Summary of Research in Marin County

(All of these studies involved Marin women and/or families directly in the research being reported)

Biology of Breast Cancer

Study/Publication	Methodology	Research Findings	Implications of Findings
Geographic Excess of Estrogen Receptor-Positive Breast Cancer: 2003	Incidence data for invasive breast cancer histological subtypes and estrogen receptor (ER) and progesterone receptor (PR) status were obtained from the 1992-2000 Surveillance, Epidemiology, and End Results program. Expected numbers for Marin County were computed based on age-specific rates for five other SFBA counties. Incidence rates were age-adjusted to the 2000 United States standard.	Marin County breast cancer diagnoses during 1992-2000 compared with other SFBA and other urban CA Surveillance, Epidemiology, and End Results county rates for white, non-Hispanic women consisted of a disproportionate increase in ER+/PR+ tumors. The observed absolute excess (versus expected) numbers of Marin County ER+/PR+ lobular and nonlobular (predominantly ductal) cases were similar; however, the relative increase appeared greatest for lobular breast cancer.	First study to look at the type of breast cancer (ER-positive vs. ER-negative) accounting for an excess breast cancer incidence rate in any specific US geographic region. This observation that Marin County's excess incidence is due entirely to ER-positive breast cancer development directs future studies and focus on Marin risk factors and exposures specifically able to promote the development of ER-positive breast cancer.
Risk Factors for Estrogen Receptor Positive Breast Cancer: 2005	Follow-up analysis of the Marin Adolescent Risk Factor Case-Control study focusing only on ER-positive breast cancer cases diagnosed between 1997-1999 and their potential association with surveyed risk factors, in particular the use of hormone replacement therapy.	Duration of hormone replacement therapy was the strongest predictor of ER-positive, as opposed to ER-negative, breast cancer cases.	Since initial publication of the 1997-1999 Marin case-control study showed no apparent risk association with use of hormone replacement therapy, this secondary analysis confirmed that this risk exists in Marin but only for development of ER-positive breast cancer.

Risk Factor Studies (Reproductive and Behavioral)

Study/Publication	Methodology	Research Findings	Implications of Findings
Adolescent Risk Factor Study and the Development of Breast Cancer in Marin County (ARFS) Publication : *Risk Factors for Breast Cancer in a Population with High Incidence Factors Breast Cancer Research* Breast Cancer Research/April 2003	Interviews were conducted with approximately 300 Marin County women diagnosed between July 1, 1998 and June 30, 1999 with breast cancer (cases), and 300 Marin County women without breast cancer (controls), matched for age and ethnicity.	Cases were statistically significantly more likely than controls to report being premenopausal, never having used birth control pills, a lower lifetime body mass index, four or more mammograms in 1990-1994, beginning drinking after age 21 and on average drinking two or more drinks per day. Cases and controls did not significantly differ in with regard to duration of residence in Marin, having a first degree relative with breast cancer, history of benign biopsy, previous radiation treatment, age at menarche, parity, or use of hormone therapy	This study was a first by several important milestones: i) it was the first community-based collaborative research effort funded by the California Breast Cancer Research Program.; ii) it was the first scientific study to reveal population risk factors and/or exposures linked to breast cancer development in Marin. The case-control study design was most appropriate since the homogeneous demographics of Marin indicate high risk for all Marin women even though most do not ever develop breast cancer. Public attention was drawn to the fact that alcohol consumption in Marin was revealed as a significant modifiable breast cancer risk factor.
Traditional Risk Factor Study (TRiFS) Publication: None	The study described female breast cancer risk factor distributions in Marin County using the Adolescent Risk Factor Study Database. Prevalence and population attributable fraction estimates were calculated for selected traditional breast cancer risk factors.	The study found some traditional breast cancer risk factors may account for about ½ of the breast cases in Marin County: age of menarche younger than 12, age of mother at first birth over 30, family history of breast cancer, age at menopause equal to or greater than 55 and postmenopausal body mass index greater than 27.	As found in other breast cancer study populations, much of the attributable risk appears to come from non-modifiable endogenous reproductive factors. While obesity and age-at-first-birth are considered modifiable risk factors, Marin women are actually less obese than others CA women, and deferred child-bearing also correlates with increased socio-economic status that is also a significant population risk factor affecting women in Marin and elsewhere in the world.

Marin Women's Study (MWS) Publication: *Recent trends in hormone therapy utilization and breast cancer incidence rates in the high incidence population of Marin County, California* BioMed Central Public Health Journal April, 2010	The MWS enrolled 1, 833 women following routine screening mammography between October 2006 and July 2007, Participants completed a self-administered questionnaire that included items regarding historical hormone therapy use (estrogen only, progesterone only, EPHT), age of first and last use, total years of use and reason(s) for stopping as well as information regarding complementary hormone use. Questionnaire items were analyzed for 1,083 non Hispanic white participants ages 50 and over. Breast Cancer Incidence rates were assessed overall and by tumor histology and estrogen receptor (ER) status for the years 1990-2007 using data from the Northern California SEER cancer registry.	A dramatic reduction in EPHT use was followed temporally by a significant reduction in invasive and ER+ breast cancer rates among women living in Marin County. Prevalence of EPHT use among non-Hispanic white women aged 50 and over declined from 21.2% by 2006-07. Estrogen only use declined from 26.9% in 1998 to 22.4% by 2006-07. Invasive breast cancer incidence rates declined 33.4% between 2001 and 2004 with drops most pronounced in ER+ cancers. These rate reductions corresponded to declines of about 50 cases per year, consistent with population attributable fraction estimates for EPHT-related breast cancer. Self-reported screening mammography rates did not change during this period. Use of alternative or complementary agents did not differ significantly between ever and never hormone users. Of the women who reported stopping EPHT in the past 5 years, 60% cited health risks or new reports as their primary reasons for quitting.	This first report from the MWS was one of the most highly accessed epidemiologic studies following its public release in early 2010. While US trends also show declines in breast cancer incidence occuring within 24 months of reduced population use of E +P hormone replacement therapy, Marin's declines are more pronounced than elsewhere, consistent with the excess incidence of ER-positive breast cancer in Marin and the fact that EPHT is thought to selectively promote this type of breast cancer. Notably, this county decline in EPHT (and the resulting decrease in breast cancer incidence) appears to have largely resulted from personal initiative and a well informed population, and not from any countywide medical directive or health intervention.

Marin Breast cancer risk asssessment using a candidate panel of risk-associated SNPs (OncoVue®) compared to a traditional risk assessment tool (Gail score) with or without incorporation of SNPs from genome wide association Studies (GWAS). Publication: (published abstracts from the 2008 and 2009 San Antonio Breast Cancer Symposium)	The study applied the OncoVue® risk estimation model (InterGenetics, Inc.) using DNA extracted from buccal cell samples from 174 controls and 164 age-matched, Caucasian Marin breast cancer cases previously archived as part of the 1997-1999 Marin Adolescent Risk Factor case-control study.	By using a combination of a questionnaire and a buccal or saliva DNA sample, the OncoVue® model takes into account genetic variation in single nucleotide polymorphisms, (SNPs), that the traditional Gail model, which bases risk calculation primarily on traditional risk factors like age at first live birth of a child, does not. The 22 SNPs (from 19 different genes) used in the OncoVue model were derived from earlier studies that evaluated 117 common SNPs potentially associated with breast cancer. Incorporation of these 22 SNPs in the OncoVue model proved 2.2-fold better able to identify Marin breast cancer cases from Marin controls relative to Gail model scoring alone, even when the latter was bolstered by the use of 7 other GWAS SNPs.	Since SNPs are small genetic changes within DNA that underlie individuality, including disease risk, this two-part study of 1997-1999 Marin breast cancer cases and controls essentially demonstrates that genetic variation among Marin women can help identify those most likely to develop breast cancer. Since the 7 GWAS SNPs did not significantly improve the predictive ability of the Gail model, but the 22 OncoVue SNPs made a significant improvement in risk assessment and prediction, the 19 genes represented by the 22 OncoVue SNPs are now postulatd to be involved in the gene-environment interaction underlying Marin breast cancer incidence. Further research undertaken as part of the Marin Women' Study and sponsored by the Avon Foundation are now re-assessing the value of the OncoVue model using MWS saliva samples collected since 2006.

Environmental Studies

Study/Publication	Methodology	Research Findings	Implications of the Findings
Breast Cancer and the Environment Research Centers *Pubertal Assessment Method and Baseline Characteristics in a Mixed Longitudinal Study of Girls.* Pediatrics, April 2010	Over 1,000 girls between the ages of 6 and 8 from the San Francisco Bay Area (including Marin) the Cincinnati Area, and East Harlem, N.Y. participated in the study.	This study from the Breast Cancer and the Environment Research Center found more girls are starting breast development at age 7 and 8, which is earlier than reported in studies from more than 10 to 20 years ago. At 7 years old, 10% of white girls, 23% of black girls, 15% of Hispanic girls and 2% of Asian girls started breast development. Previous studies found that 5% of white girls and 15% of black girls had started breast development at age 7. Some regional differences were found. The girls in the Bay Area were less likely to have experienced onset of puberty at age 7 or 8 years than the girls in Cincinnati or New York.	Initial observations indicate consistency of assessments of pubertal maturation across 3 BCERC sites. The ability to capture with reasonable accuracy the timing and tempo of pubertal breast maturation will allow the sites to pool data for detecting associations between specific factors, including diet and environmental chemicals with variations of pubertal development, including early onset of breast development and age of menarche which is a moderate, yet consistent risk factor for future breast cancer.
Breast Cancer and the Environment Research Centers *Body Burdens of Brominated Flame Retardants and Other Persistent Organohalogenated Compounds and Descriptors in U. S. Girls.* Environmental Research 2010.	Blood samples from about 600 girls from the San Francisco Bay Area (including Marin) and Cincinnati, Ohio who are enrolled in the Breast Cancer and the Environment Research Centers were analyzed at the national Centers for Disease Control and Prevention (CDC).	This study from the Breast Cancer and the Environment Research Centers found higher levels of chemicals that act like hormones in girls in the Bay Area than in a comparison group in Ohio. These include some brominated chemicals used as flame retardants (PBDEs), pesticides, and polychlorinated biphenyls (PCBs).	This study demonstrated that banned chemicals are turning up in the blood of young girls being studied in Ohio and California. The levels of the chemicals in the girls varied by race, body mass index and geography.

Breast Cancer and the Environment Research Center *Investigation of Relationships between Urinary Biomarkers of Phytoestrogens, Phthalates, and Phenols and Pubertal Stages in Girls.* Environ Health Perspectives: 118(7):2010	The study included 1,151 girls from the three BCERC sites in the San Francisco Bay Area, New York City and greater Cincinnati who were between age six and eight at enrollment and between age seven and nine at analysis. Researchers collected urine samples from the study participants and they were analyzed for phthalates, phenols and phytoestrogens, including 19 separate urine metabolites, at the CDC.	The data showed that these chemical compounds were detected in nearly all the samples in the study population, and that higher exposure to some of the chemicals affected breast development slightly. Generally, weak effects were seen, on the order of a 3-6% difference. One phenol, two phytoestrogens and a subset of phthalates (those found in building products and plastic tubing) were associated with slightly later puberty. The phthalates found in personal products like lotion and shampoo, especially those with fragrance, were related to slightly earlier breast and pubic hair development.	This study is one of the first to find links between the time when girl's breasts begin to develop and exposure of these girls to certain chemicals. Exposure to different chemicals among those studied influenced the timing of breast development which is important because age of menarche is associated with future breast cancer risk.
Endocrine-Disrupting Compounds in Paired Indoor and Outdoor Air in Two Northern California Communities Environmental Sciences and Technology: August 3, 2010	Researchers analyzed 104 chemicals in 40 non-smoking homes in Richmond, CA. and 10 in Bolinas CA, including both chemicals that penetrate indoors from outdoor industrial and transportation sources and those from indoor use of consumer and building products. House dust and air samples were analyzed for phthalates, phenols, flame retardants, polycyclic aromatic hydrocarbons (PAHs), polybrominated biphenyls (PCBs) and pesticides	39 chemical analytes in outdoor air and 63 in indoor air were detected. Data demonstrated higher indoor concentrations for 32 analytes, suggesting primarily indoor sources as compared with only 2 that were higher outdoors. Outdoor air concentrations were higher in Richmond than Bolinas for 3 phthalates, 10 PAHs and o-phenyphenol, while indoor air levels were more similar between communities.	This study is one of the first to characterize indoor endocrine disruptors (EDCs) in an urban, industrial, low-income community and analyze the relative importance of indoor and outdoor sources of exposure. Findings support previous observations that indoor concentrations of EDCs are higher than those outdoors.

Summary of Community Input and Public Databases on the Environment in Marin County

Study/Publication	Methodology	Findings	Implications of the Findings
Personal Environmental Risk Factor Pilot Study (2002) Publication: None	Ideas about possible environmental exposures that may be breast cancer risk factors were collected from the Marin Community via e-mail, mail, telephone and three mapping workshops held in three different locations in Marin (Point Reyes, San Rafael and Corte Madera). A third source of community input was a list that summarized responses to a question "Do you have ideas about what might cause breast cancer" included in the Adolescent Risk Factor and Development of Breast Cancer Study	Ideas received formed a bank of nearly 1,500 submitted comments. Approximately, 336 unique concerns were expressed. Concerns most frequently mentioned were pesticides, water quality (chlorine, arsenic, asbestos in pipes, copper, and degrading cement pipes), air contamination (vehicle emissions and Richmond oil refineries), serpentine rock erosion and military installations (Hamilton Air Base and Marin Headlands)	The high response to ZBCs request for community ideas and input indicates a strong interest locally in investigating the role environmental factors may play in the initiation and development of breast cancer.

Marin Environmental Data Study (2003) Publication: None	The purpose of the Study was to begin a community-specific environmental data base by identifying and describing sources of environmental data and data sets specific to Marin County	The following community specific datasets were identified, described and GIS mapped for Marin County: ARIP- The USEPA's Accidental Release Information Program Database, CalPIP- The California Department of Pesticide Regulation's California Pesticide Information Portal, CAQ- California Air Quality data collected by the California Air Resources Board, CERCLIS- The USEPA's Comprehensive Environmental Response, Compensation, and Liability Information System, GEIMS- The Geographic Environmental Information Management System of the California State Water Resources Control Board, PUSE- The state of California's Pesticide Use Summaries Database, STORET- The USEPA's Storage and Retrieval Database, SSURGO- The USDA's Soil Survey Geographic Database and WTB/ULS- The Wireless Telecommunications Bureau's Universal Licensing System Database.	Unique environmental databases and resources are available at the county level to conduct a comprehensive investigation of breast cancer and the environment.

Residential Mobility Studies

Study/Publication	Methodology	Findings	Implications of the Findings
Marin Residence Study Publication: None	An "add on" to the Adolescent Risk Factor Study and the Development of Breast Cancer in Marin County (ARFS) study, detailed histories of residential, schools and place worked in Marin was collected from cases and controls	There were no suggestive or significant differences between cases and control over all ages for total years resided, worked or attended school in Marin. There were no substantial differences in geographic areas of birth or places ever lived before age 21 among women overall or women over 50. Under age 50, a significantly higher percentage of cases than controls reported having been born in or having lived in the Northeast or Great Lakes before age 21.	Using the total years resided, worked or attended school in Marin did not yield statistically significant differences. This suggests that more sensitive analyses may be needed to determine the link between health and place of residence. More sensitive analyses could include smaller geographic areas (neighborhoods rather than counties) for instance.
Cancer Clusters and Residential Histories Publication in progress	This project is exploring space-time clustering of breast cancer cases relative to controls in the Marin County data set while accounting for residential mobility and the risk factors and covariates identified in the prior study by Wrensch et al.	Statistically significant clusters of breast cancer in Marin County were identified that occur at local scales and persist through time. These are statistically significant regardless of the three geographic scales considered (a) Marin only (b) California (c) The entire US.	The case-control sample is mobile and a portion of the cases comprising the cluster in Marin came from Long Island (an area of known elevated BC risk) and south central Wisconsin. The challenge is to discriminate between excess breast cancer risk attributable due to migration from that due to environmental risk factors in Marin.