk from PCB exposure associated with **menopausal status** and genetic variant in a recent study.

#### Flame Retardants: PBDEs

- ◆ Measurable quantities of these persistent chemicals found in almost every human. Limited data indicate the potential for carcinogenic and endocrine disrupting effects.

#### Combustion By-Products: PAHs

- ◆ From active/passive smoking, diet and air; current research is focused on **genetic susceptibility** affecting DNA repair.



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## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Plastics/Plasticizers

- ◆ Manufacturing and use of PVC (polyvinyl chloride) and other plastics has resulted in near universal exposure to compounds linked to cancer and endocrine disruption including **dioxins, metals** and **phthalates**.

- ◆ Workers, communities near manufacturing and disposal facilities, infants and other groups are more likely to be exposed to higher levels and/or may be more susceptible to harmful effects.



GAPS: We do not know ...

- ◆ The sources and pathways of human exposure and the relative contribution to health impacts of the various chemicals associated with the lifecycle of PVC.



Dioxins are released into the environment when plastics are made or incinerated.




Lead added to PVC piping is released into water.

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## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Bisphenol A (BPA)

- ◆ Virtually everyone has low-levels of BPA in their body, primarily due to canned foods and plastic beverage containers.
- ◆ There is strong evidence of estrogenic effects of BPA, and of a link between low-levels of exposure and breast cancer in animal studies. There have been no human studies.
- ◆  Gaps: We do not know ...
  - ◆ About the health of workers who may be exposed to BPA on the job.
  - ◆ About the levels and impacts of human exposures and body burdens over time.



Campbell's soup advertisement, 1945



## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Compounds in Personal Care Products

- ◆ There is strong reason for concern about the compounds in personal care products:
  - Widely used;
  - Applied directly to and able to enter the body;
  - Little is known about the thousands of ingredients;
  - Made from compounds linked to breast cancer and hormonal disruption; and
  - Are minimally regulated.



5 ingredients posing potential breast cancer risks

Source: Environmental Work Group



Hair products that contain placenta and estrogen are heavily marketed to African American women and girls

- ◆  Gaps: We do not know ...

- ◆ The nature and extent of the impact of compounds in personal care products and breast cancer.



## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Pesticides

A wide range of chemicals used to control insects, weeds, fungus, etc. Virtually everybody has measurable levels due to exposure through food, air and water.

- ◆ DDT/DDE – Still found in human tissues, including breast milk. Evidence does not support increased incidence, but is suggestive for disease progression.
- ◆ Other Organochlorines – Dieldrin and 13 other OC have been linked to risk, but evidence is inconsistent and mostly negative.
- ◆ Atrazine – Linked to hormonal changes in wildlife, this herbicide induces mammary gland tumors in *some* rats.



Gaps: We do not know ...

- ◆ How long-term, lower level exposure from an early age is affecting breast cancer risk.



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## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Hormones in Food

- ◆ Dairy: The use of growth hormone (rBGH or rBST) increases levels of insulin-like growth factor I (IGF-I), which promotes mammary tumor growth and has been linked to increased risk of breast cancer in premenopausal women.
- ◆ Meat: More than 90% of U.S. beef cattle are treated with up to 6 hormones—2 estrogenic.
- ◆ Higher rates of breast cancer have been associated with meat and dairy consumption.



Gaps: We do not know ...

- ◆ The effects of IGF-I and hormones in food on human levels.
- ◆ The relationship between specific components of milk and the development of breast cancer.



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II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

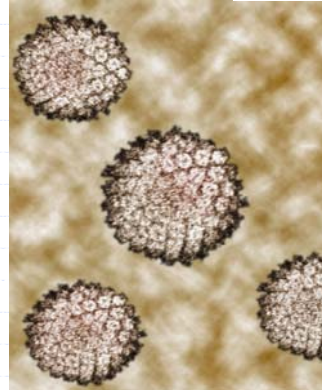
Infectious Agents/Microbes

- ◆ Microbes may have an impact on breast cancer; the limited work to date has focused on possible etiologic roles of specific microbes.
- ◆ There are virtually no data on the role of common infectious agents, sexually transmitted diseases (other than HIV), parasites, and intestinal bacteria.
- ◆ Infectious causes of inflammatory breast cancer are suggested by the clinical features.



Gaps: We do not know ...

- ◆ The role of chronic viral or parasitic infections, or the importance of age at infection or vaccination, in breast cancer.



Example of a link between infectious agents and cancer: A few infections caused by high-risk *Human Papilloma Viruses* end up triggering cervical cancer over many years.

Photo Credit: Science VU/NCI, Visuals Unlimited Collection, Getty Images

II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

Environmental Tobacco Smoke/Second Hand Smoke (ETS/SHS)

- ◆ ETS/SHS causes lung cancer, and contains at least 20 compounds known to be mammary carcinogens.
- ◆ Extensively studied, but estimating exposure has been difficult and inconsistent.
- ◆ Cal-EPA has concluded that there is a causal relationship between ETS/SHS and breast cancer among premenopausal women, but consensus on the strength of the association is lacking.



Gaps: We do not know ...

- ◆ How exposure to ETS/SHS during different time periods of life influences breast cancer risk.

**Mammary Carcinogens Identified in Tobacco Smoke**

- Benzene
- N-nitrosodiethylamine
- Acrylamide
- Benzo[a]pyrene
- N-nitrosodi-n-butyl-amine
- Acrylonitrile
- Dibenz[a,h]anthracene
- 4-Aminobiphenyl
- 1,3-Butadiene
- Dibenzo[a,e]pyrene
- Nitrobenzene
- Isoprene
- Dibenzo[a,h]pyrene
- Ortho-Toluidine
- Nitromethane
- Dibenzo[a,i]pyrene
- Propylene oxide
- Dibenzo[a,j]pyrene
- Urethane
- Vinyl chloride



## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Radiation

- ◆ Causes breast cancer and no level of exposure is without risk.
- ◆ Exposure at a younger age is more harmful than later in life and subgroups of women appear to be more susceptible.
- ◆ While medical use can be beneficial, it can increase cancer risk.
- ◆ Gaps: We do not know ...
- ◆ What screening and treatment recommendations to make to susceptible subpopulations.



Photo Credit: Larry Dale Gordon, The Image Bank Collection, Getty Images

## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Electric and Magnetic Fields (EMF)

- ◆ Extensively studied for decades. So far the evidence does not support a relationship between EMF and breast cancer.
- ◆ Gap: We do not know ...
- ◆ Of a plausible mechanism for a relationship between EMF and breast cancer.



Electricity by Man Ray

II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

Light At Night



Los Angeles 1908



Los Angeles 1988

Source: International Dark-Sky Association <http://www.darksky.org/images/sat.html>

II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

Light At Night

- Substantial evidence that exposure is a risk factor for breast cancer.
- Strong evidence that light at night affects the circadian rhythms and melatonin levels affecting tumor growth, with potential to impact risk and breast cancer treatment.
- Public health consequences of light at night exposures are enormous.

Research Article

Melatonin-Depleted Blood from Premenopausal Women Exposed to Light at Night Stimulates Growth of Human Breast Cancer Xenografts in Nude Rats

David E. Blask, George C. Brainard, Robert T. Dauchy, John P. Hamifin, Leslie K. Davidson, Jean A. Krause, Leonard A. Sauer, Moises A. Rivera-Bermudez, Margarita L. Dubocovich, Samar A. Jasser, Darin T. Lynch, Mark D. Bollag, and Frederick Zalatan

Laboratory of Chrono-Neuroendocrine Oncology, Roswell Research Institute, The New York Hospital-Cornell University Medical Center, New York; Department of Neurology, Thomas Jefferson University, Philadelphia, Pennsylvania; Department of Molecular Pharmacology and Biological Chemistry, Northwestern University, Feinberg School of Medicine, Chicago, Illinois; and Department of Anatomy, Physiology, and Genetics, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Abstract

The increased breast cancer risk in female night shift workers has been postulated to result from the suppression of pineal melatonin production by exposure to light at night. Exposure of rats bearing rat hepatomas or human breast cancer xenografts to increasing intensities of white fluorescent light

nearly 50% of breast cancers cannot be accounted for by conventional risk factors (1, 2). Westernized nations have increasingly become 24-hour societies with greater numbers of people being exposed to more artificial light during the night both at home and particularly in the workplace (3). Stevens postulated that light exposure at night may represent a unique risk factor for breast cancer in industrialized societies with the advent of continuous

## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Light At Night



Gaps: We do not know ...

- ◆ How to best measure exposure.
- ◆ How the *CLOCK* gene that regulates the circadian rhythm may alter susceptibility.
- ◆ The effectiveness of melatonin/light-dark therapies or of timing anticancer drug regimes according to the circadian clock.
- ◆ Ways to limit or reduce the harmful effects of night-shift work.



**USA At Night**

Source: International Dark-Sky Association

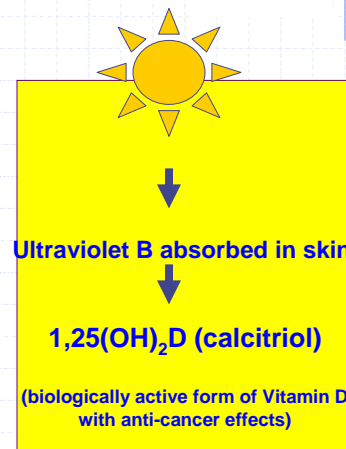
Photo Credit: Defense Meteorological Satellite Program (DMSP) satellites

## II. EXPOSURES FROM THE PHYSICAL ENVIRONMENT

### Vitamin D/Sunlight

Vitamin D may be protective for breast cancer:

- ◆ Experimental studies have shown that the biologically active form of vitamin D has anti-cancer effects.
  - ◆ A few epidemiologic studies support this, but are inconclusive.
  - ◆ Sun exposure may have a positive effect on prognosis.
- Gaps: We don't know ...
- ◆ How and when in life to measure sun exposure or the underlying mechanisms.
  - ◆ The impact in non-white populations.
  - ◆ The role of vitamin D in tumor progression and survival or treatment.



### III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT


What is the relationship between the place where we live, our neighborhood environment and breast cancer?

- ◆ Place matters, but we don't know when or why.
- ◆ To prevent breast cancer we need to address influences that occur at the neighborhood level.



### III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT

#### Urban-Rural

- ◆ In general, the highest rates of breast cancer are seen in urban areas.
- ◆ Urban-rural patterns are not simple and are not well understood.
- ◆  Gaps: We do not know ...
- ◆ Which factors contribute to the observed higher urban incidence.
- ◆ The relative importance of urban or rural residence at different life stages.



III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT

Neighborhood Socioeconomic Status (SES)



- ◆ Breast cancer occurs more often in affluent women, and both individual and community-level SES are important.
- ◆ Poorer women:
  - Are less likely to have mammograms, the recommended frequency of clinical breast exams, an early diagnosis or breast conserving surgery;
  - Have higher mortality rates compared to more affluent women.
- ◆ Neighborhood SES, race, ethnicity and immigration status are all interrelated and vary over time.



Chronicle / Deanne Fitzmaurice  
Photo Credit: San Francisco Chronicle, Deanne Fitzmaurice

III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT

Neighborhood Socioeconomic Status (SES)




- ◆ Gaps: We do not know ...
  - ◆ All of the reasons for SES disparities.
  - ◆ What specific attributes of SES, such as environmental exposures, may contribute to risk.
  - ◆ The impact of neighborhood SES over a lifetime.



### III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT

#### Institutional Discrimination

- ◆ We know that segregation and racism have negative impacts on health.
- ◆ Studies of the relationship between discrimination and health indicate that discrimination could impact breast cancer outcomes.
- ◆  Gaps: We do not know ...
- ◆ The effect of discrimination on breast cancer.
- ◆ How to fully assess discrimination and distinguish the roles of area-level and individual measures of discrimination.


Injustice anywhere  
is a threat to  
justice everywhere

*Martin Luther King, Jr.*

It is also a threat to  
health

### III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT

#### Neighborhood Social Environment

- ◆ Some research exists on the influence of stress, coping and social support at the individual level; these studies suggest an association with breast cancer outcomes, especially the role of social support in survival.
- ◆  Gap: We do not know ...
- ◆ How neighborhood or societal level stressors impact breast cancer.



Source: Ventura College Breast Cancer Support Group

### III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT Built Environment

- ◆ Aspects of the built environment impact public health outcomes ranging from birth to death.
- ◆ There are strong and consistent associations between the built environment and obesity and physical activity, two known risk factors for breast cancer.



### SECTION III. NEIGHBORHOOD BUILT AND SOCIAL ENVIRONMENT Built Environment

#### ◆ Gaps: We do not know ...

- ◆ The nature and extent to which attributes of the built environment influence breast cancer.
- ◆ How to measure interactions between SES, race/ethnicity, age, physical exposures, and social environments.
- ◆ If an environmental justice framework would help to holistically consider neighborhood-level disparities, cumulative risks, and multi-stressors.





## These Topics Are All Interrelated



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## The Brainstorming Question:

One specific *research topic and approach* that will create solutions to the environmental causes and/or unequal burden of breast cancer is.....

For more information about this project, please go to:

[www.cabreastcancer.org/sri](http://www.cabreastcancer.org/sri)

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