

The Breast Cancer Family Registries (Breast CFRs): Diet Collection Methodology for Studies of the Genetic Epidemiology of Breast Cancer

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NCI Web Site for the Breast CFRs:
epi.grants.cancer.gov/BCFR



BACKGROUND:

In 1995, the National Cancer Institute (NCI) initiated support for the Breast Cancer Family Registries (Breast CFRs), a research infrastructure dedicated to: a) the support of interdisciplinary and translational studies in the genetic epidemiology of breast and ovarian cancer, and b) the identification of at-risk populations to be enrolled in prevention and clinical trials. The Breast CFR is a consortium of six academic and research institutions and their medical affiliates in the United States, Canada, and Australia. In 1998, an Informatics Center was established at the University of California–Irvine to collate, manage, and distribute core and ancillary data collected and generated by the participating sites and their collaborators. The participating institutions are collecting epidemiological, clinical, diet, and molecular data and biospecimens from families that span the continuum of risk for breast cancer. Families are ascertained either through cases identified from population-based cancer registries (affected probands, population-based families) or from index persons recruited through clinical and community settings (affected or unaffected probands, clinic-based families). Additional effort is dedicated to recruitment from ethnic and racial groups, including Ashkenazi Jewish and minority families.

PURPOSE:

- Describe the methodology used by the Breast CFRs in ascertaining dietary data collected via a food frequency questionnaire (FFQ). In future studies, these data will be used to assess the relation between dietary intake and breast cancer risk and prognosis in a population of families across the spectrum of genetic risk.
- Discuss the challenges associated with the collection of dietary data in a sample of heterogeneous and multinational populations.
- Present preliminary dietary data collected in the currently accrued Breast CFRs participants.

METHODS:

- Six sites enroll index persons and their families from either cancer registries through an affected proband or subjects seen in clinical and community settings.
- A self-administered FFQ developed and validated by the University of Hawaii for the multiethnic cohort is used by the five North American sites. Nutrient data are analyzed using a food composition database maintained at the Cancer Research Center of Hawaii. This FFQ includes:
 - Portion size and usual intake of 180 foods and beverages that respondents consumed during the past year (at two sites, participants diagnosed with breast cancer completed the FFQ based on intake in the year prior to diagnosis; see Table 1);
 - Instructions to mark one of eight frequency choices using photographs of three different portion sizes of representative foods; and
 - Questions about usual intake of alcoholic beverages and vitamin and mineral supplements.
- The Melbourne and Sydney sites use a locally validated dietary FFQ developed by the Cancer Council Victoria for epidemiologic studies of Australian populations. The FFQ chosen by the North American sites was not considered appropriate due to

differences in the food lists as well as large differences in portion sizes. The Australian FFQ:

- Includes 74 items with 10 frequency options with more detailed information on consumption of alcoholic beverages than the Hawaii questionnaire but no questions on vitamin or mineral supplements,
- Calculates a Portion Size Factor (PSF) for each respondent from responses based on photos depicting three different serving sizes for each of potatoes, vegetables, steak, and casserole; and
- Uses a program developed by the Cancer Council Victoria to calculate nutrient intakes using primarily Australian nutrient data, along with USDA carotenoid data.
- Dietary analyses are restricted to only females who consumed >600 calories but <4,500 calories per day within three years of the diagnosis of breast cancer. After applying these exclusion criteria, 14,983 FFQ respondents were included, and preliminary dietary analyses were restricted to: energy, percent energy from fat, dietary fiber, beta-carotene, and vitamin C intake.

FINDINGS:

- As of July 2004, the six sites enrolled 12,305 families, including 6,225 population-based case families; 2,999 population-based control families; and 3,081 clinic-based families.
- The varied ethnic distribution of the Breast CFRs includes 78% whites to 9% Asians (Table 2).
- Response rates for completing the FFQ ranged from 68% to 97% (Table 3).
- Diet collection methodology, including referent time, differed slightly among sites (see Table 1). Since Australia used a different dietary instrument from the five North American sites, the energy and nutrient estimates for Australian participants were relatively lower and not directly comparable. Comparisons for vitamins and minerals are also not comparable because the Australian data do not include the intake of dietary supplements.
- Preliminary data are presented for mean Body Mass Index (BMI= kg/m²) and five nutrients, for clinic-based (affected and unaffected) participants, and for population-based (probands, controls, affected relatives, and unaffected relatives) participants.
 - Overall mean BMI for clinic-based participants ranges from 23.7 to 27 and, for participants at the population-based sites, ranges from 24.7 to 27.0 (Figure 1).
 - Mean energy intake ranges from 1,665 to 1,932 kilocalories per day for clinic-based participants and from 1,639 to 2,012 for population-based participants (Figure 2).
 - Mean percent energy from fat ranges from 28% to 32% for participants from the North American sites. In Australia, there is a higher mean percent energy from fat, in the range of 33 to 40% (Figure 3).
 - Mean intake of dietary fiber for all participants ranges from 19.2 to 29.5 g/day (Figure 4).
 - Mean intake of beta-carotene ranges from 4,875 to 7,836 mcg/day (3.4 to 7.2 mg/day) (Figure 5).

- Mean intake of vitamin C for participants at all sites ranges from 114 to 931 mg/day (Figure 6).
- Although there is some heterogeneity in collecting dietary data at the six sites, use of a standardized FFQ at the North American sites and a standard protocol for assessing dietary data appears to have resulted in a fairly homogeneous nutrient composition that is a valuable resource. Dietary data are still in the process of being evaluated, and future analyses are planned to compare differences by site, participant type, and ethnic group.

IMPLICATIONS:

- **Research Infrastructure:** The Breast CFRs has a comprehensive research infrastructure to support interdisciplinary and multi-institutional research in the genetic epidemiology of cancer. Information on diet and other risk factors, as well as stored DNA and tissue, is available for interested researchers to characterize diverse susceptible populations and families, identify risk factors, and examine the role of genetic and environmental factors in the development and clinical course of breast cancer.
- **Molecular Characterization:** The comprehensive characterization of deleterious BRCA1 or BRCA2 mutations—including those in minority populations and those in individuals of Ashkenazi descent (21% of the total Breast CFRs recruitment)—and of other identified cancer susceptibility genes (ATM, CHK2), as well as the genotyping of candidate genes in pertinent metabolic pathways, will allow for the identification of subpopulations at genetic risk.
- **Populations Included:** The large sample size, the dual ascertainment schemes (population-based and clinic-based), and the flexibility of design (hybrid, case-control, and family-based designs) will allow investigation of gene/diet interaction and breast cancer risk.

CHALLENGES IN MOVING THE FIELD FORWARD:

- **Methodologic Issues:** For practical reasons, some differences exist in the methods (interview or self-report) used to collect dietary data across sites, and Australia used a different questionnaire from the other sites. The principal challenge is to determine how to calibrate diet across all six sites due to differences in methodology and to validate the recorded intakes, possibly using serum markers.
- **Dietary Patterns Over Time:** FFQs were initially collected when the participants were first enrolled, and dietary changes over time need to be measured to determine whether diet affects breast cancer incidence (in respondents not affected when recruited into the Breast CFRs) or survival (for those affected). Similarly, data on BMI, physical activity, and other lifestyle changes over time should be considered along with nutrient intake.
- **Infrastructure Maintenance:** Resources are needed to maintain contact with these families and identify new cancers, recurrences, and deaths; to collect additional samples and data; and to continue data analysis.

Table 1:
Food Frequency Questionnaire (FFQ) Data Collection Methodology Used in the Breast Cancer Family Registries (Breast CFRs)

SITE	INSTRUCTIONS	QUESTIONNAIRE ADMINISTRATION	TIME ALLOTTED FOR QUESTIONNAIRES TO BE RETURNED	PROCEDURE IF QUESTIONNAIRES WERE NOT RETURNED	PROCEDURE FOR INCOMPLETE QUESTIONNAIRES
Melbourne & Sydney, Australia ¹	Modified ^b	Mailed	2-3 weeks	Multiple phone calls	Phone to try to obtain missing information.
New York, NY ²	Not-Modified ^c	Mailed (occasionally administered in person)	ASAP	Multiple phone calls	Copies of incomplete pages mailed to respondent.
Ontario, Canada ³	Modified ^b	Mailed	1 month	Multiple phone calls	Phone to try to obtain missing information (specific rules for % missing in each section).
Philadelphia, PA ⁴	Not-Modified ^d	Mailed	2-3 weeks	Reminder letter (after 3 letters, FU by phone)	Copies of incomplete pages mailed to respondent.
San Francisco, CA ⁵	Modified ^{b,d}	Mailed (occasionally administered in person)	2-3 weeks (occasionally collected at home visit)	Multiple phone calls	Phone to try to obtain missing information.
Salt Lake City, UT ⁶	Not-Modified ^d	In person (group orientation by Registered Dietitian)	Completed at group orientation	Multiple phone calls	Copies of incomplete pages mailed to respondent (if only several missing, phone call to subject).

- University of Melbourne & New South Wales Cancer Council
 - Columbia University, New York, NY
 - Cancer Care, Ontario, Canada
 - Fox Chase Cancer Center, Philadelphia, PA
 - Northern California Cancer Center, Union City, CA
 - Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT
- Respondents with breast cancer were directed to complete the FFQ based on intake in the year prior to diagnosis.
 - Respondents without breast cancer were directed to complete the FFQ based on intake in the past year.
 - Translation of the FFQ to Spanish, Korean, and Chinese.
 - Translation of the FFQ to Spanish and Chinese.

Table 2:
Frequencies by Ethnic Groups in the Breast Cancer Family Registries (Breast CFRs)

ETHNIC GROUPS	BREAST CFRs SITES	AUSTRALIA
White	78%	95%
Black	6%	0%
Hispanic	5%	1%
Asian	9%	4%
Other	2%	1%

*Includes all Breast CFRs sites except Australia.

Table 3:
Breast Cancer Family Registries (Breast CFRs) Enrollment Summary

SITE	ENROLLED* PROBANDS	ENROLLED* PROBANDS WITH COMPLETED FFQ	RESPONSE RATE (%)	ENROLLED* RELATIVES	ENROLLED* RELATIVES WITH COMPLETED FFQ	RESPONSE RATE (%)
Melbourne & Sydney, Australia ¹	1,597	1,399	88%	3,008	2,090	69%
New York, NY ²	1,143	1,104	97%	1,770	1,698	96%
Ontario, Canada ³	2,313	2,134	92%	2,974	2,887	97%
Philadelphia, PA ⁴	833	605	73%	445	380	85%
San Francisco, CA ⁵	2,182	2,000	92%	2,041	1,735	85%
Salt Lake City, UT ⁶	193	188	97%	553	515	93%

*Enrolled participants who were alive and completed the Epidemiology Questionnaire.

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Figure 1:
Mean Body Mass Index (BMI) by Site and Participant Type

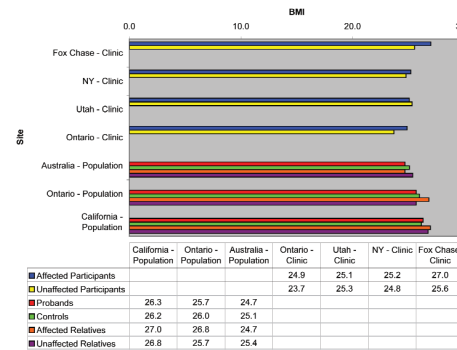


Figure 3:
Mean Percent Energy from Fat by Site and Participant Type

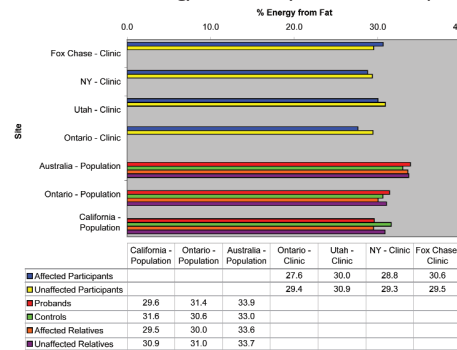


Figure 5:
Mean Beta-Carotene Intake by Site and Participant Type

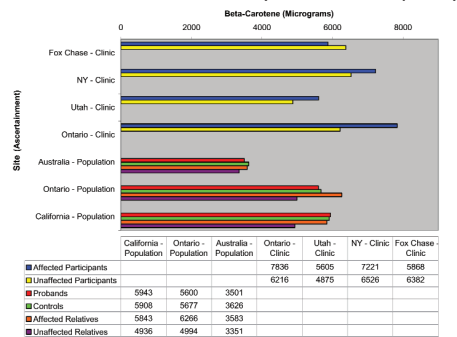


Figure 2:
Mean Energy Intake by Site and Participant Type

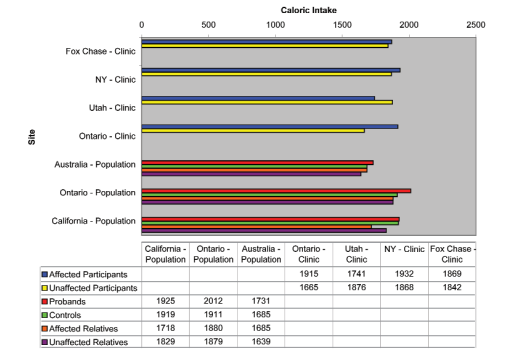


Figure 4:
Mean Dietary Fiber by Site and Participant Type

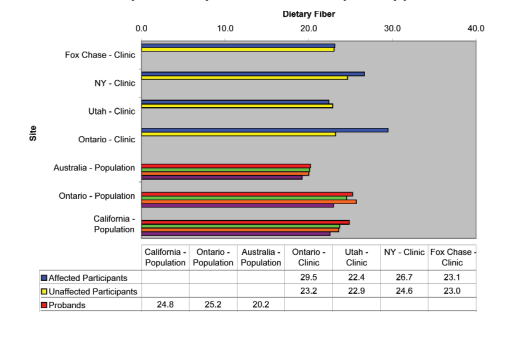
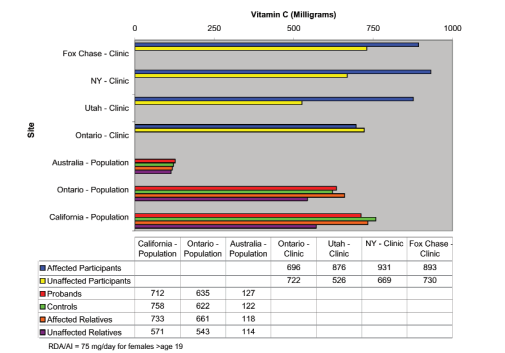


Figure 6:
Vitamin C by Site and Participant Type



RDA¹ = 75 mg/day for females >age 19