Executive Summary

Women living on Cape Cod have significantly higher rates of breast cancer than women elsewhere in Massachusetts. When this disturbing fact was discovered in the early 1990s, breast cancer activists suspected an environmental link. In 1994, their advocacy led the Massachusetts legislature to commit funds for a study on breast cancer and the environment. The Massachusetts Department of Public Health selected Silent Spring Institute to conduct the study.

The initial phase of the Cape Cod Breast Cancer and Environment Study is now complete. The Silent Spring Institute research team has developed a sophisticated geographic information system to analyze associations between breast cancer and environmental features, studied historical records on pesticide use and drinking water quality, and developed new methods for field study of environmental estrogens. We have carefully examined patterns of higher breast cancer incidence on the Cape, amassed substantial data about the Cape environment, and searched for clues about inter-relationships.

Our research has clearly shown that higher breast cancer incidence is a long-standing problem that extends to all regions of the Cape. The results also show that sustained study of breast cancer and the Cape environment should continue to be a public health priority.

Through 2001, our research team will be building on the significant accomplishments from the study’s first phase as we seek to uncover why breast cancer risk is higher on Cape Cod than statewide. We will be collecting and analyzing data to determine how women are exposed to pesticides, compounds that mimic estrogen, and other hormones in the environment.

Research on environmental links to breast cancer has only recently become a focus, and the Cape Study is at the cutting-edge of this scientific inquiry. Because of the complexity of this research—the challenge, for example, of calculating a woman’s exposure to chemicals years or even decades before her tumor was discovered—knowledge will build incrementally from many studies using multiple methods. Breast cancer activists, scientists, physicians, and legislators all have a critical role to play in supporting the research needed to solve this tragic puzzle.

Table Of Contents

Executive Summary 1
Introduction 2
Breast Cancer: An Issue Affecting The Entire Cape 3
Why Focus On The Environment In The Search For Prevention 6
Building A Foundation For Studying Breast Cancer On Cape Cod: Phase One Goals Achieved 16
The Road Ahead: Phase Two Of The Cape Cod Breast Cancer And Environment Study 17
Where We Are Today 18
Appendix 19
Introduction

Breast cancer rates in nine of Cape Cod’s fifteen towns have been significantly higher than the state average since at least 1982. When the Massachusetts Department of Public Health published town-by-town cancer statistics for 1982 to 1990, this pattern caused breast cancer activists, particularly members of the Massachusetts Breast Cancer Coalition, to wonder whether the Cape environment differs from the rest of the state in some way that stimulates breast cancer to develop. These activists—along with Cape Cod legislators, especially Representative John Klimm and Senator Therese Murray, and their fellow legislators from across the state—worked to secure money to study breast cancer. The funds, which are administered by the Massachusetts Department of Public Health, were awarded to Silent Spring Institute to conduct the Cape Cod Breast Cancer and Environment Study. The initial award in December 1994 was for a three-year, $3.6 million study.

Silent Spring Institute is a unique partnership of scientists, physicians, public health advocates, and community activists united around the common goal of studying associations between the environment and women’s health, especially breast cancer. The Institute is committed to breast cancer prevention, a research agenda with an activist vision that goes far beyond science-as-usual. To this end, we foster a different approach to research by crossing scientific disciplines and involving the public. This open process stimulates creative thinking while keeping our work grounded in the research questions that are critical to the women of Cape Cod.

For the Cape Cod Study, we formed a multidisciplinary team of leading researchers to design an innovative approach to examining possible environmental risk factors for breast cancer. Our research has found that the elevated breast cancer incidence is indeed a long-standing problem for Cape Cod, and one that is not easily explained by established breast cancer risk factors, such as reproductive and family history.

We then focused on developing a better understanding of exposure to the environmental factors on the Cape that are hypothesized to affect breast cancer. Our emphasis on environmental exposure reflected not only the striking and unexplained geographic pattern of breast cancer on Cape Cod, but also the broader scientific need for research into breast cancer prevention. By studying the environment, we hope to find preventable causes of breast cancer that will turn breast cancer statistics around for future generations.
Breast Cancer: An Issue Affecting the Entire Cape

Breast cancer incidence was significantly elevated in 9 of the 15 towns on Cape Cod, 1982-1990. Cape Cod stands out as a geographic region with elevated breast cancer incidence.

This map of the state is the picture of breast cancer that provided the impetus for the Cape Cod Breast Cancer and Environment Study. Cape Cod stands out as a region in Massachusetts where there are many neighboring towns with breast cancer rates higher than statewide.
As a result of our in-depth analysis of breast cancer data from the Massachusetts Cancer Registry, we found that

- Breast cancer is about 20 percent higher on Cape Cod than in the rest of the state.
- Breast cancer incidence is at least 15% higher than in the rest of the state in 11 of the 15 towns on the Cape. In eight of these towns, the elevation is statistically significant.
- Cape Cod women 55-64 years old are at 29% greater risk of breast cancer than women of their age in the rest of Massachusetts.
We also focused on smaller geographic units to look for patterns within towns and across town boundaries. We do see variation within the Cape, although the problem affects communities across the region.

The map shows Silent Spring Institute’s analysis of breast cancer incidence by census tract on Cape Cod, 1982-1994. These smaller geographic areas help the study team look for patterns in incidence that might suggest possible causes.
Why are Breast Cancer Rates Higher on the Cape? . . .
Known Risk Factors are Not the Answer

In addition to looking at patterns of incidence, we began looking at whether characteristics of women who live on the Cape could explain the higher breast cancer rates.

- **Age.** The older population of Cape Cod does not explain higher breast cancer rates. The statistics are adjusted for age.

- **Mammography.** Greater use of mammography does not appear to explain higher incidence on the Cape. The percent of tumors diagnosed “early” on the Cape is about the same as in the rest of the state—an indication that breast cancer isn’t higher on the Cape just because more cancers are being discovered through mammography.

- **Risk Factors.** We also wondered about risk factors that researchers have consistently shown to be associated with breast cancer—like having a close relative with breast cancer, menstrual and child-bearing history, or demographic factors like education—and risk factors that researchers have recently begun to study like alcohol, smoking, and physical exercise.

  Using data from a Harvard University study, we were able to conduct a preliminary assessment of the role these risk factors may play. Our study team found that these risk factors do not appear to fully explain the elevated breast cancer incidence on Cape Cod. Even after adjusting for all of these risk factors, breast cancer risk is still 21% higher for Cape Cod women aged 50-74 than for women in other parts of Massachusetts.

Why Focus on the Environment in the Search for Prevention

If regional elevations in breast cancer are not fully explained by characteristics of the people who live there, then the environmental characteristics of the place may be important to evaluate. The idea that environmental pollution causes breast cancer is reasonable to explore since pollution has been associated with some types of cancers. For breast cancer, researchers have found an association with ionizing radiation; however, no one has yet been able to clearly demonstrate an association between breast cancer and other environmental factors. This may be due to the small number of studies of breast cancer and the environment, and the difficulty in measuring what women were exposed to in years before a cancer was diagnosed. We in Massachusetts are contributing to solving that problem by developing new research methods as we search for links between breast cancer and the environment.
Identifying Regional Environmental Factors Relevant to Breast Cancer

With breast cancer rates elevated across the Cape, our focus during the first phase of the Cape Cod Breast Cancer and Environment Study was to identify regional environmental factor(s). We may be able to learn something about environmental risk factors for breast cancer on the Cape from what we know about non-environmental risk factors. Many of the known risk factors for breast cancer are related to lifetime estrogen exposure. Scientists are beginning to learn that synthetic chemicals—compounds in ordinary products like pesticides, detergents, and plastics—can act like estrogen. These chemicals go by many names including environmental estrogens and estrogen mimics. If natural estrogen increases breast cancer risk, we certainly should be asking whether chemicals that mimic estrogen are also linked to breast cancer.

To do that we need to learn how women are exposed. We use products with estrogenic compounds in our homes. So on Cape Cod, when we dispose of these products, they go down the drain into the septic system and can move through the Cape’s sandy soil into groundwater. From the groundwater they may ultimately move into drinking water supplied from shallow wells that are common on the Cape. Cape Cod residents are well aware that septic systems can contaminate drinking water on the Cape, but the possibility that contamination could lead to increased exposure to estrogen mimics is an aspect of the problem that hasn't been studied before. As part of the Cape Study we pilot-tested new methods to track the movement of specific estrogenic compounds from wastewater to drinking water as a possible source of exposure.

While we were testing drinking water, we compared water quality for our samples to the health standards. As we expected, all public water supply wells that we tested met the health regulations for the compounds we looked at. Local officials on the Cape regularly test public drinking water to be sure that it meets the health standards. The US Environmental Protection Agency is studying whether environmental estrogens should be regulated in the future.

Researchers analyzed wastewater, groundwater, and drinking water samples collected on Cape Cod for 225 different compounds.
Detecting Exposure to Environmental Estrogens

In the Cape Cod Breast Cancer and Environment Study, we developed and tested new methods to measure estrogen mimics in the environment. In our limited testing program, we found environmental estrogens in septage, as we expected; and we found them in groundwater that we knew was contaminated by wastewater. We are the first scientific team to measure these environmental estrogens in groundwater.

We also tested some public and private drinking water wells. The environmental estrogens we were looking for are not presently regulated in drinking water. In our pilot-testing program we found only a few compounds at trace levels in a few private wells and none in public water supplies. Based on these results, we decided to look at other possible sources of exposure by testing dust and air in women’s homes. We also hope to do further testing of groundwater, expanding the list of target compounds to include other types of estrogens, such as natural estrogens and pharmaceuticals—birth control pills and hormone replacement therapy—excreted from women’s bodies.

Developing New Methods to Detect Estrogen Mimics

The Cape Study team developed and tested two types of methods for detecting compounds relevant to breast cancer. Silent Spring Institute researchers collaborated with researchers at Tufts University Medical School to apply the E-SCREEN bioassay to environmental samples. The E-SCREEN bioassay allows researchers to test samples to see if they act like estrogen in breast cancer cells.

In addition, the Cape Study team developed and used new analytical methods to identify and measure 225 different compounds. One new method was designed to detect alkylphenols, which are breakdown products of chemicals in some detergents and are estrogenic.
Looking for Environmental Estrogens in the Workplace

Using data from women in Boston University's Upper Cape Study, Silent Spring Institute's research team was able to explore a number of factors including occupational exposure to chemicals that mimic estrogen. We identified several jobs associated with exposure to estrogen mimics such as PCBs and 4-octylphenol.

- Occupations with PCB exposure include clinical pathologist, clinical laboratory technologist, and assembly jobs in electrical equipment and other manufacturing.
- Occupations with probable 4-octylphenol exposure include gasoline service station attendant, assembly worker, and machine operator.

The team found that occupational exposure to PCBs and/or 4-octylphenol was associated with a threefold increase in breast cancer risk, although these findings did not reach statistical significance. Future study of women with workplace exposure to estrogen mimics is a promising avenue for testing the hypothesis that exposure to these chemicals increases breast cancer risk.

Other analyses of data from the Boston University study showed no significant association between breast cancer and occupational or household exposure to magnetic fields, or between breast cancer and occupational physical activity.

Cape Study Co-Investigator and Associate Professor at Boston University School of Public Health Dr. Ann Aschengrau led the analysis of environmental estrogens in the workplace.
Recreating a Picture of the Cape’s Environment from 1948 to 1997

Because tumors diagnosed today began years ago, we wanted to know about historical sources of environmental exposure. We combined a wide variety of data about the Cape environment—dating back to 1948—in a computer mapping system, the Cape Study geographic information system (GIS).

- The GIS includes data on water quality measurements dating as far back as 25 years, areas where pesticides were used since 1948 when DDT was first sprayed on the Cape, and land use back to 1951. Some of these land uses are relevant to estimating historical exposure.
- The GIS can give us information that women can’t tell us in an interview. For example, we can use the GIS to identify areas where women live now that were sprayed for gypsy moths before the land was cleared and developed for residential use.
- The GIS captures a wealth of information in great geographic detail. One of the “data layers” shows all the houselots on the Cape. We have mapped the addresses at the time of diagnosis for 2,625 women diagnosed with breast cancer on Cape Cod from 1982-1994. These data are kept strictly confidential.

The Cape Study geographic information system (GIS) is the most comprehensive source of information on the Cape environment.
This chart shows the dramatic development of the Cape from forested to residential land from 1961 to 1990. Homeowners may be unaware of chemical exposures from past uses of the land, such as application of agricultural fertilizers and herbicides or aerial spraying of pesticides for gypsy moth infestations.

Cape Cod in 1951 was largely forested land (the green areas). By 1990 the landscape had changed. Homes were built on previously undeveloped land. Notice the increase in light green, residential land, between the map on the left, land use in 1951, and the map on the right, the same area in 1990.
How it Works: Using the GIS to Estimate Exposure to Pesticides

The GIS can combine information from multiple sources to learn how women might have been exposed to chemicals that may be related to breast cancer. This picture shows two hypothetical houses. Both are in areas where pesticides were used. We programmed the computer to calculate how far each house is from the nearest pesticide use area and to take into account other factors.

The exposures at these hypothetical houses probably would be different because of the presence of forest around one house and not the other. (The green area represents forest.) You can see that one house has a stand of trees between it and the pesticide area. The trees shield the house from pesticide drift. The other house has no forest buffer and would likely have higher exposure to pesticides used on the bog.

At this point in our research, we have looked at selected environmental characteristics and breast cancer incidence by census tract. Our exploratory analyses to date focused on indicators of historic drinking water quality and local pesticide application rates. To do these analyses we estimated average exposure for each census tract. We did not see any obvious association between the environmental measures that we looked at and census tracts with higher incidence.

If you look again at the example of pesticide use, you will see why that may not be so surprising. We may not see associations when we average exposure across a census tract, because two houses that are quite close together may have different exposures. In the example, one house is separated from a pesticide use area by a forest buffer and the other is not. You can see from this example why we want to look in greater detail at individuals and specific addresses.
Taking a Closer Look at Environmental Factors of Concern to Cape Residents

At the outset of the study, Cape Cod residents identified a number of environmental factors that were of concern. We evaluated each of the hypotheses based on several criteria: 1) scientific plausibility, that is, does scientific research suggest a possible link to breast cancer, and 2) Cape-specific exposure, that is, is exposure to the factor likely to be different on the Cape than in the rest of Massachusetts.

The information now available for these factors does not indicate that they explain the elevated breast cancer rates throughout the Cape. However, we have not ruled out localized effects from them.

- **PAVE PAWS Radar System**— The data we collected and analyzed suggest that exposure to the PAVE PAWS beam is not associated with the Capewide elevation in breast cancer incidence. However, these analyses are limited due to the lack of environmental measurements.

- **Radon and other Radionuclides**— Ionizing radiation, the type emitted by the radioactive decay of radon or other radionuclides, is known to be associated with the incidence of breast and other cancers. The available data do not indicate that radon and other naturally occurring radionuclides are more common on Cape Cod than in the rest of Massachusetts.

- **Massachusetts Military Reservation (MMR)**— Please see the information on pages 14 and 15 for a discussion of our work on the MMR.

- **Regional Air Pollution**— The data available generally indicate that air quality on Cape Cod is not significantly different from the rest of the state—and in fact is often better—both in terms of regional air quality and pollution from individual point sources. Most of the available data is for chemicals associated with ground level ozone (a major component of smog) and acid “rain”. Because of the limited data for other possible air pollutants on Cape Cod, we cannot draw any firm conclusions about the issue.

- **Pilgrim Nuclear Power Station**— The radiation data available from the few monitoring stations on Cape Cod are consistent with the background levels measured before Pilgrim’s startup.

- **Regional Sources of Food**— Many scientists are studying whether diet may affect breast cancer. Specific regional food supplies or eating habits may create regional difference in diet. In light of this, we focused on fish and shellfish and cattle and poultry consumption. For fish and shellfish, the limited data available show some contaminants are present in locally caught fish. For cattle and poultry, we found limited evidence to suggest certain farms were a unique food supply for portions of the Cape, but no data are available on the chemical use on these farms. The portion of women diagnosed with breast cancer between 1982 and 1992 who would have been exposed is quite small, since most of these farms had closed by the 1950s.

- **Electromagnetic Fields from Electric Power Facilities**— Our analysis suggests that EMF exposure does not explain the Capewide elevation in breast cancer. We found that major power lines and power stations are generally located away from Cape residences.

We are only beginning to understand the links between the environment and a woman’s risk of breast cancer. It will take more years of focused study before researchers know whether and what environmental factors may play a role.

Dr. Richard Clapp
Boston University School of Public Health & Silent Spring Institute Collaborating Researcher

Dr. Richard Clapp and Silent Spring Institute Board Member
Dr. Cathie Ragovin discuss some of the issues raised during the Institute’s 1998 symposium on breast cancer and the environment.
This map shows the Massachusetts Military Reservation and breast cancer incidence in the areas surrounding it. You can see elevated breast cancer to the north of the MMR.

The Massachusetts Military Reservation is a significantly contaminated site that may be associated with some local pockets of higher breast cancer incidence.

Three separate analytical techniques create a relatively consistent picture which suggests there is a concentration of breast cancer in census tracts to the north of the Massachusetts Military Reservation (MMR).

The maps shown on this page and the next are graphic representations of breast cancer incidence on the Upper Cape as calculated using different analytical techniques. When reviewing the maps, it is striking that despite the different methodologies, both show elevations to the north of the MMR. This finding is especially interesting given the fact that the two census tracts to the north and northeast of the MMR are, for nine months of the year, downwind of the MMR gun and mortar positions, so women in this area may have been exposed to air pollutants from the burning of propellants. Propellant bag burning was halted at the MMR in 1992.
Further, two compounds released during the burning of bags containing propellants may be especially relevant to breast cancer. Dinitrotoluene, a by-product of 2,4,6-trinitrotoluene (TNT) which is used in explosives, is a known mammary carcinogen in animals and di-n-butyl phthalate is an endocrine disruptor and has been shown to affect hormones in animal studies.

We would like to learn whether these compounds and other emissions from the MMR might have reached residential areas, and if so, whether they can be linked to the elevated breast cancer in those tracts. Sampling of soil and undisturbed (e.g., attic) house dust might provide clues to historical exposure, if any, to these compounds.
Building a Foundation for Studying Breast Cancer on Cape Cod: Phase One Goals Achieved

The Cape Cod Breast Cancer and Environment Study has an ambitious mission: to uncover why breast cancer is higher on Cape Cod than statewide. In December 1994 the study began with a three-year plan to begin this research. This first phase, which ended in December 1997, successfully completed the three sets of tasks that were its central priorities:

- **A rigorous and detailed description of the problem of breast cancer within the Cape— including geographic patterns, trends across time, and incidence for women of different ages.** We used Massachusetts Cancer Registry data to identify clues to the causes of higher risk. Our research confirms that breast cancer is 20% higher on Cape Cod than in the rest of the state for the period 1982-1994.

- **An exploratory analysis of possible reasons for the elevated incidence of breast cancer on Cape Cod.** Our research shows that the higher breast cancer rates on Cape Cod do not appear to be fully explained by individual characteristics of the women who live there, for example, age, family history, reproductive history, alcohol consumption, smoking, and age at onset of menstruation and menopause.

  Our research indicates that a number of specific environmental facilities of concern, including the PAVE PAWS radar system, Massachusetts Military Reservation (MMR), Canal Electric Plant, and Pilgrim Nuclear Power Station do not appear to explain why breast cancer rates are elevated Cape-wide. However, we have not ruled out localized effects from these facilities. In particular, the Massachusetts Military Reservation is a significantly contaminated site that may be associated with some local pockets of higher breast cancer incidence.

- **Proactive development and testing of new research methods to study compelling environmental hypotheses for breast cancer.**

  As a result of this study, we created the most comprehensive source of information on the Cape environment, the Cape Cod Breast Cancer and Environment Study Geographic Information System (GIS). The GIS makes it possible to assess in future studies how environmental factors might be associated with increased breast cancer incidence on the Cape.

  We also successfully developed and tested new methods to measure estrogenic activity and identify compounds that may be relevant to breast cancer incidence. With these new methods, we were able, for the first time, to identify environmental estrogens in groundwater contaminated by wastewater. We also found some of these compounds in very low concentrations in a few private drinking water wells, but not in public water supplies.

The results of the first three years of research on the Cape Cod Breast Cancer and Environment Study make a compelling case for continued exploration of environmental links to breast cancer on Cape Cod.
The Road Ahead: Phase Two of the Cape Cod Breast Cancer and Environment Study

Building on the significant accomplishments of the first phase, Silent Spring Institute is now able to study how women may be exposed to pesticides, endocrine disruptors, and mammary carcinogens. To do this, we are collecting and analyzing data from three sources:

- Interviews with 2,500 Cape women with and without breast cancer. Through the interview we will collect information on recognized risk factors (such as family and childbearing history), products (such as pesticides, cleaners, personal care), and activities (such as occupation, golf, gardening).
- Tests of air and dust and women’s urine for suspected mammary carcinogens and estrogen mimics in 140 households to learn which chemicals women are typically exposed to at home.
- Estimates of environmental exposures for all 2,500 study participants using the Geographic Information System (GIS) developed during the first study period.

At the conclusion of this research, we will be able to answer the following questions:

- Can we find associations between breast cancer risk and certain environmental exposures on Cape Cod, such as exposure to pesticides applied to a cranberry bog, from gypsy moth spraying, or used in the home?
- Do local variations in breast cancer risk across Cape Cod suggest local causes of some breast cancers, for example, near specific sources of pollution?
- What endocrine disruptors and mammary carcinogens (two types of chemicals that may affect breast cancer) are found in Cape Cod homes and at what concentrations?
- How can we improve our ability to assess women’s exposure to certain chemicals especially when the exposure occurs years before a breast cancer diagnosis?

The answers to these questions will serve our ultimate goal: to identify preventable causes of breast cancer.

As activists, we are tremendously proud of the innovative research Silent Spring has been doing on Cape Cod. Known risk factors for breast cancer account for less than 50% of this disease. We believe that Silent Spring’s research on environmental links to breast cancer will lead to the identification of preventable causes of this disease as well as many other kinds of cancer. It is imperative that we identify preventable causes, so that we can stop the breast cancer epidemic now.

Bev Baccelli
Massachusetts Breast Cancer Coalition President

The Cape Cod Breast Cancer and Environment Study is a multi-disciplinary study. Over 20 researchers at academic and private institutions collaborate in the search to learn why breast cancer is elevated on Cape Cod.
Where We Are Today

Scientists have worked through three decades and hundreds of studies to develop the current list of known breast cancer risk factors. Yet many of these factors, such as family history of the disease, are outside of a woman’s control; and what we know now explains less than half of breast cancer risk.

Only over the past decade has research begun to focus on the associations between environmental factors and breast cancer. Because of the complexity of this research—for example, the challenges of estimating a woman’s exposure to chemicals years ago when a tumor first appeared or as it proliferates before diagnosis—knowledge about environmental risk factors for breast cancer will build incrementally from many studies using multiple methods. Breast cancer activists, scientists, physicians and legislators all have a critical role to play in supporting the research needed to solve this tragic puzzle.

The mission of Silent Spring Institute is to study breast cancer and the environment with a goal of finding preventable causes.
Appendix

Cape Cod Breast Cancer and Environment Study Final Report: A Summary

Since the beginning of the Massachusetts Cancer Registry in 1982, breast cancer incidence has been significantly higher in most Cape Cod towns than statewide. The Cape Cod Breast Cancer and Environment Study was initiated by a December 1994 grant from the Massachusetts Department of Public Health (MDPH) guided by an appropriation of the legislature to study this public health problem. The multi-disciplinary study team led by Silent Spring Institute includes researchers at Applied Geographics Inc., Boston University School of Public Health, Focus Group, Menzie-Cura & Associates, the Slone Epidemiology Unit of the Boston University School of Medicine, and Tufts University Medical School. The executive summary describes these elements of our work:

• results of our detailed analyses of patterns of breast cancer within Cape Cod,

• the scientific foundations for studying exposure to environmental factors, particularly chemicals that mimic estrogen,

• new scientific methods developed and applied in the study,

• analysis of historical drinking water quality for Cape Cod water supplies,

• results of our reconstruction of historical pesticide use,

• results of field sampling for environmental estrogens in Cape Cod wastewater, contaminated groundwater, and drinking water,

• recommendations for future study.

1. ELEVATED BREAST CANCER ON CAPE COD

The initiative for the Cape Cod Breast Cancer and Environment Study came from public concerns about breast cancer incidence in Cape Cod towns during the period 1982-1990. Nine Cape Cod towns had breast cancer incidence significantly higher than statewide.

The first question to ask about these statistics is “Are they real?” That is, do they signal a regional health problem or are they artifacts of limited data or other factors?

Standardized incidence ratios (SIRs) are calculated as the ratio of the number of new breast cancers diagnosed in a group of women compared with the number that would be expected, based on breast cancer rates in a comparison group. They are adjusted for age, so we can be confident that regional differences are not due to an older population on the Cape. However, SIRs may be affected by how hospitals report breast cancer cases to the state registry or by estimates of population. In studies in other locations, researchers have reported regional variations in breast cancer rates that are related to differences in established risk factors for breast cancer. For Cape Cod, a growing population adds questions about effects of in-migration.

Results of the Cape Cod Breast Cancer and Environment Study indicate that higher breast cancer incidence on the Cape is indeed real, and the study greatly expands our understanding of patterns of incidence within the region. We rechecked Cancer Registry case data and developed new refinements of the population estimates to calculate incidence. Effects of established risk factors were explored through data from earlier case-control epidemiologic studies. However, possible effects of in-migration remain largely a question for future research. Results reveal a clear and detailed picture of breast cancer as a public health priority for Cape Cod and provide a firm foundation for sustained research to identify causes. The next phase of study should include individual-level epidemiologic study of possible environmental risk factors along with established risk factors.
Patterns of Incidence

- Breast cancer incidence was 21% higher on Cape Cod than statewide for the period 1982-1992. This finding is highly statistically significant (p < .001), so it is very unlikely to be due to chance.

- Incidence is elevated across the Cape. Breast cancer incidence is significantly elevated for all three regions of the Cape and for nine of the Cape's 15 towns. This pattern suggests that research should address factors that affect all regions of the Cape, as well as local factors.

- Patterns of incidence for census units within Cape towns and across town boundaries were calculated in detail as a resource for generating additional hypotheses about local factors in breast cancer incidence.

- Cape incidence is higher than off-Cape Massachusetts for nearly every year within the study period. The highest incidence was during the early 1980s.

- The excess in breast cancer incidence on Cape Cod is higher for post-menopausal (SIR = 125; 95% CI 119-131) than pre-menopausal women (SIR = 106; 95% CI 90-123). When incidence is calculated by ten-year age groups, SIRs for Cape women are significantly higher than the rest of the state for women aged 55 - 84. Elevated incidence for women younger than retirement years suggests that factors specific to the retirement population are unlikely to adequately explain higher breast cancer incidence on the Cape. As researchers better understand pre- and post-menopausal disease, these results showing higher post-menopausal risk may point to directions for future research on the Cape.

- Breast cancer incidence remains about 20% higher on Cape Cod than in the rest of Massachusetts during 1993-1994, the most recent years reported by the Cancer Registry.

Effects of Mammography on Incidence Data

- In order to assess the possible effects of mammography screening on breast cancer incidence, we calculated the proportion of cases diagnosed “early” on Cape Cod as compared with the rest of the state. The Massachusetts Cancer Registry began recording in situ cases only in 1992, so data for the earlier 10 years of our study period are limited to Stage 1 (local) to Stage 3 (distant) diagnoses. Available data indicate that differences in mammography are unlikely to account for differences in breast cancer incidence, particularly for the earlier years when incidence was highest on the Cape.

Established Risk Factors

- Higher breast cancer rates on the Cape are unlikely to be adequately explained by differences between the Cape and the rest of the state for established risk factors. Researchers at Harvard School of Public Health applied a multi-variate statistical model to case-control data from the Collaborative Breast Cancer Study in an analysis designed to assess how established risk factors may contribute to differences in risk between the Cape and the rest of Massachusetts outside metropolitan Boston. The model adjusted for age, education, the interaction of Jewish religion and family history of breast cancer, recent body mass index, height, age at menarche, the interaction of parity and age at first full term pregnancy, history of benign breast disease, menopausal status, age at menopause, recent alcohol consumption, pack-years of smoking, early physical activity, and carotenoid consumption. For women aged 50-74, who make up most of the study population, the relative risk adjusted for factors in the model was 21% higher for Cape Cod women than others in Massachusetts (RR =1.21; 95% CI 1.03-1.42) for 1989-1993. This finding is consistent with SIRs calculated by Silent Spring Institute from Cancer Registry data.
2. FOCUS ON THE ENVIRONMENT: SCIENTIFIC BASIS

Detailed breast cancer surveillance and analysis of existing case-control data, described above, indicate that elevated breast cancer is a long-standing regional problem that is not easily explained by established risk factors. These results point to a need for research to identify new etiologic factors that may contribute to higher breast cancer on the Cape.

At the outset of the study, Silent Spring Institute proposed to focus on developing a better understanding of exposure to environmental factors on the Cape that are hypothesized to affect breast cancer. The emphasis on environmental exposure reflects not only the striking and unexplained geographic pattern of breast cancer on Cape Cod, but also the broader scientific need for research in this emerging area. In parallel with our finding that Cape Cod women have higher breast cancer risk after statistical adjustment for established risk factors, other researchers report that numerous individual risk factors taken together — including a family history of close relatives with breast cancer, menstrual and reproductive history, and sociodemographic characteristics, such as income and education — explain less than half of breast cancer risk. The search for additional environmental factors, particularly in areas of regional high incidence, offers the opportunity to identify preventable causes.

Endocrine Disruptors and Breast Cancer

Studying environmental factors poses a challenge to advance new hypotheses and new scientific methods, since previous research about breast cancer and the environment is limited. Radiation is the only established environmental risk factor for breast cancer. About 40 chemicals have been identified by the National Toxicology Program as mammary carcinogens in animals; however, only a small fraction of chemicals in common use have been tested for carcinogenic effects. None have been adequately studied in women, although several recent studies have investigated DDT and PCBs, and others are now under way to follow up on earlier conflicting results.

Research about established risk factors for breast cancer may be a clue about which environmental chemicals to target for further research. Many of the best-studied risk factors for breast cancer, such as age at menarche and menopause and childbirth history, are associated with exposure to estrogen and related hormonal factors. As scientists have learned in recent years that synthetic chemicals, known as endocrine disruptors, affect estrogen and other hormones, environmental exposure to these chemicals becomes a priority for breast cancer research. Endocrine disruptors, including chemicals that mimic estrogen, are found in both active and inert ingredients in pesticides, and in common commercial products, such as detergents and plastics. Because they are widely used in commercial products, estrogenic chemicals are found in domestic wastewater and septic systems.

The hypothesis that endocrine disruptors affect breast cancer risk may be particularly relevant to Cape Cod because of the area’s history of substantial pesticide use and impacts of wastewater on drinking water. Nearly all drinking water on the Cape is drawn from a shallow, sandy aquifer that is vulnerable to impacts from septic systems and local land uses. Exposure to pesticides may be via drinking water, or through contact with air or soil either at the time of pesticide application or later, since residues remain in the environment. The Cape Cod Breast Cancer and Environment Study was designed to develop new data about how women may be exposed to endocrine disruptors in order to build a foundation for exploring whether exposure to these chemicals affects breast cancer risk. In response to public concerns, the study also explored the scientific plausibility and relevance to Cape Cod of a number of other environmental factors: regional food supplies, electromagnetic fields, the PAVE PAWS radar system, radiation in water, Pilgrim Nuclear Power Station, regional air pollution, and the Massachusetts Military Reservation.
3. NEW RESEARCH METHODS

With research about possible links between the environment and breast cancer still in its infancy, we needed new scientific methods as well as innovative hypotheses to investigate the causes of higher breast cancer rates on the Cape. Methods development is among the most significant contributions of the Cape Cod Breast Cancer and Environment Study.

- We compiled breast cancer and environmental data in a comprehensive computer-based Geographic Information System. The system enabled us to map the addresses of 2,173 women diagnosed with breast cancer between 1982 and 1992 on the Cape and to superimpose environmental data from our own field work, as well as local, state, federal, and university databases. The system represents a rich, permanent resource for health studies on the Cape. By combining multiple data sources to provide information at the house-lot level, the GIS can improve the accuracy of exposure assessment for future individual-level studies. Future research may expand our understanding of breast cancer on Cape Cod through use of the GIS in case-control and cohort studies, and in studies of health outcomes, such as reproductive effects and cancers, that may result from related hormonal processes.

- Study team members at Boston University School of Public Health developed sophisticated statistical analysis methods for environmental epidemiology and applied them to case-control data for the Upper Cape. One technique provides new approaches to the challenge in environmental epidemiology of identifying pockets of excess incidence with small numbers of cases. Results identified such locations on the Upper Cape. Another method evaluates the effects of different cut points in defining exposure categories for distances from possible environmental risks. These two methods could be applied in the future for the Mid and Lower Cape if new case-control data are collected, and for additional types of cancer.

- We developed new methods to test water samples for estrogenic chemicals using a cell-proliferation bioassay (E-SCREEN or estrogen-screen) developed at Tufts University and custom-designed chemical analysis methods. We are one of the first scientific teams to test environmental samples for estrogenic chemicals using complementary bioassay and chemical analysis methods. These methods enable researchers to measure specific estrogenic chemicals and total estrogenic activity in groundwater and other samples from the environment. The methods for preparing and testing environmental samples using E-SCREEN were developed and validated for the first time in this study, creating a widely applicable tool for environmental assessment for estrogenic chemicals that researchers hypothesize may be related to breast cancer.
4. EXPOSURE TO DRINKING WATER INFILTRATED BY WASTEWATER

Cape Cod draws nearly all of its drinking water from shallow wells in the sandy aquifer that underlies most of the Cape. Because of the contrast between this vulnerable water supply and the surface water supplies that are typical in the rest of Massachusetts, the Cape Cod Study focused on drinking water quality as a possible underlying explanation for higher breast cancer rates on the Cape.

Investigating a possible link between drinking water and breast cancer is a multi-faceted process that involves identifying pollutants that may be relevant to breast cancer and assessing women's exposure to these compounds in years prior to diagnosis. In this study, we developed a method to estimate historical drinking water quality in each of the Cape's water supplies. We focused on nitrates, an established indicator of wastewater infiltration, because wastewater contains endocrine disruptors and is a common pollutant on Cape Cod. We also studied volatile organic compounds (VOCs), pollutants that are commonly associated with densely developed land typical of some parts of the Cape. The advantage of using these regularly monitored parameters is that they provide systematic data for most of the Cape's population dating back to the 1970s and 1980s. Limitations stem from our incomplete understanding of how these indicators relate to compounds that may be relevant to breast cancer.

The GIS developed for the Cape Cod Breast Cancer and Environment Study provides a rich data source that allows researchers to assess historical drinking water quality for nearly every house-lot on the Cape. This means GIS data can be combined with interview data about women's addresses wherever they lived on the Cape to estimate selected aspects of their drinking water quality. GIS data sources include the following:

• locations and water quality data for the 130 groundwater wells that serve the Cape's 18 municipal water supplies and 80% of the Cape's population
  • measured nitrates for 1972 to the present
  • measured VOCs for the 1980s to the present
  • zones of contribution (the land area expected to contribute recharge to a well)
  • installation dates and composition of drinking water distribution pipes for most supplies (information that relates to possible contaminants in the distribution system and identifies when residents switched from private to public supplies)

• measured nitrates for selected private wells, a data set with approximately 13,000 test results

• land use data back to 1951 that may be used, for example, to measure residential density and identify areas of agricultural land

• MA DEP data on point-source impacts, including groundwater discharge permits, solid and hazardous waste facilities, and known contamination plumes

• USGS data on groundwater elevation contours that may be used to identify the direction of contaminant migration

Researchers present information about the Cape Cod Breast Cancer and Environment Study.
Results of our analysis of historical data show variations within the Cape in drinking water quality that reflect impacts of on-site septic systems, wastewater discharge, and other local land use. The magnitude of impacts is small in comparison to established health standards. The health implications of low concentrations of these indicators and any co-contaminants cannot be inferred from this study.

- The range of 15-year average nitrate concentrations in Cape public water supplies between 1970-1985 is 25-fold (0.05 to 1.31 mg/L). Average nitrate levels have more than doubled in many supplies between 1980 and 1990. Nitrate levels are well below health standards, but they are of interest in this study because they indicate impacts to the aquifer.

- The estimated percent of water drawn from wells with a history of detectable VOCs ranges from 0% in some public water supplies to 93% of water impacted in one supply. Concentrations of VOCs are low in comparison to established health standards.

Comparing Cape and off-Cape public water supplies shows that Cape Cod residents are more likely to drink water from wells with a history of impacts from VOCs other than trihalomethanes (THMs). More than three-fourths of Cape residents on public water supplies are served by wells with a history of non-THM VOCs, compared with fewer than half of residents supplied by public water off-Cape. However, the population-weighted average exposure to these contaminants is only slightly higher on-Cape than off-Cape.

This study contributes to a better understanding of regional impacts of land use on drinking water supplies, and it provides a new method for constructing exposure variables that reflect historical drinking water quality. These variables can be included, along with other environmental and personal risk factors, in regression analyses for individual-level health studies. The study leaves unanswered questions about how nitrates and VOCs, which are indicators of land use impacts, are associated with related compounds that may be relevant to breast cancer. Our field sampling results, discussed below, provide additional information about the impacts of wastewater and local land use on drinking water.

5. EXPOSURE TO PESTICIDES

The history of exposure to pesticides on Cape Cod is of interest for several reasons:

- Some previous studies have linked blood concentrations of DDE, a breakdown product of DDT, with breast cancer
- Some pesticides are endocrine disruptors
- Some are mammary carcinogens in animals
- Pesticides have been widely used on the Cape and may move differently in sandy Cape Cod soils than in other regions
- Development of residences in areas previously sprayed with persistent pesticides and in close proximity to cranberry bogs and golf courses may lead to greater exposures than in other regions.

To develop a resource for evaluating historical exposure to pesticides, we extensively searched local, state, and federal records of wide-area spraying and investigated pesticide use practices for cranberry bogs and golf courses.

- Results of this search confirm widespread use of persistent pesticides dating from the 1948 introduction of DDT and continuing through the mid 1960s.
- Results highlight the importance of forest spraying in addition to the more-often-studied agricultural uses.
• Using our Geographic Information System, we developed the capability to estimate exposure at the house-lot level. Multiple variables can be considered simultaneously; for example we combined distance to a pesticide source with other environmental factors, such as presence of a forest buffer that may reduce exposure.

• GIS data show variation within Cape Cod in potential exposure to pesticides from golf courses and cranberry bogs, and certain types of wide-area spraying.

• Data mapped in the GIS underestimate historical pesticide use on Cape Cod. The extent of unrecorded pesticide use cannot be estimated from our data.

Our results and the limitations we identified in historical records suggest areas for future research:

• Because areas of pesticide use do not match well with census boundaries, future use of our data in an individual-level study will be more informative than the exploratory ecologic analyses reported here.

• An individual-level study also could include household pesticide uses, for example termiteicides and lawn care chemicals, that are not included in this study.

• Additional research using questionnaires, field and household sampling, or biological measurements would be useful to complement historical records.
  
  • Questionnaires would provide information about the use of non-persistent pesticides that are not identified in sampling programs.
  
  • Soil and sediment sampling would provide information to complement and validate historical records and improve our ability to model exposure from GIS data. These data also would allow for comparisons with published data for other parts of Massachusetts and the US. Core samples of undisturbed sediments from wetlands would be useful because they reveal the history of pesticide deposition and provide information about how residues vary locally and regionally. Our research suggests that Eastham may have been an area of relatively low pesticide use, and this possibility warrants further exploration through field sampling because Eastham consistently shows lower breast cancer incidence than most other Cape towns.
  
  • Samples of house dust and soil near homes and blood serum measurements would be useful to provide a fuller picture of pesticide exposure in an individual-level study. Because of the opportunity to combine biological measurements with environmental data in our GIS, Cape Cod is a particularly appropriate place to follow up on pilot blood serum research by MDPH in western Massachusetts.
  
  • Our data do not allow for a comparison between Cape Cod pesticide use and other parts of the state. Future research could better provide a perspective on whether pesticide use on Cape Cod differs from elsewhere in a way that may be related to differences in breast cancer.

6. FIELD TESTING FOR ENVIRONMENTAL ESTROGENS AND OTHER COMPOUNDS IN GROUNDWATER

In addition to studying historical records for drinking water quality and pesticide use, the Cape Cod Breast Cancer and Environment Study conducted an innovative program of field testing designed to contribute to our understanding of how women may be exposed to contaminants in drinking water, including chemicals that may be related to breast cancer. We custom-designed chemical analysis methods to test for specific compounds identified as environmental estrogens in earlier research, and we developed a method of preparing environmental samples that allows them to be tested for estrogenic activity using the E-SCREEN bioassay. The E-SCREEN is an estrogen screening assay that researchers at Tufts Medical Former Cape Study Public Advisory Committee member Nancy Swift reviewed materials at a public information session. Nancy Swift died of breast cancer in April 1998.
School adapted to measure total estrogenicity in environmental samples. In order to investigate how environmental estrogens may travel from their sources in wastewater through groundwater into drinking water, we sampled septage, wastewater influent and effluent, groundwater known to be contaminated by wastewater, and drinking water. Our methods and results are national as well as regional importance, as the recently re-authorized Safe Drinking Water Act directs the US Environmental Protection Agency to study endocrine disruptors over the next few years to assess measurement techniques, research needs, and health implications.

- We detected substantial concentrations of environmental estrogens in septage and wastewater samples: nonylphenol (1000 µg/L), nonyl and octylphenol ethoxylates (11,000 µg/L) and carboxylates (50 µg/L), bisphenol A (1 µg/L), butylbenzyl phthalate (10 µg/L), and organochlorine pesticides (6 µg/L).

- We found many of the same compounds at lower concentrations in groundwater contaminated by wastewater, indicating that some endocrine disruptors can move from their source in wastewater through the aquifer.

- Given the history of wastewater contamination of Cape Cod drinking water supplies, we anticipated that environmental estrogens found in wastewater might also be frequently detected in drinking water. However, in the few dozen drinking water wells we sampled, we found only a few private wells with low concentrations of selected environmental estrogens at levels unlikely to be due to sample contamination. Bisphenol A (0.005-0.05 µg/L) was detected in six private wells above levels in any field blanks (used as quality control measures), and nonylphenol ethoxycarboxylate (0.1 µg/L) and nonyl/octylphenol tetraethoxylate (33 µg/L) were each also detected in one well.

- E-SCREEN results show substantial estrogenicity in wastewater, with lower activity in groundwater contaminated by wastewater. Drinking water samples and field blanks showed no or slight activity. The overall range in estrogenic activity in the samples was 6 orders of magnitude (0.003 - 3,000 pmol/L estradiol equivalents).

- Comparison of chemical analyses and E-SCREEN results shows a strong correlation between concentrations of estrogenic compounds and measured activity across sample types. Most estrogenic activity can be accounted for based on the relative estrogenic potency of compounds detected by chemical analysis, an indication that the sample extracts do not contain substantial amounts of additional estrogenic compounds that were not on our target list.

- Our findings of very low concentrations of a few estrogenic compounds in only a few drinking water samples suggest that drinking water may not be a primary source of exposure on Cape Cod. We cannot reject the possibility of drinking water as an important source of exposure, however, because we may have failed to detect compounds in drinking water for several reasons: (1) contaminants from wastewater may be transformed in the aquifer into compounds not detected by our methods; (2) drinking water may be impacted by more polar, water soluble wastewater constituents that our methods were not designed to detect, including endogenous and pharmaceutical estrogens excreted by women; and (3) our small number of samples is a limited picture of drinking water quality.

Results of the field sampling program are a fertile source of research questions for the future. Because we found high levels of estrogenic target compounds in wastewater sources and some indication of three of these compounds in drinking water, further research remains important. We recommend two approaches to further study how endocrine disruptors affect the environment and how women may be exposed.

First, our findings of substantial concentrations of environmental estrogens in wastewater and lower concentrations of the same compounds in groundwater contaminated by wastewater raise important questions about how specific endocrine disruptors migrate in the Cape Cod aquifer. Continued rapid development of residential septic systems on the Cape makes this question particularly significant for protecting environmental quality for the future. An efficient strategy for investigating the impact of wastewater on groundwater would be sampling that begins at septic systems or other wastewater sources and moves outward, tracing target compounds at specified distances from the source. In addition to
applying the methods already developed in the Cape Cod Breast Cancer and Environment Study, these
methods should be expanded to look for more mobile, water-soluble compounds. This testing should
include analysis for endogenous and pharmaceutical estrogens excreted by women since they were recently
reported by other researchers in wastewater samples. This research is critical before we can confidently
reject drinking water as an important exposure route.

Second, the methods developed in this study to test drinking water could be applied to other
environmental samples, particularly household air and dust, and to blood to identify other exposures
to endocrine disruptors. Our results showing substantial concentrations of estrogenic compounds in
domestic septage confirms that these chemicals are used in residential environments. Continued field
study of endocrine disruptors is a priority because the hypothesis that these chemicals affect breast
cancer is consistent with a large body of research showing associations between natural estrogen and
breast cancer risk.

7. CONTEXT FOR FUTURE RESEARCH

At the close of two and a half years of research, we have carefully analyzed patterns of higher breast cancer
incidence on Cape Cod, amassed substantial data about the Cape environment, and searched for clues
about inter-relationships.

We have clearly documented that higher breast cancer incidence is a long-standing public health problem
that extends to all regions of the Cape. We developed a sophisticated geographic information system to
compile and analyze associations between breast cancer and environmental features, completed an analysis
of historical records for pesticide use and key aspects of drinking water quality, and developed new methods
for field study of environmental estrogens. Our results show that sustained study of breast cancer and the
environment on Cape Cod should continue to be a public health priority. In addition to the specific
recommendations interwoven throughout this executive summary, we recommend these fundamental
approaches to future research:

• Continued breast cancer surveillance using methods developed in this study should track incidence
  through the 1990s.

• Using the Cape Cod Breast Cancer and Environment Study GIS, environmental data should be
  included along with established risk factors in a case-control study to assess the relative contribution
  of multiple factors.

• Effects of in-migration of women to the Cape and of environmental exposure during particular
  periods of a woman’s life should be studied using cohort and/or case-control methods.

• Additional targeted field work to strengthen and validate environmental exposure data should remain
  a priority.

In addition to the scientific innovation in the Cape Cod Breast Cancer and Environment Study, this
study represents a different approach to research, because it crosses scientific disciplines and includes the
public through our Public Advisory Committee, community information sessions, and numerous interviews
and focus groups on Cape Cod. This open process stimulates creative thinking while keeping our work
grounded in the research questions that matter to Cape Cod residents. Continuing in this spirit of
partnership, it is our hope that our results and recommendations for future research will prompt broad
discussion, involving scientists, public officials, and citizens, of the best directions for future efforts to
better understand breast cancer on Cape Cod and find clues to prevention.
Acknowledgments

We want to thank the many individuals who helped found Silent Spring Institute and who contributed to the Cape Cod Breast Cancer and Environment Study. In particular we would like to acknowledge the contributions of the following individuals: the Silent Spring Institute Board of Directors, chaired by Ellen Parker; members of the Massachusetts Legislature, especially Representative John Klimm and Senator Therese Murray; the Massachusetts Breast Cancer Coalition; and the many Silent Spring Institute volunteers.

Our Public Advisory Committee has also made tremendous contributions throughout the process by working with us in planning, gathering data, interpreting our results, and sharing their experiences. Of the 26 original members, five women had been diagnosed with breast cancer. Now, three years later, two have died of breast cancer and another has been diagnosed with metastatic disease. The experiences of these five women and all the other women who have shared their lives with us strengthen our resolve as we search for preventable causes of breast cancer.

* * *
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Silent Spring Institute builds on a unique partnership of scientists, physicians, public health advocates, and community activists who are dedicated to identifying— and breaking— the links between the environment and breast cancer. The Institute is committed to breast cancer prevention, a research agenda with an activist vision that goes far beyond the science-as-usual approach.

For more information, to order a copy of the December 1997 Cape Cod Breast Cancer and Environment Study Final Report, or to volunteer with Silent Spring Institute, contact us at

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We tolerate cancer-causing agents in our environment at our peril.... For those in whom cancer is already a hidden or a visible presence, efforts to find cures must of course continue. But for those not yet touched by the disease and certainly for the generations as yet unborn, prevention is the imperative need.

— Rachel Carson, Silent Spring