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Report

The Long Island Breast Cancer Study Project: description of a multi-institutional collaboration to identify environmental risk factors for breast cancer

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Summary

The Long Island Breast Cancer Study Project is a federally mandated, population-based case-control study to determine whether breast cancer risk among women in the counties of Nassau and Suffolk, NY, is associated with selected environmental exposures, assessed by blood samples, self-reports, and environmental home samples. This report describes the collaborative project's background, rationale, methods, participation rates, and distributions of known risk factors for breast cancer by case-control status, by blood donation, and by availability of environmental home samples. Interview response rates among eligible cases and controls were 82.1% ($n = 1{,}508$) and 62.8% ($n = 1{,}556$), respectively. Among case and control respondents who completed the interviewer-administered questionnaire, 98.2 and 97.6% self-completed the food frequency questionnaire; 73.0 and 73.3% donated a blood sample; and 93.0 and 83.3% donated a urine sample. Among a random sample of case and control

respondents who are long-term residents, samples of dust (83.6 and 83.0%); soil (93.5 and 89.7%); and water (94.3 and 93.9%) were collected. Established risk factors for breast cancer that were found to increase risk among Long Island women include lower parity, late age at first birth, little or no breast feeding, and family history of breast cancer. Factors that were found to be associated with a decreased likelihood that a respondent would donate blood include increasing age and past smoking; factors associated with an increased probability include white or other race, alcohol use, ever breastfed, ever use of hormone replacement therapy, ever use of oral contraceptives, and ever had a mammogram. Long-term residents (defined as 15+ years in the interview home) with environmental home samples did not differ from other long-term residents, although there were a number of differences in risk factor distributions between long-term residents and other participants, as anticipated.

Introduction

The Long Island Breast Cancer Study Project (LIBCSP) is an umbrella of projects funded by the National Cancer Institute and National Institute of Environmental Health Sciences in response to federal legislation (Public Law 103–43, June 10, 1993), which mandated that a study be conducted to assess environmental and other potential risk factors contributing to the incidence of breast cancer in the Long Island counties of Nassau and Suffolk in New York, as well as the two other counties in the Northeastern United States with the highest mortality rates (Schoharie, NY, and Tolland, CT). The multi-institutional collaborative study described here, which is the centerpiece of the LIBCSP and is commonly referred to by that global name, is a population-based case-control study undertaken to determine whether the risk of breast cancer among women residing on Long Island is associated with polycyclic aromatic hydrocarbons (PAH) and organochlorine compounds, such as DDT and polychlorinated biphenyls (PCBs), assessed in blood samples, by self-reports, or in environmental home samples. This report includes a brief summary of the background and rationale that catalyzed the multidisciplinary approach that benefitted from scientific oversight of two external advisory groups as well as lay community collaboration. The primary focus of the manuscript is to provide a detailed description of the study methods, success of the study recruitment efforts, and distributions of the known breast cancer risk factors by case-control status, by blood sample donation, and by availability of environmental home samples. Characteristics of persons willing to donate blood in an epidemiologic setting will aid in the interpretation of our study results, and facilitate comparisons with other investigations. Results on the primary, and other, hypotheses of the LIBCSP will follow in separate reports.

Background

The residents of Long Island have long been concerned about the potential adverse effects of environmental contaminants, including the pesticide DDT as described in Rachel Carson's Silent Spring [1]. In addition, the high incidence rates of breast cancer observed in this geographic region (117.8 per 100,000 in Nassau county and 113.6 in Suffolk county in 1992–1996) [2], which translates into some 2,000 newly diagnosed *in situ* and invasive breast cancer cases annually, have galvanized grass-root activism on the Island, particularly on issues relating breast cancer with environmental contaminants (Members of the Long Island Breast Cancer Network, 1994, personal communication). Linking the two issues, breast cancer risk and environmental pollution, seems to many lay people to be a logical association. In fact, it appears that many more members of the US general public, in contrast to those in the scientific community, associate environmental contaminants with breast cancer incidence. For example, respondents of a pilot survey [3] were asked to rate their confidence that a stated factor contributed to increasing incidence rates of breast cancer during the 1980s. A significantly higher proportion of the female and male lay sample of 1,019 Americans rated chemical use (56.3 and 47.3%, respectively), pesticide residues (34.5 and 28.3%), and electromagnetic fields (29.6 and 18.4%) as contributing to the increasing incidence as compared with the sample of 264 scientists (25.6, 14.1, and 5.1%, respectively) [3]. Thus, despite the perception shared by many taxpayers that some environmental pollutants contribute to breast cancer incidence, federal legislation may well have been necessary to stimulate systematic research efforts among the more skeptical scientific community. Specific breast cancer-related environmental concerns listed in the federal legislation include contaminated drinking water, indoor and out-

door air pollution, electromagnetic fields, pesticides and other toxic chemicals, and hazardous waste.

The dramatic variation in the incidence of breast cancer worldwide coupled with the observation that immigrants and their offspring have incidence rates that approach those of their adopted country, rather than their country of origin [4], strongly support a role for the environment in the etiology of breast cancer. These observations have led extensive research on some environmental factors, including dietary intake [5] and active [6, 7] and passive [8, 9] cigarette smoking, on which results are inconclusive. Other environmental factors which are supported by more conclusive epidemiologic research include alcohol consumption [10, 11] and ionizing radiation to the chest in moderate to high doses [12], both of which are considered important risk factors for breast cancer [13].

Endogenous estrogen and other hormones are proposed as plausible biologic pathways by which breast carcinogenesis is influenced by its many established risk factors [14, 15], including menstrual characteristics (early age at menarche and late age at menopause), reproductive patterns (late age at first birth, low parity or nulliparity, and little or no lactation), postmenopausal body size (increased weight, height, and body mass index (weight adjusted for height)), and high alcohol intake. Further, a number of factors suspected of affecting breast cancer risk (such as dietary patterns, physical activity, or cigarette smoking) may act through an estrogenic or anti-estrogenic pathway as well. Estrogen has primarily been described as a cancer promoter, as it causes an increase in cell turnover, which may disrupt the normal cellular process of DNA repair, thereby promoting any existing DNA damage. In contrast, some factors such as ionizing radiation may initiate breast carcinogenesis through direct induction of mutations in DNA.

More recently, researchers have focused on the breast carcinogenic potential of several ubiquitous environmental agents that received little scientific attention prior to the 1990s [12, 16–28]. Those that are included in the LIBCSP for evaluation in relation to breast cancer risk on Long Island appeared in the early to mid 1990s to be among the most biologically plausible environmental exposures that could be assessed with biomarkers that were feasible for use in a population-based epidemiologic study [29]. These include: persistent organochlorine compounds [17, 19], such as PCBs or DDT, and its metabolite DDE, which are hormonally active agents that were used as electrical insulators and pesticides, respectively, and whose manufacture has been banned in the US since the 1970s; and PAHs [17, 18], which are combustion products (e.g., present in cigarette smoke, grilled and smoked foods, and vehicle exhaust), are proven mammary carcinogens in rodents, and may have estrogenic or anti-estrogenic effects [30]. The primary exposure assessment methods used to evaluate the effect on breast cancer risk in the LIBCSP were blood levels of organochlorines, which can be interpreted as a life-time cumulation of exposure, and PAH-DNA adducts, which reflect more recent exposures and the body's metabolic response to the exposure. Environmental samples of water (for assays primarily of chlorinated and carbamate pesticides and metals), soil (PAH), and dust (organochlorines and PAH) were also collected primarily for use in the validation of geographical models that are being developed to estimate past exposure levels that may be specifically associated with residence on Long Island. Another environmental concern and focus of a companion project in the LIBCSP, is electromagnetic fields (EMF), for which there is some biological plausibility for a role in breast carcinogenesis. EMF may increase risk by influencing melatonin levels, and thus estrogen levels [16, 25].

Like other recent research efforts [31–37], the LIBCSP will also explore whether molecular variations, in the biology of the tumor of cases or in the estrogen or carcinogen metabolism among cases and controls, affect breast cancer risk or modify the relation between breast cancer risk and environmental exposures. One strategy employed in the LIBCSP is to determine whether breast cancer risk is influenced by the pathways by which an individual metabolizes estrogen, assessed through measurement of urinary estrogen metabolites. Specifically, the study will evaluate whether 16alpha-hydroxyestrone and 2-hydroxyestrone are associated with the risk of breast cancer, or whether they modify the association between breast cancer and environmental exposures. The metabolic pathways for each of these estrogen metabolites are mutually exclusive, however, with 16alpha-hydroxyestrone considered the more potent estrogen and possibly mutagenic [34]. Further, levels of 2-hydoroxyestrone are enhanced by exogenous factors that influence endogenous estrogen levels. Thus, the relative abundance of the two metabolites may be more important than the absolute level of either.

Materials and methods

The LIBCSP is a population-based case-control study of breast cancer that focuses on female residents of Nassau and Suffolk counties in Long Island, New York. To assess the primary exposures of interest, organochlorine compounds and PAH, as well as potential confounders, and effect modifiers, three assessment methods were employed: a comprehensive in-person questionnaire, collection of biologic samples (blood and urine), and environmental home sampling (dust, water, and soil). All assessments were obtained at the time of the personal interview, and each will be described in detail below. The study protocol was approved by the Institutional Review Board (IRB) of all participating institutions (the 14 collaborating scientific institutions and the additional 25 participating hospitals) and in accordance with an assurance filed with and approved by the US Department of Health and Human Services.

Study subject identification

Cases

Cases were women newly diagnosed with a first primary *in situ* or invasive breast cancer between August 1, 1996, and July 31, 1997, confirmed by the physician and the medical record, who were residents of either Nassau and Suffolk counties in New York at the time of their diagnosis, and who spoke English. (Over 97% of all residents in these two counties are English-speaking.)

The exposure assessment for the primary hypotheses of the LIBCSP are based on measurements in blood. Pilot data [38, 39] indicated that blood collection from cases after commencement of most therapies, with perhaps the exception of chemotherapy, would not influence the accuracy of the measures of organochlorine levels in blood. (It is also possible that biomarkers of exposure are affected by the disease itself, although for the two markers under study this concern has not been clarified.) To facilitate collection of blood samples from cases prior to chemotherapy, a 'super-rapid' identification network was established to ascertain potentially eligible case women with newly diagnosed breast cancer. Two to three times per week, study personnel contacted the pathology departments of all 28 hospitals on Long Island, as well as three large tertiary care hospitals in New York City. Seven institutions in the LI-NYC area with the largest numbers of newly diagnosed cases of breast cancer among LI women were contacted daily.

Physicians of potentially eligible case women were then contacted to confirm the subject's diagnosis and the date of her diagnosis, and for permission to contact the subject. To promote physician cooperation, prior to initiating subject identification, over 400 physicians on Long Island, who as general practitioners, internists, surgeons, or oncologists had the potential to diagnose or treat women with breast cancer, were mailed a packet describing the study and asking them to indicate their willingness to participate in the study in writing. No physician refused to participate. A total of 2,271 women were initially identified and considered as potentially eligible cases for the study. Of these, 2,030 were determined likely to be eligible by the physician and physician consent was obtained for 1,837 (90.5%); physician refusal for contact was generally based on a subject's poor health status (which was often due to age-related co-morbidity).

Controls

Control women were a sample of current residents of Nassau and Suffolk counties who spoke English, who did not have a personal history of breast cancer, and who were frequency matched to the expected distribution of case women by 5-year age group. Potentially eligible control women were identified by Waksberg's method of random digit dialing (RDD) [40] for those under 65 years of age, and by Health Care Finance Administration (HCFA) rosters for those 65 years of age and older. HCFA selection occurred twice during the 12-month identification period that coincided with the 12 months of case ascertainment. RDD selection began July 1, 1996, and continued in eight waves over the following 12 months. The response rate to the RDD telephone screener was 77.9%, which can only be directly multiplied to the control response rate for persons who are under age 65 years (and comprise 57.9% of the control group).

Subject recruitment

Potentially eligible controls and cases with physician consent were first contacted by the study team by overnight letter. Initial recruitment efforts that used overnight service generated undue concern among some potential control women who were 65 years of age and older; subsequently older potential controls were contacted by a regularly mailed letter. The recruitment letter explained the study purpose, the vari-

ous components of the study interview (the in-person questionnaire, the biologic specimen collection, and the home sampling component), that the study was completely voluntary, and that they could choose to participate in any or all of the components for which they were selected. The packet sent to potential participants also included a brightly colored flyer that answered commonly asked questions about the study. In addition, the packet included a form letter signed by the Long Island Breast Cancer Network members, a community-based organization, explaining that this unique study was a direct result of the community's activism and urging women to consider participation. To further enhance study recognition and credibility, community activists placed IRB-approved public service announcements in local newspapers and on television and radio, and circulated study newsletters and brochures in multiple settings such as libraries, physicians' offices, and health fairs. Study recruiters contacted the study subjects to answer questions and arrange for a study interview. For most women, recruiters contacted potential respondents by telephone; for some control women who were difficult to locate by telephone, potential respondents were approached in person. Written signed informed consent was obtained from participants prior to conducting any component of the interview.

Subject participation

The main questionnaire was completed by 1,508 (82.1%) of eligible case women ($n = 235$ with *in situ* and 1,273 with invasive breast cancer) and 1,556 (62.7%) of eligible control women (Table 1). The reasons for non-response to the interview among cases and controls included subject refusal ($n = 218$ (12.4%) and 573 (21.6%), respectively); too ill, cognitively impaired, or deceased (76 (4.1%) and 193 (7.8%)), and unlocatable, moved out of area, or other (26 (1.4%) and 195 (7.9%)). Study subjects ranged in age from 20 to 98 years and, as shown in Table 1, response to the interview varied with the age of the respondents, with 88.9% of cases and 76.1% of controls under age 65 years participating versus 71.6 and 43.3%, respectively, among those 65 and older. The average length of time between the referent date (date of diagnosis for cases and date of identification for controls) and interview date was 96 days for cases and 167 days for controls.

For case women, final study eligibility was based upon thorough review of the medical record (for an accurate date of diagnosis of a first primary), which could only be obtained with a signed medical record consent form. For controls, final eligibility (no history of prior breast cancer and a resident of Long Island at the reference date) could only be obtained after direct contact with the subject. Therefore, the interview response rates presented may be underestimates, as they include in the denominator 25 potentially eligible case women and 193 potentially eligible control women for whom study eligibility could not be determined because they were never located or had moved out of the area. If unlocatable women are omitted from the denominator, as suggested by Slattery (41) and others (42), then the overall interview response rates (also known as cooperation rates) are 83.2 and 68.0% for cases and controls, respectively, as shown in Table 1. The true response rates probably lie between the two sets of estimates.

Questionnaires

Prior to implementation in the field, the main questionnaire was pilot tested among residents of Long Island and developed with contributions from scientific and community collaborators. During field activities, the instrument, which averaged 101 min in duration, was administered by a trained interviewer in the respondent's home. Respondents were asked about their pregnancy history; occupational history; residential history in Nassau and Suffolk counties; their use of pesticides in and around their home or on a farm; electrical appliance use; lifetime history of consumption of smoked or grilled foods; medical history; family history of cancer; body size changes by decade of life; lifetime participation in recreational physical activities; active and passive cigarette smoking; use of alcohol by decade of life; menstrual history; use of exogenous hormones; and demographic characteristics.

After administration of the main questionnaire, study respondents were invited to self-administer a modification of the Block food frequency questionnaire, which has been previously validated (43–45). This instrument was completed by 98.2% ($n = 1{,}481$) of case and 97.6% ($n = 1{,}518$) of control participants; all participants self-completed the instrument in an average of 36 min immediately after the main questionnaire had been completed. Response for this component did not appear to vary with age of the respondent (Table 2).

As a quality control measure, a random 20% of all respondents were recontacted by telephone to in-

Table 1. Response, cooperation, and contact rates to the main questionnaire (Qx) by age at reference among case and control subjects, Long Island Breast Cancer Study Project, 1996–1997

Study subject status	All	Age at reference (in years)				
		<45	45–54	55–64	65–74	75+
Cases						
Sampled	2271	307	526	504	567	367
Ineligible	241	37	48	44	68	44
MD refusal	193	20	38	38	42	55
Eligible (A)	1837	250	440	422	457	268
Unlocatable or out of area (B)	25	4	2	8	5	6
Subject refusal	217	23	33	33	67	61
Too ill	31	1	1	3	8	18
Cognitively impaired	29	1	2	2	7	17
Deceased	16	0	2	4	3	7
Other	1	0	1	0	0	0
Partially completed main qx	10	0	2	1	3	4
Completed main qx (C)	1508	221	397	371	364	155
Contact rate = (A−B)/A = D	98.6%	98.4%	99.5%	98.1%	98.9%	97.8%
Cooperation rate = C/(A−B) = E	83.2%	89.8%	90.6%	89.6%	80.5%	59.2%
Response rate = D*E = C/A	82.1%	88.4%	90.2%	87.9%	79.6%	57.8%
Controls						
Sampled	2714	411	575	587	661	480
Ineligible	233	19	35	50	72	57
Eligible (A)	2481	392	540	537	589	423
Unlocatable or out of area (B)	193	17	21	24	69	62
Subject refusal	530	70	98	89	161	112
Too ill	101	3	4	10	34	50
Cognitively impaired	67	2	0	1	11	53
Deceased	25	0	0	4	5	16
Other	2	1	1	0	0	0
Partially completed main qx	7	1	3	2	1	0
Completed main qx (C)	1556	298	413	407	308	130
Contact rate = (A−B)/A = D	92.2%	95.7%	96.1%	95.5%	88.3%	85.3%
Cooperation rate = C/(A−B) = E	68.0%	79.5%	79.6%	79.3%	59.2%	36.0%
Response rate = D*E = C/A	62.7%	76.0%	76.5%	75.8%	52.3%	30.7%

sure that the interview actually occurred, verify the length of the interview, and to briefly re-interview the subjects. Completed questionnaires were shipped to Westat, Inc., Bethesda, MD, for data verification, coding, data entry, and initial range and logic checks.

Biologic sample collection

Study interviewers, who were certified phlebotomists or nurses, obtained biologic samples; 73.1% ($n = 1{,}102$) and 73.3% ($n = 1{,}141$) of case and control respondents who had completed the main interview, respectively, donated a nonfasting 40 ml blood sample, and 93.0% ($n = 1{,}403$) and 83.3% ($n = 1{,}296$) donated a 25 ml spot urine sample at the time of the interview. Donation of biologic samples varied with age, with a lower proportion of older control women donating blood and urine (Table 2). The proportion of case respondents with biologic specimens collected prior to chemotherapy was 77.2% (851/1102) for blood and 75.1% (1053/1403) for urine. To further investigate whether samples collected after chemotherapy differed from samples collected prior to chemotherapy [38], 190 case women for whom prechemotherapy samples had been collected were selected for recontact at a later date to obtain samples after commencement of chemotherapy. Of these, 148 (77.9%) cases donated

Table 2. Response rates by study interview component and age at reference among respondents, Long Island Breast Cancer Study Project, 1996–1997

Study interview component		All	Age at reference				
			<45 yrs	45–54 yrs	55–64 yrs	65–74 yrs	75+ yrs
Cases							
Questionnaires	Main	1508	221	397	371	364	155
	%	100%	100%	100%	100%	100%	100%
	FFQ	1481	213	389	371	357	151
	%	98.2%	96.4%	98.0%	100.0%	98.1%	97.4%
Biologic Specimens	Blood	1102	163	292	268	268	111
	%	73.1%	73.8%	73.6%	72.2%	73.6%	71.6%
	Urine	1403	209	370	343	337	144
	%	93.0%	94.6%	93.2%	92.5%	92.6%	92.9%
Environmental	Dust	320	15	86	99	97	23
Home samples	%	83.6%	83.3%	85.1%	90.0%	81.5%	65.7%
	Soil	360	18	98	104	111	29
	%	93.5%	100.0%	95.1%	94.5%	93.3%	82.9%
	Water	363	17	98	106	112	30
	%	94.3%	94.4%	96.1%	96.4%	93.3%	85.7%
Medical records	Signed	1473	213	383	365	357	155
	%	97.7%	96.4%	96.5%	98.4%	98.1%	100.0%
	Retrieved	1402	206	361	344	343	147
	%	95.2%	96.7%	94.3%	94.2%	96.1%	94.8%
Controls							
Questionnaires	Main	1556	298	413	407	308	130
	%	100%	100%	100%	100%	100%	100%
	FFQ	1518	292	405	401	300	120
	%	97.6%	98.0%	98.1%	98.5%	97.4%	92.3%
Biologic specimens	Blood	1141	229	318	312	206	76
	%	73.3%	76.8%	77.0%	76.7%	66.9%	58.5%
	Urine	1296	254	370	354	231	87
	%	83.3%	85.2%	89.6%	87.0%	75.0%	66.9%
Environmental	Dust	356	15	88	133	91	29
Home samples	%	83.0%	65.2%	77.9%	87.5%	85.8%	82.9%
	Soil	360	21	99	142	92	31
	%	93.5%	91.3%	87.6%	93.4%	86.8%	88.6%
	Water	363	20	106	145	100	32
	%	94.3%	87.0%	93.8%	95.4%	94.3%	91.4%

a postchemotherapy blood sample and 155 (81.6%) donated a postchemotherapy urine sample.

At the time of the blood and urine collection, donors were asked to self-complete a specimen checklist which inquired about the date of the subject's last menstrual period (if she was still menstruating); selected foods consumed and medications used, and cigarettes smoked over the past several days; intake of PAH-containing foods over the past 4 weeks, and any breast surgeries or treatment undergone in the past 6 months. With the blood (which was collected in EDTA-treated, lavender-top tubes) at room temperature and the urine (with vitamin C added to about one-half the volume of each donation) on ice, the biologic samples were shipped overnight to a single laboratory at Columbia University. Biologic specimen

collection was avoided on days and times when overnight services were not available. Thus, processing and aliquoting of the biologic samples occurred for most subjects within 24 h of collection. Aliquots of plasma, red blood cells, mononuclear cells, and granulocytes from 40 ml of blood and aliquots with and without vitamin C from 25 ml of urine are stored at −80 degrees centigrade with bar-code labels, which are preprinted with the subjects' randomly selected study identification number. All lab personnel are blinded to the case-control status of the specimens.

Environmental home sampling

An invitation to participate in the environmental home sampling component was extended to all long-term residents who self-identified themselves as African-American or black, and a random sample of long-term residents who self-identified as white. Long-term residence was defined as living in the current home for 15 years or longer. About 58% of all participants were potentially eligible for this component of the study; of these, a random sample of about 36% were targeted for sampling. Environmental home samples were obtained directly after the completion of the main questionnaire and the food frequency questionnaire, and the donation of blood and urine. The samples were collected by the interviewer and included: carpet dust (83.6% (320/383) and 83.0% (356/429) of selected long-term case and control residents, respectively); tap water (94.3% (363/385) and 93.9% (403/429)), and soil outside the home (93.5% (360/385) and 89.7% (356/429)). The proportion of the selected case and control respondents who refused to permit collection of the home samples was modest (3.4 and 5.9%, respectively, for dust; 3.9 and 4.0% for water; and 3.5 and 3.5% for soil). Response to the environmental home sampling component did not appear to vary substantially with age among cases and controls, although soil samples were obtained for a slightly lower proportion of case women 75 years of age and older (Table 2).

Using high-volume small surface samplers ((HVS3), CS_3, Inc., Bend, OR), dust was collected from the carpet located in the room of the home in which the respondent reported spending the most time. The carpet area to be vacuumed was measured and recorded along with the age and other characteristics of the rug. After vacuuming, the Teflon collection bottles with the collected dust were shipped by overnight mail to Southwest Research Institute, San Antonio, TX; sieved (<150 micron) aliquots were stored at −12 degrees centigrade. The 79 homes (44 cases, 35 controls) from which sample collection was not feasible (9.7%) lacked a carpet, or sufficient amount of dust required for the assays (0.1 gm) could not be obtained.

Water samples were collected from the kitchen tap in both glass and plastic bottles using a standard protocol. Along with duplicates and quality control samples, all water samples were delivered on ice by the interviewer to one of two centralized locations on Long Island, where they were kept refrigerated. Personnel from the Suffolk County Department of Health, Hauppauge, NY, retrieved the refrigerated samples several times per week. Water assays were completed at the Suffolk County Department of Health within seven 7 of sample collection.

Soil was collected according to a protocol established in collaboration with members of the study's external advisory committee based on unpublished results from a pilot study conducted by members of the study team. With a stainless steel soil sampler (Oakfield 12″ Tube Kit (Model G), Forrestry Suppliers, Inc., Jackson, MS), samples were obtained from four locations in each of the participants' yards: center of yard closest to the road; center of yard farthest from the road; foundation by most frequently used entry; and foundation of next most frequently used entry. Quality control samples and soil samples were placed in plastic bags, individually labeled with the location from which the sample was obtained, and shipped by overnight mail to the American Health Foundation, Valhalla, NY, and stored at −20 degrees centigrade. Failure to collect soil was usually due to lack of a yard rather than weather conditions, because the 1996–1997 winter season on Long Island was unusually mild.

All environmental home samples were labeled by the interviewer with a bar code label preprinted with the subjects' randomly selected study identification number. All laboratory personnel are blinded to the case-control status of the environmental home samples.

Other field activities

Cases were asked to sign a medical record release form that would permit determination of final study eligibility as well as the clinical characteristics of her breast cancer diagnosis (e.g., stage of disease, hormone receptor status). Signed medical record release forms were obtained for 1,473 (97.7%) case respondents, and

records were successfully located and abstracted for 1,402 (95.2%). Because a goal of the study was to collect blood samples prior to chemotherapy [38, 39], most case women were interviewed prior to the completion of their course of treatment; thus, complete treatment information is not available on the majority of case subjects.

After completing the interview, subjects were informed that they might be contacted in the near future by researchers at the State University of New York at Stony Brook about the opportunity to participate in a companion study of electromagnetic fields and breast cancer risk. An informational brochure was left with the study subject, along with a telephone number to call with any questions.

Professional and community collaboration

Broad scientific expertise in epidemiology, clinical care, toxicology, environmental assessment, carcinogenesis, and other disciplines was drawn from local, as well as nationally-based, institutions, to adequately address the study aims of this federally mandated project. In addition, this study has had the benefit of close working relations with community activists in developing the study hypotheses and design, and during pilot-testing and field activities. Lay persons were often able to provide a fresh outlook to our plans and procedures, but at no time were they permitted access to confidential subject information. Scientific oversight was provided by two external advisory committees that included both scientists and lay persons. The committees formally convened in-person annually, and informally by telephone more frequently.

Statistical analyses

For the results reported here, chi-square statistics were calculated [46]. Unconditional logistic regression [47] was used to estimate the odds ratios for donating a blood sample to the study in relation to known and suspected risk factors for breast cancer including age (at reference = date of diagnosis for cases and identification for controls), case-control status, race (self-identified as white/African-American or black/or other), ethnicity (Hispanic or Latino/not Hispanic or Latino), education (less than high school/high school graduate/some college/college graduate/post college), marital status (ever/never), religion (in which the respondent was raised), income (self-reported), age at menarche (<12 years/12 years/13 years/14+ years), parity (nulliparous/parous and number of children), age at first birth (<22 years/22–24 years/25–27 years/28+ years), lactation (<2 months/2–5 months/6–13 months/14+ months), menopausal status (pre-/postmenopausal), cigarette smoking (never/current (within 12 months of reference date)/quit more than 12 months before reference date), alcohol use (ever (at least once a month for 6 months or more)/never), body mass index (BMI)) weight in kilograms/height in meters squared) at age 20 years and at reference, family history of breast cancer (in mother or sister), oral contraceptive use (ever/never), and hormone replacement (ever/never). To determine the best predictors of donating blood, a best-fitting multiple logistic regression model was identified using backwards selection, where covariates were systematically removed from the model by comparing the log likelihood ratios derived from a model with and without the covariate, using a nominal significance criteria of 10%.

Menopausal status was defined using information provided by the subject on her date of last menstrual period, prior surgical information on hysterectomy or oophorectomies, her cigarette smoking status, and use of hormone replacement. A subject was defined as postmenopausal if her last menstrual period was more than 6 months before the reference date or if she had both ovaries removed prior to reference date. If a subject was taking hormone replacement therapy or had a hysterectomy without removal of both ovaries, her menopausal status was initially classified as unknown (11.81% of subjects). To reduce the number of subjects with unknown menopausal status, we utilized information about the subject's reference age. That is, any smoker with unknown menopausal status was categorized as postmenopausal if her age at reference was ≥54.8 years (90% percentile for natural menopause among smoking controls), and any nonsmoker with unknown menopausal status was categorized as postmenopausal if her age at reference was ≥55.4 years (90% percentile for natural menopause among nonsmoking controls). Subjects whose final classification of menopausal status was missing was 3.04%.

Results

Many established risk factors for breast cancer that have been identified in previous studies [13] were confirmed to affect risk among women of all ages on Long Island (Table 3). These included parity (age-

Table 3. Age-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer in relation to known and suspected risk factors, Long Island Breast Cancer Study Project, 1996–1997

Factor		Cases ($n = 1{,}508$)		Controls ($n = 1{,}556$)		Age-adjusted OR (95% CI)
		No.	%	No.	%	
Demographic factors						
Age at reference	<35 years	39	2.6	45	2.9	
	35–44 years	181	12.0	245	15.7	
	45–54 years	397	26.3	423	27.2	
	55–64 years	372	24.7	403	25.9	
	65–74 years	365	24.2	310	19.9	
	75–84 years	134	8.9	112	7.2	
	85+ years	20	1.3	18	1.2	
	Missing	0		0		
Race	White	1411	93.8	1429	91.8	1.00
	Black	69	4.6	85	5.5	0.85 (0.61, 1.18)
	Other	25	1.7	42	2.7	0.64 (0.39, 1.05)
	Missing	3		0		
Latina or hispanic	No	1448	96.2	1487	96.0	1.00
Ethnicity	Yes	57	3.8	62	4.0	0.99 (0.69, 1.43)
	Missing	3		7		
Education	<High school	183	12.2	150	9.7	1.00
	High school graduate	538	35.8	526	33.9	0.89 (0.70, 1.15)
	Some college	360	24.0	415	26.7	0.78 (0.60, 1.03)
	College graduate	191	12.7	236	15.2	0.75 (0.56, 1.02)
	Post college	230	15.3	225	14.5	0.94 (0.69, 1.26)
	Missing	6		4		
Marital status	Ever married	1443	95.8	1486	95.5	1.00
	Never married	64	4.2	70	4.5	1.00 (0.70, 1.42)
	Missing	1		0		
Religion	Catholic	859	57.1	916	59.0	1.00
	Protestant	360	23.9	373	24.0	1.02 (0.86, 1.21)
	Jewish	259	17.2	239	15.4	1.16 (0.95, 1.42)
	None	14	0.9	12	0.8	1.28 (0.59, 2.80)
	Other	13	0.9	13	0.8	1.13 (0.52, 2.45)
	Missing	3		3		
Income	<$15,000	115	8.9	84	6.4	1.00
	$15,000–$19,999	70	5.4	83	6.3	0.60 (0.39, 0.93)
	$20,000–$24,999	78	6.0	98	7.5	0.59 (0.39, 0.90)
	$25,000–$34,999	176	13.6	139	10.6	1.05 (0.72, 1.52)
	$35,000–$49,999	192	14.8	203	15.5	0.82 (0.57, 1.17)
	$50,000–$69,999	214	16.5	245	18.7	0.81 (0.56, 1.16)
	$70,000–$89,999	169	21.7	177	13.5	0.90 (0.62, 1.32)
	$90,000+	281	13.1	281	21.5	0.96 (0.67, 1.38)
	Missing	213		246		

Table 3. (*continued*)

Factor		Cases ($n = 1{,}508$)		Controls ($n = 1{,}556$)		Age-adjusted OR (95% CI)
		No.	%	No.	%	
Reproductive factors						
Age at menarche	<12 years	391	26.1	437	28.2	1.00
	12 years	418	28.0	400	25.9	1.16 (0.95, 1.41)
	13 years	379	25.4	359	23.2	1.17 (0.96, 1.43)
	14+ years	307	20.5	351	22.7	0.94 (0.7, 1.16)
	Missing	13		9		
Parity status	Nulliparous	198	13.1	171	11.0	1.00
	Parous	1310	86.9	1385	89.0	0.78 (0.63, 0.98)
	1 child	166	12.7	148	10.7	0.97 (0.72, 1.32)
	2 children	508	38.8	518	37.4	0.83 (0.65, 1.05)
	3 children	358	27.3	379	27.4	0.78 (0.60, 1.00)
	4+ children	278	21.2	340	24.5	0.63 (0.48, 0.82)
	Missing	0		0		
Age at first birth	<22 years	305	23.3	358	25.9	1.00
(among parous)	22–24 years	375	28.6	417	30.1	1.03 (0.84, 1.27)
	25–27 years	272	20.8	297	21.4	1.06 (0.85, 1.33)
	28+ years	357	27.3	313	22.6	1.36 (1.10, 1.69)
	Missing	1		0		
Lactation	Never lactated	841	64.2	840	60.7	1.00
(among parous)	<2 months	118	9.0	124	9.0	0.95 (0.72, 1.24)
	2–5 months	103	7.9	128	9.2	0.82 (0.62, 1.09)
	6–13 months	146	11.1	140	10.1	1.06 (0.82, 1.36)
	14+ months	102	7.8	153	11.0	0.70 (0.54, 0.92)
	Missing	0		0		
Lifestyle factors						
Body Mass Index	<22.3	341	22.9	382	25.0	1.00
at reference	22.3–25.1	367	24.6	391	25.6	1.02 (0.84, 1.26)
	25.2–29.2	391	26.2	376	24.6	1.10 (0.90, 1.36)
	>29.2	392	26.3	379	24.8	1.10 (0.90, 1.35)
	Missing	17		28		
Body Mass Index	<19.0	371	25.1	373	24.4	1.00
at age 20	19.0–20.2	346	23.4	364	23.8	0.95 (0.77, 1.16)
	20.3-22.2	442	29.8	399	26.0	1.10 (0.91, 1.34)
	>22.2	321	21.7	396	25.8	0.82 (0.67, 1.00)
	Missing	28		24		
Alcohol use	Never	588	39.0	593	38.1	1.00
	Ever	920	61.0	963	61.9	1.00 (0.86, 1.15)
	Missing	0		0		
Cigarette	Never smoked	675	44.8	698	45.0	1.00
smoking	Former smoker	543	36.0	564	36.3	1.00 (0.85, 1.17)
	Current smoker	290	19.2	291	18.7	1.09 (0.90, 1.32)
	Missing	0		3		

Table 3. (*continued*)

Factor		Cases ($n = 1{,}508$)		Controls ($n = 1{,}556$)		Age-adjusted OR (95% CI)
		No.	%	No.	%	
Medical factors						
Family history of breast cancer	No first degree	1166	79.8	1321	87.0	1.00
	First degree	295	19.2	197	13.0	1.66 (1.36, 2.02)
	Missing	47		38		
Use of oral contraceptives	Never	848	56.3	840	54.0	1.00
	Ever	657	43.7	715	46.0	1.06 (0.90, 1.24)
	Missing	3		1		
Use of hormone replacement	Never	1096	72.9	1159	74.5	1.00
	Ever	408	27.1	396	25.5	1.06 (0.90, 1.25)
	Missing	4		1		

adjusted OR = 0.63 for 4+ children v.s. none, 95% CI = 0.48, 0.82), breastfeeding (OR = 0.70 for 14 months v.s. none, 95% CI = 0.53, 0.89), age at first birth (OR = 1.36 for 28+years v.s. <22 years, 95% CI = 1.10, 1.69), and family history of breast cancer in mother or sister (OR = 1.66 v.s. none, 95% CI = 1.36, 2.02). In this initial evaluation, factors found not to influence risk in this study included education, age at menarche, weight adjusted for height, and alcohol use.

Using blood donation as the outcome variable, multivariate models were constructed to identify factors associated with the likelihood of donating blood (expressed as the odds ratio for blood donation) among interviewed subjects with adjustments made for the potential confounders including case-control status, as described in the methods. Factors found to be associated with a decreased probability of blood donation among case and control respondents were past smoking (multivariate-adjusted OR = 0.75 v.s. never, 95% CI = 0.61, 0.92) and increasing age (OR = 0.99 per year, 955 CI = 0.98, 1.00) (Table 4). Factors that were associated with an increased probability of blood donation (Table 4) included white or other race (OR = 1.65 and 1.74, respectively, v.s. black, 95% CI = 1.09, 2.46 and 085, 3.55), ever use of alcohol (OR = 1.28, 95% CI = 1.06, 1.55), ever use of hormone replacement (OR = 1.63 v.s. never, 95% CI = 1.30, 2.03), breast fed for six or more months (OR = 1.47 v.s. never, 95% CI = 1.14, 1.90), and ever had a mammogram (OR = 1.51 v.s. never, 95% CI = 1.14, 2.00). Case-control status was not a predictor of blood donation among interview respondents.

As anticipated, respondents who reported living in their current home for 15 years or longer differed on a number of breast cancer risk factors from those who were not long-term residents (Table 5). Long-term residents as compared with other LIBCSP participants were significantly more likely to be older ($p = 0.001$), white ($p = 0.001$), less educated ($p = 0.001$), postmenopausal ($p = 0.001$), older at menopause ($p = 0.007$), and never or past smokers ($p = 0.001$); and to have lower incomes ($p = 0.001$), more children ($p = 0.001$), never breastfed ($p = 0.001$), a higher body mass index ($p = 0.001$), ever drank alcohol ($p = 0.001$), never used oral contraceptives ($p = 0.001$), and ever used hormone replacement ($p = 0.001$); and to have ever had a mammogram ($p = 0.001$).

The random sample of 589 respondents for whom a complete set of environmental home samples (dust, water, and soil) were obtained did not differ from all long-term residents on the overwhelming majority of breast cancer risk factors assessed (Table 6). The exception was body size; those with dust, water, and soil samples available reported a lower BMI at age 20 ($p = 0.03$) than other long-term residents. African-Americans comprise a larger proportion of those for whom environmental home samples were collected, as compared with those for whom samples were not obtained, because all black respondents were invited to participate in this component, whereas only a random sample of white respondents were invited.

Table 4. Multivariate-adjusted* odds ratios (OR)** and 95% confidence intervals (CI) for the phlebotomy component in relation to known and suspected risk factors for breast cancer among case and control respondents, Long Island Breast Cancer Study Project, 1996–1997

Factor		Multivariate-adjusted OR	95% CI
Age at reference	(Per year)	0.99	0.98, 1.00
Race	African-American	1.00	
	White	1.65	1.10, 2.48
	Other	1.74	0.85, 3.55
Cigarette smoking	Never smoked	1.00	
	Former smoker	0.75	0.61, 0.92
	Current smoker	0.89	0.69, 1.15
Alcohol use	Never	1.00	
	Ever	1.28	1.06, 1.55
Use of oral	Never	1.00	
contraceptives	Ever	1.21	0.99, 1.49
Use of hormone	Never	1.00	
replacement	Ever	1.63	1.30, 2.03
Lactation	None	1.00	
	<6 months	1.02	0.79, 1.32
	6+ months	1.47	1.14, 1.90
Mammography	Never	1.00	
	Ever	1.51	1.14, 2.00

*Odds ratios adjusted for all other factors listed in the table.
**Odds ratios greater than 1.0 indicate that the factor is associated with a greater probability of blood donation; less than 1.0 indicates the factor is associated with a lower probability of blood donation.

Discussion

The Long Island Breast Cancer Study Project is a large epidemiologic study designed to evaluate whether several environmental factors are associated with elevated risk of breast cancer. The study is complex and ambitious on a number of levels including efforts to involve community members in the design and conduct of various components of the study; a multi-disciplinary, multi-institutional scientific collaboration; oversight from two external advisory committees composed of both scientific and community leaders; implementation of a super-rapid reporting method in a geographic location that has had limited experience with population-based studies of cancer; inclusion of women of all ages; utilization of multiple enhancements designed to boost study participation (including contacting physicians prior to the inception of field operations, first contacting most subjects by overnight service, including in the recruitment package a form letter from local breast cancer activists that explained the unique origins of the study, employment of skilled subject recruiters, and an in-person recruitment strategy, where possible); multiple methods employed to assess environmental exposures; and establishment of a biologic specimen bank, that includes blood (including DNA) and urine, and an environmental sample bank of dust and soil. Nevertheless, a number of important concerns must be considered in interpreting any results emanating from this study or related projects.

Subject participation

Despite our extensive identification and recruitment efforts, response rates were lower among controls than in cases, which was driven by poor participation among elderly control women. Lower response among elderly women have been previously reported in case-control studies of breast cancer [42] and other diseases, such as hip fractures [48]. This project is unique among epidemiologic studies of breast

Table 5. Percent distribution of known and suspected risk factors for breast cancer among case and control respondents by residency status, Long Island Breast Cancer Study Project, 1996–1997

Factor		Long-term residents (%) ($n = 1{,}769$)	Non-long-term residents (%) ($n = 1{,}295$)	Chi-square P-value
Demographic factors				
Age at reference	<35 years	0.6	5.6	0.0001
	35–44 years	4.1	27.2	
	45–54 years	26.2	27.6	
	55–64 years	30.9	17.6	
	65–74 years	27.4	14.7	
	75–84 years	9.6	5.9	
	85+ years	1.2	1.4	
Race	White	94.7	90.2	0.0001
	Black/African-American	3.6	7.0	
	Other	1.8	2.8	
Education	Less than high school	10.8	11.0	0.0001
	High school graduate	38.4	30.0	
	Some college	25.1	25.8	
	College graduate	11.7	17.1	
	Post college	14.0	16.1	
Religion	None	1.0	0.6	0.034
	Protestant	23.4	24.7	
	Catholic	58.3	57.7	
	Jewish	16.8	15.6	
	Other	0.4	1.4	
Income	<$15,000	5.9	10.0	0.0001
	$15,000–$19,999	6.3	5.3	
	$20,000–$24,999	7.5	5.8	
	$25,000–$34,999	12.6	11.5	
	$35,000–$49,999	16.5	13.4	
	$50,000–$69,999	18.5	16.5	
	$70,000–$89,999	13.0	13.6	
	$90,000+	19.8	23.9	
Reproductive factors				
Age at menarche	<12 years	28.1	27.2	0.31
	12 years	26.7	26.7	
	13 years	23.0	25.6	
	14+ years	22.2	20.5	
Parity status	Nulliparous	9.9	15.0	0.001
	Parous	90.1	85.0	
	1 child	9.4	15.0	0.0001
	2 children	37.3	39.2	
	3 children	29.0	25.0	
	4+ children	24.4	20.8	

Table 5. (*continued*)

Factor		Long-term residents (%) ($n = 1{,}769$)	Non-long-term residents (%) ($n = 1{,}295$)	Chi-square P-value
Age at first birth (among parous)	<22 years	23.0	27.1	0.0001
	22–24 years	22.8	17.3	
	25–27 years	26.5	19.1	
	28+ years	27.7	36.6	
Lactation (among parous)	Never lactated	67.8	54.6	0.0001
	<2 months	9.3	8.5	
	2–5 months	6.5	11.6	
	6–13 months	9.8	11.8	
	14+ months	6.7	13.5	
Menopausal status	Premenopausal	20.2	50.1	0.0001
	Postmenopausal	79.8	49.9	
Lifestyle factors				
Body Mass Index at reference	<22.3	20.8	28.2	0.0001
	22.3–25.1	25.1	25.1	
	25.2–29.2	26.5	23.9	
	>29.2	27.6	22.8	
Body Mass Index at age 20	<19.0	23.6	26.3	0.12
	19.0–20.2	24.5	22.2	
	20.3–22.2	28.8	26.7	
	>22.2	23.1	24.8	
Alcohol use	Never	41.9	34.0	0.0001
	Ever	58.1	66.0	
Cigarette smoking	Never smoked	45.4	44.1	0.0001
	Former smoker	38.6	32.9	
	Current smoker	16.0	23.0	
Medical factors				
Family History of Breast Cancer	No first degree	83.8	83.0	0.56
	First degree	16.2	17.0	
Use of oral contraceptives	Never	60.7	47.6	0.0001
	Ever	39.3	52.4	
Use of hormone replacement	Never	70.6	78.0	0.0001
	Ever	29.4	22.0	
Mammography Within last 5 years	None	11.5	17.5	0.0001
	1+	88.5	82.5	

cancer in that there was no upper or lower age limit for subject eligibility. Comorbidity among the elderly and the protective efforts of the subjects' families prevented full study participation among these older women. Thus, if the older respondents somehow differ systematically from older non-respondents, results based on this segment of LIBCSP data should be interpreted cautiously and may not be generalizable to all older women. Nevertheless, the LIBCSP will be among the few studies that can provide extensive data on the epidemiology of breast cancer among women 65 years of age and over, who comprise over a third of all those newly diagnosed with the disease.

Table 6. Percent distribution of known and suspected risk factors for breast cancer among case and control respondents who are long-term residents by completion of environmental home sampling component, Long Island Breast Cancer Study Project, 1996–1997

Factor		Complete set of water/dust/soil (%) ($n = 589$)	No complete set of water/dust/soil (%) ($n = 1{,}180$)	Chi-square P-value
Demographic factors				
Age at Reference	<35 years	0.5	0.6	0.23
	35–44 years	2.6	3.2	
	45–54 years	22.7	24.1	
	55–64 years	34.5	30.8	
	65–74 years	30.7	26.9	
	75–84 years	8.7	12.4	
	85+ years	0.4	2.0	
Race	White	92.0	96.0	0.0001
	Black/African-American	6.6	2.0	
	Other	1.4	2.0	
Education	Less than high school	8.2	12.1	0.14
	High school graduate	40.7	37.2	
	Some college	25.0	25.1	
	College graduate	11.6	11.7	
	Post college	14.5	13.8	
Religion	None	1.4	0.9	0.61
	Protestant	24.8	22.7	
	Catholic	56.0	59.5	
	Jewish	17.3	16.5	
	Other	0.5	0.4	
Income	<$15,000	4.2	6.7	0.14
	$15,000–$19,999	6.4	6.2	
	$20,000–$24,999	7.6	7.4	
	$25,000–$34,999	14.2	11.7	
	$35,000–$49,999	18.8	15.4	
	$50,000–$69,999	16.8	19.4	
	$70,000–$89,999	11.2	19.0	
	$90,000+	20.8	19.2	
Reproductive factors				
Age at menarche	<12 years	27.9	27.4	0.86
	12 years	25.7	27.5	
	13 years	23.3	23.1	
	14+ years	23.1	22.0	
Parity status	Nulliparous	9.2	10.3	0.47
	Parous	90.8	89.7	
	1 child	9.2	9.2	0.31
	2 children	35.7	38.0	
	3 children	28.4	29.3	
	4+ children	26.1	23.5	

Table 6. (*continued*)

Factor		Complete set of water/dust/soil (%) ($n = 589$)	No complete set of water/dust/soil (%) ($n = 1{,}180$)	Chi-square P-value
Age at first birth (among parous)	<22 years	24.7	22.1	0.64
	22–24 years	23.0	22.7	
	25–27 years	26.0	26.8	
	28+ years	26.3	28.4	
Lactation (among parous)	Never lactated	69.4	67.0	0.41
	<2 months	8.0	10.0	
	2–5 months	7.1	6.1	
	6–13 months	9.4	10.0	
	14+ months	6.2	6.9	
Menopausal status	Premenopausal	19.8	20.4	0.74
	Postmenopausal	80.2	79.6	
Lifestyle factors				
Body Mass Index at reference	<22.3	20.9	20.8	0.25
	22.3–25.1	26.7	24.3	
	25.2–29.2	23.6	28.0	
	>29.2	28.8	26.9	
Body Mass Index at Age 20	<19.0	26.4	22.1	0.028
	19.0–20.2	25.5	24.0	
	20.3–22.2	28.9	28.8	
	>22.2	19.2	25.1	
Alcohol use	Never	44.6	40.7	0.14
	Ever	55.4	59.3	
Cigarette smoking	Never smoked	45.2	45.5	0.34
	Former smoker	40.4	37.7	
	Current smoker	14.4	16.8	
Medical factors				
Family history of breast cancer	No first degree	84.4	84.0	0.74
	First degree	16.6	16.0	
Use of oral contraceptives	Never	60.5	60.8	0.87
	Ever	39.5	39.2	
Use of hormone replacement	Never	69.1	71.4	0.32
	Ever	30.9	28.6	
Mammography Within last 5 years	None	9.0	12.8	0.064
	1+	91.0	87.2	

Another contribution to the lower participation response rates observed among controls is the lower screener rate obtained during RDD, which affects results based on women under age 65 years. RDD has been an effective and common technique to identify a pool of potentially eligible population-based controls since the technique was introduced by Waksberg [40] in the late 1970s. Olson and colleagues [49] observed few differences between a group of hypothetical controls identified through RDD versus those identified through a household census of the same community, although the RDD screener rate in the Olson study

was higher than the rate reported here. With the increasing use of telephone message machines and caller ID, particularly in high-income areas such as Long Island where residents are subjected to extensive telephone marketing, the RDD technique may be less effective.

It is reassuring to note that in general we observed in the LIBCSP many of the established risk factors for breast cancer noted in other epidemiologic studies [13], including family history of breast cancer and reproductive history. For those risk factors for which little relation was observed among women of all ages in our sample, future more detailed analyses may help to clarify these apparent inconsistences with previous studies. For example, risk of breast cancer is likely to vary with age or menopausal status (e.g., important when examining body mass index). Other possibilities to consider include variations in the patterns of use (relevant, e.g., when examining use of alcohol, tobacco, or hormones); or variations in molecular markers. Alternatively, it may also indicate that other non-traditional factors, such as environmental exposures, play a role in breast cancer risk in this Long Island population.

There was a difference between cases and controls in the time lag between the reference date and the interview date, with cases interviewed on average within about 3 months of diagnosis and the controls within about $5\frac{1}{2}$ months of identification. This is a common feature of case-control studies when cases are deliberately recruited more quickly than controls, particularly when survival rates for the disease under study are low. We employed this strategy for another reason, namely to obtain prechemotherapy blood samples. The impact of this recruitment strategy on recall has not been well studied. For most factors, cases and controls are asked to recall lifetime or historical exposures that occurred prior to the reference date, and in this scenario a difference of 2–3 months has been presumed to make little difference when recalling events that occurred long ago. However, a few-month differential could possibly affect recall of those exposures that occur at the reference date. However, our pilot data [39] indicate that serial blood measures of organochlorines taken several months apart are very highly correlated among women without breast cancer.

Blood donation

To address the primary hypotheses of the LIBCSP, blood sample collection to assess the exposures of interest was a key component of the study. Although response rates were lower among controls than anticipated (to the telephone screener among those under 65 and to the interview among those 65 years and older), among respondents who completed the interview there was no case-control differential with nearly three-quarters of case and control participants donating a blood sample. Although there are some differences between blood donors and non-donors, the proportion of eligible subjects who donated blood is comparable to other population-based studies with a phlebotomy component [50]. Thus, LIBCSP study results are likely to be as representative of the general population as those from other major population-based studies of breast cancer.

Environmental samples

Long-term residents differed from other LIBCSP respondents on a number of breast cancer risk factors as would be expected, given that length of residence is often associated with age and other demographic and socioeconomic characteristics. However, the random sample with a complete set of dust, water, and soil samples available did not differ from other long-term residents. Thus, the results based on these measurements should be applicable to all adult female long-term residents on Long Island.

Future directions

A number of members from the Long Island lay community are concerned about the potential role in breast cancer development of chemicals other than those under study in the LIBCSP. Thus, the bank of stored sera and urine may prove to be a valuable resource in the future for other biomarker studies with environmental exposure hypotheses.

Several LIBCSP investigators have collaborated on a component study that demonstrates the feasibility of using geographic modeling to estimate a subject's past exposures (e.g., to PAH) based on a mathematical model that incorporates ecologic measures, dispersal mechanisms, and the subject's self-reported history of residential addresses [51]. These techniques could be useful for estimating past exposures to agents for which feasible biomarkers of long-term exposures have yet to be developed.

Current research activities of many of the LIBCSP collaborators are focused on the molecular epidemiology of breast cancer and potential gene-environment interactions. These include examination of oncogenes,

estrogen and carcinogen metabolizing enzymes, polymorphisms associated with oxidative stress and DNA repair, and other molecular markers, and how they may affect breast cancer risk, or whether they modify the risk associated with environmental exposures and breast cancer among women on Long Island. Examination of these markers in an epidemiologic context could help to clarify the association between an environmental agent and breast cancer risk by identifying subgroups of susceptible individuals who may be at a particularly high risk of breast cancer. Such a strategy has begun to help illuminate the relation between cigarette smoking (a major source of PAH exposure) and breast cancer, for example, by identifying subgroups who are slow metabolizers of tobacco carcinogens [33]. The already established LIBCSP blood bank is being drawn upon to conduct some of these assays.

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