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Racial and Ethnic Differences in Breast Cancer Risk Factors

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Data collection for a population-based case-control study of breast cancer conducted in the San Francisco Bay Area has been on-going since July 1996. Cases include African-American and White women aged 35-79 years and diagnosed with breast cancer between 1995 and 1998. Controls are identified through random-digit dialing. Information on physical activity, sunlight exposure, dietary intake of vitamin D and phytoestrogens, and other risk factors, is collected by in-person interview. The home visit also includes measurements of anthropometry and skin pigmentation using a Chromameter. To date, 607 case and 736 control interviews have been completed. Data from this study will be pooled with the data collected in two on-going case-control studies in African-American, Latina, and White women that use the same methodology and questionnaire. The combined data for an estimated 1300 cases and 1650 controls will allow us to examine the risk factor profile among White (high risk), African-American (moderate risk), and Latina (low risk) women. This study will make an important contribution to the sparse epidemiologic literature on breast cancer risk factors in African-American and Latina women.

Breast Cancer, Physical Activity, Phytoestrogens, Vitamin D, Multiracial/Ethnic, Epidemiology

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1. INTRODUCTION

1.1. Background

Breast cancer incidence rates in the San Francisco Bay Area are among the highest in the world [1]. In 1996, breast cancer affected 137.1 per 100,000 White women, the racial-ethnic group with the highest incidence rate, and as the leading incident cancer in women accounted for 32% of all cancers diagnosed in women from 1992-1996 [2]. Although incidence rates (per 100,000) are lower in African-Americans (91.1), Asians (73.5), and Latinas (71.4), breast cancer is the leading cancer in these populations as well [2].

The pronounced racial-ethnic differences in breast cancer incidence between Latinas, African-Americans, and White women remain largely unexplained for several reasons: (1) Few analytic studies with an etiologic focus have been conducted in Latina and African-American populations [3-11]; (2) few breast cancer studies included non-White populations that were large enough for separate analysis and racial-ethnic comparisons of risk factors [5,7,8]; and (3) in the few studies that included African-American women only [3,4,6,9-11], the comparison of risk factors with those of other racial-ethnic groups is limited by differences in methodology and data collection instruments used in different studies. It therefore is not known to what extent the differences in incidence rates are attributable to racial/ethnic differences in (1) the magnitude of relative risks associated with known and suspected risk factors, (2) the prevalence of known and suspected risk factors, (3) the magnitude of relative risks and/or prevalence of risk factors yet to be identified, and (4) genetic susceptibility.

1.2. Purpose of On-going Research

The San Francisco Bay Area offers a unique opportunity to conduct etiologic research in a multiracial/ethnic population given the large number of breast cancer cases diagnosed each year, 25% of whom are non-White. The on-going population-based case-control study funded by DOD is collecting interview data for African-American and White breast cancer cases and population controls. It uses the same protocol and data collection instruments as two complementary case-control studies: (1) an on-going case-control study of breast cancer in Latina women aged 35-79 years, which will complete data collection by the end of August 1999 (PI: Dr. Esther M. John, funded by the National Cancer Institute), and (2) a recently completed case-control study of breast cancer in Latina, African-American, and White women aged 50-79 years (PI: Dr. Pamela Horn-Ross, funded by the California Breast Cancer Research Program). The three studies carried out from 1995 to 1999 are administered as one single case-control study, and the data from the three studies will be pooled for the DOD-funded analyses described below.

The purpose of the on-going study is to collect interview data on a broad array of known, suspected, and newly hypothesized factors, with the ultimate goal of pooling the data from the three case-control studies. The pooled data will allow us to examine racial/ethnic differences in breast cancer risk factors in a large multiracial/ethnic population from a single geographic area. This research will make a significant contribution to the lack of knowledge about the etiology of breast cancer in non-White populations and will help elucidate the reasons for the striking racial/ethnic differences in breast cancer incidence.
2. BODY

2.1. Research Materials and Methods

2.1.1. Study Population

Cases for the entire study (funded by DOD, NCI, and BCRP) include women meeting the following eligibility criteria: (1) newly diagnosed with histologically confirmed, primary invasive breast cancer; (2) diagnosed between April 1, 1995 and April 30, 1998; (3) no previous history of in-situ or invasive breast cancer; (3) Latina, African-American or White (based on self-identification); (4) aged 35-79 years at diagnosis; (6) alive at the time of contact; (7) residing in Alameda, Contra Costa, San Francisco, San Mateo, or Santa Clara counties, California, at the time of diagnosis; and (8) English or Spanish speaking.

Cases for the DOD component include (1) African-American and White women aged 35-49 years and diagnosed between April 1, 1995 and April 30, 1998; (2) African-American and White women aged 50-79 years and diagnosed between April 1, 1995 and June 30, 1995; and (3) African-American and White women aged 50-79 years and diagnosed between November 1, 1996 and April 30, 1998.

The BCRP funded case-control study completed by Dr. Horn-Ross in 1998 includes Latina, African-American and White breast cancer cases aged 50-79 years and diagnosed between July 1, 1995 and October 31, 1996. The on-going NCI funded case-control study conducted by Dr. John includes Latina breast cancer cases aged 35-79 years and diagnosed between April 1, 1995 and April 30, 1998.

The cases are identified through the two population-based cancer registries covering the Greater San Francisco Bay Area which are operated by the Northern California Cancer Center. All Latina and African-American cases are eligible for the home interview; White cases are randomly sampled at 10%.

Controls for the entire study (funded by DOD, NCI, and BCRP) include a probability sample of women who meet the following criteria: (1) No previous history of breast cancer; (2) alive and between the ages of 35 and 79 years at the time of selection into the study; (3) residing in Alameda, Contra Costa, San Francisco, San Mateo, or Santa Clara counties, California, at the time of selection into the study; (4) Latina, African-American or White based on self-identification; and (5) English or Spanish speaking.

Controls are identified through random-digit-dialing (RDD) and frequency-matched to cases by race/ethnicity (Latina, African-American, White) and five-year age group (35-39, ..., 75-79). Latina controls are matched to Latina cases in an approximate ratio of 1.5 controls per case, African-American controls are matched to African-American cases in an approximate ratio of 1.2 controls per case, and White controls are matched to White cases in a ratio of 1 control per case.

2.1.2. Data collection procedures
Physician contact. As required by the Bay Area cancer registries, each breast cancer patient's physician listed on the cancer abstract is contacted to inquire about medical or psychological contraindications prior to our contacting his or her patient.

Random-digit dialing. To identify population controls between the ages of 35 and 79 years, a modification of the Waksberg method RDD method is used, which has been successfully applied in other population-based case-control studies conducted at the Northern California Cancer Center. This method greatly increases the efficiency of locating residential households and non-White controls.

Study contact. Breast cancer patients without physician-reported contraindications and controls selected randomly from the RDD lists of eligibles are sent a letter inviting them to participate in an interview conducted at the participant's home or elsewhere if preferred.

Screening interview. Following the letter, trained professional interviewers contact the potential study participant by phone to arrange a convenient time for the home interview. They also administer a brief screening questionnaire which inquires about current age, racial/ethnic background, adoption status, Jewish heritage, personal history of breast or ovarian cancer, and history of cancer in first-degree relatives (a copy of the screening questionnaire was submitted along with last year's annual report).

Home interview. The in-home interview involves the administration of the consent form and structured questionnaire, and the measurement of anthropometry (i.e., weight, height, waist and hip circumferences), and skin pigmentation using a Minolta Chromameter. The questionnaire inquires about demographic background, physical activity, sunlight exposure, diet, supplement intake, anthropometry, residential history, occupational history, pregnancy history, menstrual history, hormone use, and medical history (a copy of the questionnaire was submitted along with last year's annual report). The interview and measurements take 2 to 2 1/2 hours to administer for most participants. All study participants receive a compensation of $25.00 for their time and effort in completing the home interview.

2.1.3. Data management

Progress in RDD and data collection (e.g., screening, in-person interview, measurements) is monitored through two computerized FOXPRO tracking systems. Data entry of screening and questionnaire data is also performed through FOXPRO data entry screens.

2.1.4. Quality control

Several quality control procedures have been implemented to ensure the collection of high quality data. (1) All interviewers participate in a thorough training course conducted by the Principal Investigator and Program Manager to ensure data collection according to a standardized protocol. (2) Interviewers meet every two weeks with the Program Manager to discuss progress and quality of the completed work. (3) Interviewers participate in quarterly staff meetings, or more often as needed, to discuss specific issues arising in the field (e.g., refusals, no-shows, home visits, organization of work load, incentives, etc) and to participate in refresher sessions on specific questionnaire items and measurements. (4) Each interviewer is observed by the Program Manager while conducting an interview in the field. A report on the observation
is prepared and discussed with the interviewer. (5) Each completed questionnaire is edited by the interviewer immediately following the interview. (6) Each edited questionnaire is reviewed by the Program Manager. Missing data items and obvious error and inconsistencies in answers are identified and clarified by re-contacting the study participant. (7) Equipment (i.e., scales, chromameters) is periodically calibrated by office staff. (8) A sample of study participants is being re-contacted and questioned about specific sections of the questionnaire (see below on reliability study). (9) Data entry is on-going and is done twice to easily identify data entry errors.

2.2. Results

2.2.1. Completed field work

Data collection for the overall study began in May 1996 and is expected to be completed by the end of August 1999. Development of analyses programs began in January 1999. Data cleaning and statistical analyses of the final dataset will be conducted between September 1999 and June 2000. Progress in data collection is described below for the overall study (funded by DOD, NCI, and BCRP), as well as specifically for the DOD component.

Random-digit dialing. For the overall study, we dialed a total of 73,477 random numbers between July 1996 and February 1999 and identified a total of 8,137 Latina, African-American and White women aged 35-79 living in the San Francisco Bay Area.

Case ascertainment. As of July 26, 1999, the Bay Area cancer registries reported a total of 8,013 Latina, African-American and White breast cancer cases diagnosed between April 1, 1995 and April 30, 1998. Physician-reported contraindications were received for 120 cases (1.5%), who were therefore not contacted by study staff.

Screening interview. Although only 10% of White cases are eligible for inclusion in the study, all White cases are included in the screening with the primary purpose of assessing self-reported race/ethnicity. A recent study conducted at the Northern California Cancer Center found substantial misclassification of Hispanic race/ethnicity in the cancer registry records. We are therefore screening all breast cancer cases aged 35-79 years who are listed in the registry records as Latina, African-American or White, in order to identify all Latina cases (based on self-identification rather than potentially inaccurate medical records). Additional Latina cases are identified as part of a screening interview performed for a separate study of breast cancer in Asian women.

Excluding cases who are not eligible for inclusion in the study (147 with self-identified race other than Latina, African-American, or White; 293 deceased cases; 360 cases with a prior history of breast cancer), the population eligible for the screening interview includes 7,093 cases. Of these, 139 are still pending (mostly individuals who cannot be located). Among the remaining 6,954 cases eligible for screening, 6,009 cases (86.4%) completed the telephone screening interview, 404 refused to participate, 83 were too ill to participate, 53 did not speak English or Spanish, 335 could not be located despite intensive search conducted by office staff, and 77 could not be reached after more than 10 telephone contacts.

Among the 2,348 controls selected into the study, 7 were deceased at the time of contact, and 62 had a prior history of breast cancer. Among eligible controls, 59 are still pending at the screening level. Among the remaining 2,220 controls eligible for screening, 1,947 (86.8%)
completed the telephone screening interview, 143 refused to participate, 13 were too ill to participate, 6 did not speak English or Spanish, and 111 could not be reached at the phone number dialed during RDD.

**Home interview.** Among the 1,479 cases eligible and selected for the home interview (all Latinas and African-Americans, 10% sample of Whites), 25 are pending. Among the remaining 1,486 cases eligible for the home interview, 1,295 (87.6%) completed the home interview, 135 refused participation, 40 were too ill to participate, 6 could not be located, and 3 did not speak sufficient English or Spanish to complete the interview.

Among the 1,947 controls who completed the screening interview, the home interview is pending for 28 controls, 1,639 controls (85.4%) completed the home interview, 235 refused participation, 28 were too ill to participate, 15 could not be located following the screening interview, and 2 did not speak sufficient English or Spanish to complete the interview.

In summary, current response rates to the screening questionnaire are 86.4% for cases and 86.8% for controls, whereas the response rates to the home interview are 87.6% for cases and 85.4% for controls. Thus, the DOD analyses which will pool the data from the 3 studies will be based on a minimum of 1,295 cases and 1,639 controls. Additional data will come from the currently pending work load, which includes 139 cases and 59 controls pending at the screening level and 25 cases and 28 controls pending at the interview level. These pending individuals will be closed out by the end of August 1999.

**Study progress of DOD component.** During year 3 of the DOD component, 1,640 cases meeting the DOD eligibility criteria were ascertained by the cancer registries and processed for physician-reported contraindications, and 1,824 telephone screening interviews and 269 home interviews were completed with cases. RDD conducted during year 3 identified 368 eligible controls, and 381 telephone screening interviews and 352 home interviews were completed with controls. Thus, a total of 2,205 telephone screening interviews and 621 home interviews were completed for the DOD component in year 3.

### 2.2.2. Completed interviews vs. work scope

Based on field experience accumulated during two years of data collection, we revised the work scope in the summer of 1998 (see last year's annual report) based on actual case ascertainment, survival, and response rates. We projected to complete home interviews for 380 African-American and 455 White cases and equal numbers of controls, and 505 Latina cases and 760 Latina controls (1.5 controls per case), or a total of 2,935 participants. As of July 26, 1999, home interviews have been completed for 465 cases and 682 controls among Latinas; 386 cases and 460 controls among African-Americans; and 438 cases and 495 controls among Whites.

With regard to the DOD component, we estimated last summer we would complete home interviews with 260 African-American and 310 White cases and equal numbers of controls. To date, we have completed home interviews for 296 cases and 360 controls among African-Americans, and 311 cases and 376 controls among Whites, or a total of 1,343 individuals. The original grant proposal had estimated the completion of 1,390 completed interviews. Thus, we have nearly reached the originally set goal in terms of completed interviews funded by the DOD. Additional interviews will be completed by the end of August 1999.
2.2.3. Reliability study

In year three of DOD funding, we completed a reliability study with a random sample of 210 study participants who were re-contacted and asked a set of questions included in the original questionnaire. The reliability questionnaire focused on the questions contained in the sections on physical activity, sunlight exposure, and occupational history which deal with the major hypotheses of this study. Of those re-contacted and invited to complete the reliability questionnaire by telephone, 174 (83%) participated, 18 refused to participate, 2 had passed away, and 16 could not be reached.

2.2.4. Data analysis

In year three, we began developing statistical analysis programs in SAS to assess the relation between breast cancer and three sets of exposures: physical activity, sunlight exposure, and occupational exposures. No results, however, are available yet as data collection is still ongoing.

As part of the BCRP-funded companion study conducted by Dr. Horn-Ross, the NCCC nutrient database was updated to include phytoestrogen values and statistical analysis programs were developed to assess the association of breast cancer with dietary phytoestrogen intake. The updated nutrient database and Dr. Horn-Ross' analysis programs will be available for the DOD data analyses to be conducted in year four for the overall study.

2.2.5. Objectives for year four of DOD funding

We will complete field work for the overall study by the end of August 1999 and then begin data cleaning and definition of exposure and confounding variables. We will also update the NCCC nutrient database to include vitamin D nutrient values. We will rerun the analyses programs currently under development for the entire study population and develop additional analyses programs to assess racial/ethnic differences in breast cancer risk factors and perform attributable risk calculations. The focus of the analyses will be on the relation of breast cancer with physical activity, vitamin D from sunlight exposure and diet, dietary phytoestrogen exposure, and other known risk factors such as reproductive, menstrual, and hormonal factors. We will also analyze the data collected as part of the reliability study.

3. KEY RESEARCH ACCOMPLISHMENTS

Key research accomplishments achieved in year three of the DOD funded project include:

- Ascertained 1,640 newly diagnosed breast cancer cases meeting the eligibility criteria for the DOD study.
- Processed 1,640 newly diagnosed breast cancer cases for physician-reported contraindications.
- Identified 368 eligible controls through random-digit dialing.
- Completed 2,205 telephone screening interviews.
• Completed 621 home interviews with African-American and White cases and controls.
• Completed double data entry for completed screening and home interview questionnaires.
• Developed statistical analyses programs in SAS to assess the relation between breast cancer and physical activity.

4. REPORTABLE OUTCOMES

As data collection for the overall study is still on-going, no results are available yet and no manuscripts or abstracts have been published at this time.

In March 1999, Dr. Esther M. John received an R01 award from the National Cancer Institute to continue the on-going case-control study of breast cancer in Latina, African-American, and White women for three years. This new study has two objectives: (1) Additional newly diagnosed breast cancer cases and controls will be invited to complete the home interview and measurements and to provide a blood sample. (2) Cases diagnosed between May 1, 1997 and April 30, 1999 and their controls who have completed the home interview as part of the on-going study (funded by DOD and NCI) will be re-contacted and asked to provide a blood sample. Combining the interview data with the blood sample, the new study will (1) examine the relation between breast cancer and polymorphisms in the vitamin D receptor (VDR) gene, as well as interactions between polymorphisms in the VDR and vitamin D from sunlight exposure and diet; and (2) bank DNA, serum, and plasma for future molecular epidemiologic studies of breast cancer.

5. CONCLUSIONS

Data collection is on schedule and over 95% complete. The remaining interviews will be completed by the end of August 1999 according to the originally proposed time line.
6. LITERATURE CITED


