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13. ABSTRACT *(Maximum 200*

The following describes results of a two year descriptive study, with a nested case-control design, aimed at determining relationships between risk factors and genetics in breast cancer etiology among pre-menopausal African American women. One hundred breast cancer cases (cases) (n = 100) and their primary female relatives (PFRs) (n = 154) were administered several questionnaires (psychosocial, reproductive, genetic and lifestyles) related to disease risk. Cases were matched by ethnicity and age (within 10 years) to one cancer-free woman participating in a screening mammography program (n = 100). Results showed less than 35% of Cases & Siblings believed *there is a lot they can do from getting cancer* compared to 9% of Mothers and 21% of Offspring. More than 50% of Cases & Siblings are *pleased with the emotional support provided by family and friends, respectively.* Cases reported starting their menstrual cycle at age 13 and Controls, age 12. DNA samples have been extracted from the blood of all cases and PFRs. Eight participants (19%) had a positive reported family history for breast/ovarian cancer with at least one more affected relative. Over 30% of Cases & Siblings were overweight as opposed to 2% of Mothers and 19% of Offspring.

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Sunia A. Smith 10/11/96

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INTRODUCTION

Breast cancer is the most commonly diagnosed nondermatologic cancer and is the second leading cause of cancer-related deaths among women in the United States (1-3). The overall incidence rate increased from 82.5 to 110.6 during 1973-1992 (4), with varying race-specific rates. For white women, the age-adjusted rate increased 34% (from 84.3 to 113.1) and for black women, increased 47% (from 68,7 to 101.1) during that same time period (2).

Reasons cited for this increase incidence among African Americans have been numerous. Increases in screening mammography rates, earlier detection of cancer and increased access to care for a group disproportionately represented at the low socioeconomic status level are among reasons cited. Although these explanations may represent partial answers for the growing trend of breast cancer diagnosis for black women, none account fully for ethnic differences in breast cancer incidence.

Epidemiologic studies have shown risk factors such as age; socio-economic class; race/ethnicity; lifestyle; and reproductive factors increase a woman's chance of developing breast cancer. There have been few epidemiologic studies of breast cancer focusing explicitly on African-American women, and it is not established whether the standard risk factors apply. Evidence relative to younger versus older African American women is also scarce. In work by Robert Mayberry (5), risk of breast cancer among black women younger than 40 years of age was nearly three times greater for those who used oral contraceptives for more than 10 years relative to never-users (odds ratio, 2.8; 95% confidence interval, 1.2 to 6.8) and more than four times greater for severely obese women (body mass index $\geq$ 32.30 kg/m^2) relative to women whose relative weights were less than 24.90 kg/m^2. The report also indicated similarities among younger and older black women with regards to additional breast cancer risk factors (i.e., surgical menopause, age at first full term pregnancy and multiple births).

Women with a family history of breast cancer are also at increased risk for developing breast cancer. Studies indicate women with a familial pattern of this disease are thought to have a lifetime risk of breast cancer as high as 50% (6). This risk varies from woman to woman, depending on the presence of other risk factors. Research suggests the risk is two to three times higher in women who have first-degree relatives with breast cancer (7). There is also evidence that, for women with first-degree relatives with bilateral, premenopausal breast cancer, the risk is even higher (7,8).

In 1990, linkage studies localized an inherited susceptibility gene for breast cancer aggregates in certain families to chromosome 17q (9). Generally, women who inherit the BRCA1 gene are more likely to develop cancer than those who do not. Female carriers of BRCA1 mutations are estimated to have an 85% lifetime risk of developing

breast cancer, with more than 50% of the breast cancers occurring before the age of 50 years (10). It is, however, very likely that other genes may be responsible for inherited breast cancer. Since the cloning of the BRCA1 gene (10,11), it is possible to detect the presence of mutations in this gene in about 45% of the families with a clearly inherited pattern of this disease.

The purpose of this research is to determine the relationship between risk factor and genetics in the etiology of breast cancer. The objectives include: 1) analyze multigenerational reproductive and lifestyle risk factors; 2) dietary assessment ; 3) psychological assessment; and 4) complete pedigree data and storing DNA samples for the study of mutations on the BRCA1 gene.

Several questionnaires, including a Breast Cancer Risk Appraisal (BCRA), Food Frequency Questionnaires (HHHQ), and Psychosocial Questionnaire were administered to study risk factors for breast cancer in premenopausal African American women by identifying genetic and environmental influences in the etiology of breast cancer in cases and their family groups.

BODY

Recruitment For Study Year 2, the project is on target in terms of the timeline with 100 breast cancer cases on study. There are 254 women, including breast cancer cases and their primary female relatives (PFR) (mother, sister(s), and/or female offspring) and disease-free controls, enrolled. Each family group member has completed the BCRA, HHHQ, 24 Hour Dietary Recall and Psychosocial Questionnaires and had their blood drawn for DNA extraction. Family history forms were administered to capture information related to illnesses and causes of deaths within family groups.

Cases were identified from several sources including: 1) the Jackson Memorial Medical Center Tumor Registry (JMMC/TR); 2) Cedars Hospital Tumor Registry; and 3) South Miami Hospital Tumor Registry, to enlist the required cases. Permission was obtained from the Florida Department of Health and Rehabilitative Services (HRS) to obtain the names and addresses of African American women age 50 years or less diagnosed with breast cancer in the past five years entered into the Florida Cancer Data System (FCDS). This FCDS identified a total of 3,174 age-eligible breast cancer cases in the State, with a large percentage of them residing in South Florida. These efforts ensured the availability of the projected sample size. We reported these recruitment methods in the paper: Use of tumor registry data in minority health programs. Selina A. Smith, Edward Trapido, Stephen Richman, Amelie Jean Francois, Stephanie Lojko, Clyde B. McCoy. Journal of Registry Management Vol 23: pp 68-73, May 1996 (Appendix A). Letters were mailed to eligible women in the South Florida area. A total of 50 breast cancer cases (50% of total sample) have been recruited as a result of this effort.

Because recruitment sources varied, participants were contacted in-person, by telephone or by letter. Participants were given the option of completing the assessment interview by phone or by home visit. Informed consent and blood for DNA testing were obtained prior to the arranged interview, which lasted approximately 90 minutes. Allowing several options for interview location increased participant enrollment.

Controls were randomly selected from the total number of participants undergoing screening mammography in the Early Detection Program (EDP). A control was defined as the first woman enrolling in the EDP immediately following the identification of the case matched by age (within 10 years) and ethnicity. Following study protocol, one control was identified for each case.

A Risk Appraisal Project or RAP (an acronym for the Multigenerational Breast Cancer Risk Factors in African American women) database was developed in Study Year 1 to ensure data are continuously accumulated to meet study objectives. Data were entered on a routine basis, following editing and checks for outliers by the data manager. Data analysis for cases and controls was completed by linking RAP and EDP databases.

Objective 1: Analyze multigenerational reproductive and lifestyle risk factors in African American family groups. Aim 1: Conduct a breast cancer risk factor appraisal. A breast cancer risk appraisal (BCRA), designed to capture all known and suspected risk factors for breast cancer, developed and pilot tested in Study Year 1, has been administered to all participants. Risk factors such as diet, reproductive factors, activity level, body build, alcohol use and fat distribution for cases, primary female relatives and controls, were analyzed. In our last annual report, we presented preliminary data on these factors among family groups. These findings will be presented at the 124th Annual Meeting of the American Public Health Association, November 17-21, 1996 New York, NY (Appendix A). Multigenerational reproductive and lifestyle risk factors will continue to be examined in Study Years 3 and 4. Table 1 represents demographics and health characteristics analyses completed to-date on the total project sample for Study Years 1 and 2. Sixteen percent of Cases & Siblings received a high school diploma compared to 1% of Mothers and 12% of Offspring. Fourteen percent of Cases & Siblings and 13% of both Mothers and Offspring have monthly income less than $9,999 or less. Both Cases & Siblings (36%) and Offspring (37%) have never been on a special diet, compared to 2% of mothers. In addition, analyses showed both Cases & Siblings (38%) and Offspring (32%) rarely/never exercise.

Table 1. Sociodemographic and Health Characteristics of Breast Cancer Cases, and their Siblings, Mothers, & Offspring*

	Cases & Siblings (n = 134)		Mothers (n = 11)		Offspring (n = 109)	
	Mean	%	Mean	%	Mean	%
Sociodemographic						
Age (years) (n/SD)	44.07	9.09	61.18	9.05	20.12	9.33
Education (years)						
No formal schooling	1.00	0.39	----	----	5.00	1.95
8th grade or less	9.00	3.52	----	----	20.00	7.81
< high school	21.00	8.20	4.00	1.56	25.00	9.77
high school diploma	41.00	16.02	4.00	1.56	33.00	12.89
trade/tech school	3.00	1.17	----	----	1.00	0.39
some college	31.00	12.11	2.00	0.78	21.00	8.20
college grad	28.00	10.94	1.00	0.39	4.00	1.56
Income						
< $4,999	17.00	6.64	3.00	5.86	15.03	5.86
$5,000-9,999	37.00	14.45	2.00	13.67	5.00	13.67
$10,000-14,999	15.00	5.86	1.00	9.00	9.00	3.52
$15,000-19,999	20.00	7.81	2.00	12.00	12.00	4.69
$20,000-24,999	12.00	4.69	2.00	4.69	3.00	1.17
$25,000-29,999	7.00	2.73	----	----	----	----
$30,000-34,999	4.00	1.56	1.00	0.39	1.00	0.39
$35,000-39,999	5.00	1.95	----	----	----	----
$40,000-44,999	1.00	0.39	----	----	1.00	0.39
$45,000-49,999	3.00	1.17	----	----	----	----
$50,000-54,999	3.00	1.17	----	----	1.00	0.39
Special Diet						
No	102.00	36.96	7.00	2.54	103.00	37.32
Weight loss	10.00	3.62	----	----	5.00	1.81
For medical reasons	10.00	3.62	1.00	0.36	3.00	1.09
Low salt	1.00	0.36	1.00	0.36	----	----
Low cholesterol	2.00	0.72	----	----	----	----
Weight gain	----	----	----	----	1.00	0.36
Exercise						
> 1/wk	22.00	7.97	----	----	33.00	11.96
About 1/wk	4.00	1.45	----	----	1.00	0.36
Few times/month	3.00	1.09	2.00	0.72	3.00	1.09
Few times/year	2.00	0.72	----	----	----	----
Rarely/never	105.00	38.04	9.00	3.26	89.00	32.25

*Does not include missing responses.

Of the captured risk factors, those associated with reproduction have the strongest scientific support in breast cancer etiology. However, the salient absence of African American women in previous large scale case-control epidemiological studies examining breast cancer risk factors has left a void in our understanding of which factors are applicable to black women and which factors or not.

Estrogen is of special interest in breast cancer etiology. It's role in breast cell multiplication, the total number of menstrual cycles and possible genetic alterations in cells during this replication are thought to be important in disease development. The typical woman is thought to have approximately 300-400 menstrual cycles in her lifetime, exposing her breasts to several estrogen-progesterone cycles (12). Factors affecting this number, as well as cycle duration, are implicated in breast cancer. Repeated cellular multiplication is believed to increase the likelihood of genetic accidents. Women with fewer menstrual periods, i.e., those beginning their menstrual cycles later, having their first child young, repeated pregnancies, longest breast feeding durations and earlier menopause, are at lowest breast cancer risk.

To address the issue of estrogen and breast cancer risk, we examined reproductive factors among breast cancer cases and their age-ethnicity matched controls. Using cited values as the goal standard and comparing breast cancer cases to controls, Table 2 summarizes results of analyzed reproductive factors.

Table 2. Probable Reproductive Risk Factors Among African American Breast Cancer Cases and Age-Ethnicity Matched Controls

Reproductive Factor	Established Risk Levels*	Breast Cancer Cases** (N = 100)	Controls** (N = 100)
Age @ Menarche	≥12 Years	13 Years	12 Years
Age @ First Full Pregnancy	>30 Years	21 Years	18 Years
Number of Full Term Births	+	4	5
Breast Feeding Duration	≥9 months	2	3
Age @ Menopause	≤55 Years	42	35
Exogenous Hormones	–	17	9
Oral Contraceptives	–	76	52

*Values associated with reduced breast cancer risk.
**Does not include missing responses

Age at menarche: women starting their menstrual cycles later in life (i.e., $\geq$ 12 years of age) are thought to be at lower risk for breast cancer (13). Cases reported starting their menstrual cycle at age 13 compared to Controls, age 12. *Age at full p*regnancy: having the first child at or before age 30 years lowers breast cancer risk (14). Cases reported having their first birth at an average age of 21, compared to Controls, who reported first birth at age 18. *Number of full term births:* Parity is thought to modify disease risk (15). Controls reported having an average of 5 full term birth compared to Cases reporting an average of 4. *Breast feeding:* Because lactation interrupts the estrogenic cycle (i.e., nursing women menstruate less), breast feeding duration is important in examining breast cancer risk. Breast feeding nine months or more is associated with lower risk (16). Both Cases and Controls reported breastfeeding their children less than 9 months. *Age at menopause:* women undergoing menopause later as opposed to earlier (i.e., age 55 years or less) are at greater breast cancer risk (17). *Exogenous hormone use:* current use of birth control pills and/or estrogen replacement therapy, because of their influence on estrogen in the body, may also elevate risk (18).

Aim 2: Evaluate the role of food choice and food practices and breast cancer. The Health, Habits, History Questionnaire (HHHQ) has been administered to all participants. The HHHQ estimates total calories, dietary fat intake including total Vitamin A, beta carotene and retinol from both dietary sources and vitamin supplementation, vitamin C, Vitamin E, fruit, vegetables and meat consumption, and fiber intake for the year prior to the interview. This instrument also captures food practices, i.e., frying versus baking meats, which may be related to breast cancer risk. Responses to each HHHQ are recorded on scannable forms which are forwarded in bulk to a commercial analyzer, Survey and Ballot Systems, Inc., Minnesota. Results are sent back to the project office on diskette, which is then down loaded to the RAP database.

In addition to the HHHQ, a 24 Hour Dietary Recall (24 HDR) was also administered. The 24 HDR asks participants to recall everything they had to eat /or drink in the 24 hours preceding the interview. Survey results are being used to augment the HHHQ food database with target population culturally specific foods. The Minnesota Nutrition Data System (NDS), a microcomputer-based system for collection and analysis of dietary data, is being used to analyze 24 HDR data. The NDS has been updated to provide a more accurate analysis during the past Study year.

A third measure, the Nutrition Survey, included in the BCRA, is also administered. Developed by Alan Kristal of the Fred Hutchinson Cancer Research Center, Seattle, this instrument provides a fat and fiber score which allows researchers to estimate total dietary content of these items (19). Additionally, recent changes made in fruit and vegetable consumption can also be determined. A manuscript, Family Resemblance in Modifiable Breast Cancer: A study among three generations of African American women, is in progress and will be submitted to the Journal of the American Dietetics Association. Salient findings from this paper are presented in Table 3 and 4.

Table 3. Daily Frequency of Selected Food Items among Breast Cancer Cases, Siblings, Mothers and Offspring

Food item or group	Case & Siblings (N = 134)	Mother (N = 10)	Offspring (N = 140)
	Mean(STD)	Mean(STD)	Mean(STD)
Fruit & Fruit Juice	1.51(1.08)	1.21(0.62)	1.25(1.05)
Bread, Cereal, Rice, Pasta	2.24(1.14)	1.64(0.61)	2056(1.37)
Milk, Yogurt & Cheese	1.03(1.21)	0.94(0.63)	1.67(2.08)
Meat, Poultry, Fish, Beans, Eggs	2.02(1.46)	1.13(0.69)	2.48(1.90)
Fats, Oils, Sweets & Snacks	3.08(2.04)	1.69(1.00)	3.66(2.58)
Dark Green, Deep Yellow Fruit/Veg	0.58(0.52)	0.68(0.64)	0.45(0.42)
Citrus Fruits & Juices	0.73(0.69)	0.58(0.36)	0.62(0.63)

Table 4. Mean Daily Nutrient Intakes of Breast Cancer Cases, their Siblings, Mothers & Offspring

	Cases & Siblings (N = 134)		Mothers (N = 10)		Offspring (N = 140)	
	Mean	SD	Mean	SD	Mean	SD
Nutrient						
Energy, kcal	1319.88	684.61	809.69	294.44	1615.14	895.
Fat, g	52.53	34.79	28.64	15.66	66.12	44.
Saturated	17.95	12.78	10.43	5.22	23.85	16.
Cholesterol, mg	230.83	175.18	143.04	69.96	280.35	200.
Protein, g	51.15	29.49	31.01	14.07	64.98	39.
Carbohydrate, g	159.52	75.97	106.42	41.65	189.54	98.
Dietary Fiber, g	10.05	5.14	7.10	2.94	9.81	5.
Vitamin A, IU	6770.42	5866.75	6413.50	4542.02	5940.48	4877.
Beta Carotene	3057.21	2685.72	2889.67	2320.08	2461.03	2370.
Retinol	630.09	891.77	514.44	439.09	587.70	573.
Vitamin C, mg	162.01	115.52	146.57	118.86	168.26	127.
Vitamin E, ug	7	4.10	4.28	2.15	7.90	5.
Nutrient Density						
Fat, % kcal	34.48	8.52	30.54	11.59	35.13	8.
Protein, % kcal	15.74	3.71	14.93	3.76	15.93	3.
Carb, % kcal	49.64	9.44	54.50	14.71	48.22	10.
Nutrient Estimates from Supplements						
Vitamin A, IU	3534.12	6216.10	3500.00	4743.42	1846.97	4437.
Beta-Carotene, mcgs	304.91	544.81	120.00	379.47	316.74	968.
Vitamin C, mg	114.72	221.75	106.00	137.94	98.48	463.
Vitamin E, a-TE	27.71	71.95	28.81	33.43	17.73	66.

Results showed participants had an average daily Vitamin A intake of >5,000 IU, which is above the Recommended Dietary Allowance (RDA) of 4,000 IU. Cases and Siblings consumed the highest levels of Vitamin A (6,770 IU); however, results from the nutrient estimates from supplements show none of the participants' average intake exceed the RDA for Vitamin A. All participants exceeded the RDA for Vitamin C (60 mg) with Offspring averaging the highest intake (168 mg). Furthermore, none

of the participants exceeded the RDA for Vitamin E (8 mg). Mothers had the lowest average of Vitamin E (4 mg) as opposed to an average of 7 mg for both Cases & Siblings and Offspring. In addition, the percent of calories from fat, excluding alcohol, was tabulated for participants from the HHHQ. Results demonstrated all members, excluding Mothers, had diets higher in fat than is recommended. Cases & Siblings and Offspring had an estimated fat intake $\geq$ 34%. Mothers' fat intake was at the recommended level ($\leq$ 30%).

Our health attitudes survey (a part of the Psychosocial Questionnaire) has allowed the examination of dietary beliefs related to breast cancer risk. These findings were reported during the recent American Psychological Association's Psychological and Behavioral Factors in Women's Health, September 17-20, 1996, Washington, D.C. (Appendix A). Table 5 outlines dietary health attitudes results from the Psychosocial questionnaire. Results indicate 79% of Offspring believed *eating a low-fat diet reduces one's risk of getting breast cancer* as opposed to 48% of Cases & Siblings and 9 % of Mothers. Over 50% of Cases & Siblings believed *It is important to eat foods low in fat.*

Table 5. Dietary Health Attitudes of Breast Cancer Cases and their Siblings, Mothers and Offspring

STATEMENT	CASES AND SIBLINGS %	MOTHERS %	OFFSPRING %
EATING A LOW-FAT DIET REDUCES ONE'S RISK OF GETTING BREAST CANCER	48	9	79
EATING A DIET HIGH IN VITAMIN A REDUCES ONE'S RISK OF GETTING BREAST CANCER	44	9	73
IT IS IMPORTANT TO EAT FOODS LOW IN FAT	53	9	21

Examine the role of obesity and adipose distribution in breast cancer risk. There is some evidence that regional distribution of adipose tissue is related to breast cancer risk (20). Women carrying excess weight on their upper bodies are at increased risk of getting breast cancer. For this aim, the role of obesity and adipose distribution in breast cancer risk were examined. Analyses showed the majority of participants had

an even distribution of fat.

Table 6. Self-Reported Mean Body Adipose Distribution & Weight Loss History of Breast Cancer Cases, their Siblings, Mothers and Offspring

	Cases & Siblings			Mothers			Offspring	
	Mean	SD	n	Mean	SD	n	Mean	SD
Weight Status								
Height (cm)*	162.50	20.87	137	162.56	4.25	11	142.44	53.1
Weight (kg)*	82.03	18.90	135	79.71	18.98	11	66.47	23.2
BMI (kg/m)**	49.76	10.97	134	49.11	12.19	11	42.05	11.6
Body Build (%)								
Underweight	1.09	----	3	0.00	----	0	0.00	---
Normal	7.61	----	21	1.09	----	3	19.93	---
Overweight	39.86	----	110	2.90	----	8	19.20	---
Obese	.72	----	2	0.0	----	0	0.72	---
Body Fat Distribution (%)								
Above Waist	9.06	----	25	0.36	----	1	5.43	---
Below Waist	16.30	----	45	1.45	----	4	7.97	---
Even	23.55	----	65	2.17	----	6	28.62	---
Age @ Overweight	31.00	8.33	105	35.00	11.81	7	16.00	8.2
Highest Weight	202.99	48.24	109	201.43	41.90	7	190.94	46.9
Weight Loss History								

As illustrated in Table 6, 23% of Cases & Siblings' body fat was evenly distributed compared to 2% of Mothers and 19% of Offspring. Less than 9% of Cases & Siblings had adipose distribution above the waist. Over 30% of Cases & Siblings were overweight, 2% of Mothers and 19% of Offspring.

Objective 2: Determine psychosocial profiles of breast cancer family groups.

Aim 1: Examine the impact of psychosocial factors on breast cancer. A psychosocial assessment was completed in three components: 1) Social Networks section, assessing participants' ties with friends, family and the community; 2) Health Attitudes section, examining cognitive/affective dimensions of personality which have been associated with health behaviors; and 3) General functioning determining the association between general emotional functioning, mood and health behavior. Preliminary findings related to this aim were presented in our last report as well as during the recent American Psychological Association's Psychological and Behavioral Factors in Women's Health, September 17-20, 1996, Washington, D.C. (Appendix A).

TABLE 7. PSYCHOSOCIAL HEALTH ATTITUDES OF BREAST CANCER CASES AND THEIR SIBLINGS, MOTHERS AND OFFSPRING

STATEMENT	CASES AND SIBLINGS* %	MOTHER* %	OFFSPRING* %
THERE IS A LOT I CAN DO TO KEEP FROM GETTING SICK	53	9	24
THERE IS A LOT I CAN DO TO KEEP FROM GETTING CANCER	35	9	21
I WORRY A LOT ABOUT DEVELOPING CANCER	38	5	23
I AM PLEASED WITH THE EMOTIONAL SUPPORT PROVIDED BY MY FAMILY	59	9	24

***PERCENTAGES ARE BASED ON NON-MISSING VALUES**

Data in Table 7 represents psychosocial health attitudes responses to date on the total project sample for Study Years 1 and 2. More than 50% of Cases & Siblings were *pleased with the emotional support provided by family and friends, respectively.* Thirty eight percent of Cases & Siblings *worry a lot about developing cancer,* compared to 5% of Mothers and 23% of Offspring. Over 50% of Cases & Siblings and 24% of Offspring believed *there is a lot they can do from getting sick.*

Objective 3: Construct pedigree data and bank DNA samples for conducting linkages studies to map breast cancer genes by analyzing the co-transmission of candidate markers, breast cancer

and risk factors in multiple-case families. Cases and PFRs have completed family histories and had blood drawn. DNA extractions have been completed on the total sample. Family pedigrees were drawn using the Canvas computer-based program. Results are maintained in the project office in participant files (in a locked file cabinet), RAP database and the CANVAS computer program/Macintosh computer. **Aim 1: Identification of families carrying the BRCA1 gene. a) identify common risk factors in high risk families** Family history data were collected. Inherited mutations of BRCA1 gene are associated with a high risk of breast (82%), ovarian (44%), prostate (8%) and colon (6%) cancers in some families (21). Family history data, including self-reported family history of cancer, was collected on 51 breast cancer cases and their PFRs (total n=151). Breast cancer cases reported 34 of their female relatives had breast cancer, 3 ovarian, 5 prostate and 3 colon cancer. Other cancers reported included cervical, brain, bone, stomach, lung, throat, uterine, spinal, rectal, sarcoma, gland, head and neck. Preliminary findings related to family history are being presented in the Epidemiology Section of the American Public Health Association's 124th Annual Meeting, New York, NY, November 17-21, 1996 in a poster entitled: Genetic Investigation of African American Families with Breast Cancer (Appendix A).

b) Determine if breast cancer is familial due to specific genes or because risk factors themselves are familial DNA was extracted for each of the family groups and stored for later testing for BRCA1 mutations. Our participation in an adjunct study funded by the Health Foundation of South Florida (Fernando Arena, MD, PhD, Principal Investigator), allowed testing of selected DNA samples for BRCA1 mutations. Mutations were found in three cases and all were previously unreported mutations in exon 11 (943 ins 10bp, 3888 del GA and 4160 del AG). Because of these findings, 42 additional study participants with early-onset breast cancer were investigated for the presence of mutations in exon 11 of BRCA1. Eight (8) participants, or 19% had a positive reported family history for breast/ovarian cancer with at least one more affected relative. Our search, using four sets of PCR primers, was directed to the regions in exon 11 surrounding these mutations. Only one (1) mutation was found, a second 943 ins 10bp mutation, in an unrelated family. However, we found a previously undescribed polymorphism in exon 11 (A3557/g), which was present in 4 of 100 chromosomes from African American controls and in none of 46 chromosomes of white controls. These results were submitted in an abstract form to the 46th Annual Meeting of the American Society of Human Genetics, to be held in San Francisco, CA from October 29 - November 2, 1996 and was accepted for platform presentation at the section Cancer Genetics II: Breast Cancer. The abstract, BRCA1 mutations in African American Women. J.F. Arena. S. Smith, M. Plewinska, L. Gayol, E. Perera, P. Murphy and H. Lubs. is already published in Am. J. Hum. Genet. 59 Supplement A 34, 169,1996 (Appendix A).

CONCLUSIONS

Multigenerational Breast Cancer Risk Factors in African American Women or the Risk Appraisal Study (RAP), has gained momentum among breast cancer survivors and their primary female relatives. Because this is a descriptive study, the recruitment rate has approached 100% and the retention rate has been equally successful. The use of tumor registry data in participant

recruitment has added considerably to our confidence to obtain an appropriate sample size. Controls, recruited from the nine-and-a-half year old EDP, is also on target in terms of the expected numbers. Continued success in recruitment and retention for duration of the project is anticipated.

Personnel were reconfigured early within Study Year I to accommodate the needs of the project. A percent effort of a data manager and research assistant were included to facilitate data acquisition. Originally, the intent was to complete all interviews in the homes of breast cancer cases and their primary female relatives. However, interviews were restructured to take place in the most convenient location for the participant. Additionally, many local women were interested in participating in the project but didn't have PFRs residing in Dade County. In order to meet recruitment goals, relatives living in other parts of the country were included. Strict quality control issues were considered in blood handling and informed consent is obtained from all study participants, prior to data collection.

Family history and age are accepted risk factors for breast cancer. Pedigree data collected on study participants indicates a strong relationship between family history and our breast cancer cases. Age, however, has not been as strong an indicator. Cases in the present study are below 50 years of age. For the most part, cases in the study reporting a family history of breast cancer had older female relatives (i.e., mothers, aunts, grandmothers) with personal histories of breast cancer at ages within 10 years of their diagnoses.

Primary prevention of breast cancer through lifestyle intervention has become increasingly important in epidemiologic research. Antioxidant vitamins, in particular, are in the forefront of this research. Data on vitamins A, E, C and beta carotene from the present study are valuable in that they will assist in determining diet-genetic links in breast cancer risk and these data will also assist in designing breast cancer interventions. Based on the participant enrollment at this time, it is difficult to draw conclusions related to dietary intake.

Psychosocial results from the study imply that more than 30% of the Cases & Siblings feel they can keep from getting breast cancer. This is an important finding in that most female relatives of breast cancer survivors often feel helpless in terms of preventing this disease. More than 50% of Cases/Siblings are pleased with the emotional support provided by family and friends, respectively. Additional psychosocial data analysis will continue in Study Years 3 & 4.

At the time the original grant application was submitted, methods included the extraction of DNA for later testing for BRCA1 mutations. Since the award, the location of the gene presented unique opportunities for actual testing for mutations of the gene. Through collaboration with Fernando Arena, MD, PhD, the project geneticist, we were able to present previously unreported BRCA1 mutations in a sub-sample of high risk cases. Further work is in progress to identify mutations in the BRCA1 gene in patients with one or more affected relatives with breast/ovarian cancer.

Study Years 3 & 4 will include a continuation of the descriptive study. The development of the RAP System database has equipped project leadership with ability to track project participants. Risk factors will be assessed on an additional 100 breast cancer cases and their primary female relatives. Cases will continues to be matched to age-ethnic-specific controls. Through linkage studies, likely cases for BRCA1 mutations will complete genetic assessments. As genetic and epidemiological links to breast cancer continue to be uncovered (as is anticipated by the end of this research), counseling programs will emerge. A better understanding of the interaction between environmental factors and genes will prepare the scientific and medical community to cope with breast cancer and issues of prevention.

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*APPENDICES

APPENDIX A	PUBLICATIONS/ABSTRACTS
APPENDIX B	BUDGET JUSTIFICATION

Appendix A

Publications

Use of Tumor Registry Data in Minority Health Programs

Selina A. Smith, PhD; Edward Trapido, ScD; Stephen P. Richman, MD; Amélie Jean-François, MPH; Stephanie A. Lojko, BA; and Clyde B. McCoy, PhD

Abstract: **Tumor registries contain clinical information that can be used to develop effective intervention programs. In 1987, analysis of a tumor registry in Dade County, Florida, the Florida Cancer Data System (FCDS), revealed morbidity from breast cancer was worse in black women than white women, which led to the conclusion that medically underserved women in Dade County were in need of breast cancer screening. As a result, the University of Miami Jackson Memorial Medical Center and the Sylvester Comprehensive Cancer Center implemented the Miami Early Detection Program (EDP) to enhance cancer screening. With the addition of five research projects and two community outreach programs, the EDP has expanded into the Breast Cancer Early Detection/Prevention Program (BCEDPP). All the projects involve research in minority women. The majority of BCEDPP research projects have used tumor registries for recruitment purposes. BCEDPP will continue to use tumor registry data as a key source to collect information.**

Introduction

Tumor Registries have traditionally focused on counting and examining disease frequency rates for the purpose of gathering and calculating patterns of disease incidence, prevalence, treatment, and survival. Cancer registries contain clinical information about individual patientsthat which can be used as additional data in the care of patients, in studying the care of groups of patients, as resources for projects, as well as assisting in planning.[1] This information can also be used in the implementation of clinical practice parameters, educational programs, health resource delivery, and minority health programs.[1] According to Harding,[1] cancer registries have the potential to answer research questions to the same extent that any retrospective study (without random allocation into experimental and control groups) can.

Breast cancer is the most common type of cancer among women in the United States. A woman's lifetime risk is now 1 in 8 of developing breast cancer [2] although in Florida, it is 1 in 7.[3] In general, incidence rates for breast cancer are higher in older white women and in younger African American women.[4] However, for more than 20 years, black women with breast cancer have been reported to have a lower survival rate than white women with breast cancer.[5] This difference in survival rate can be explained by differences in stage at presentation and by differences in the quality of care received.[5] According to McCoy et al.[6] individuals with a lower socioeconomic status are less educated about the causes and prevention of cancer; engage more frequently in cancer risk-promoting activities, such as the use of tobacco and alcohol; and have less access to health care services. These factors combine to make the issue of breast cancer in minority groups important. In order to achieve significant reductions in breast cancer incidence and mortality, minority women must have access to prevention and screening interventions. Several studies have demonstrated that screening mammography has had a significant impact on breast cancer diagnosis, morbidity, and mortality.[6-11]

In 1981, the State of Florida initiated a statewide, population -ased, tumor registry, the Florida Cancer Data System (FCDS), at the Sylvester Comprehensive Cancer Center (SCCC). The registry is estimated to be more than 90% complete. Figure 1 shows FCDS stage of breast cancer by race/ethnicity for Dade County. Analysis of data for Dade County from the FCDS, in 1987, revealed that the morbidity from breast cancer was worse in black women than white women.[6] Further analyses of these data led to the conclusion that medically underserved black and Hispanic women in Dade County were in need of breast cancer screening and that these were problems due to a combination of availability, accessibility, and acceptability.[6] As a result, the Sylvester Comprehensive Cancer Center and the University of Miami Jackson Memorial Medical Center (UM/JMMC) entered into a coalition with Dade County Public Health Department, American Cancer Society, and eight primary health care centers (PHCCs) to implement the Miami Early Detection Program (EDP). The EDP was implemented to enhance cancer screening and early detection services in general and specifically to overcome obstacles associated with the delivery of these services. Early Detection Program, using a mobile mammography unit, provides free or low -cost mammograms to underserved women who attend the eight PHCCs. The primary health care centers are the primary public sources where medically underserved women seek and receive health services.

As the number of daily screenings increased to more than 20 mammograms per day, a database system (DETECT) was developed.[10] DETECT captures a wide array of demographic, epidemiologic, and clinical data that is being collected on these women.

"USE OF TUMOR REGISTRY DATA IN MINORITY HEALTH PROGRAMS"
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Submitted 2/01/96, Revised and Accepted 3/04/96.

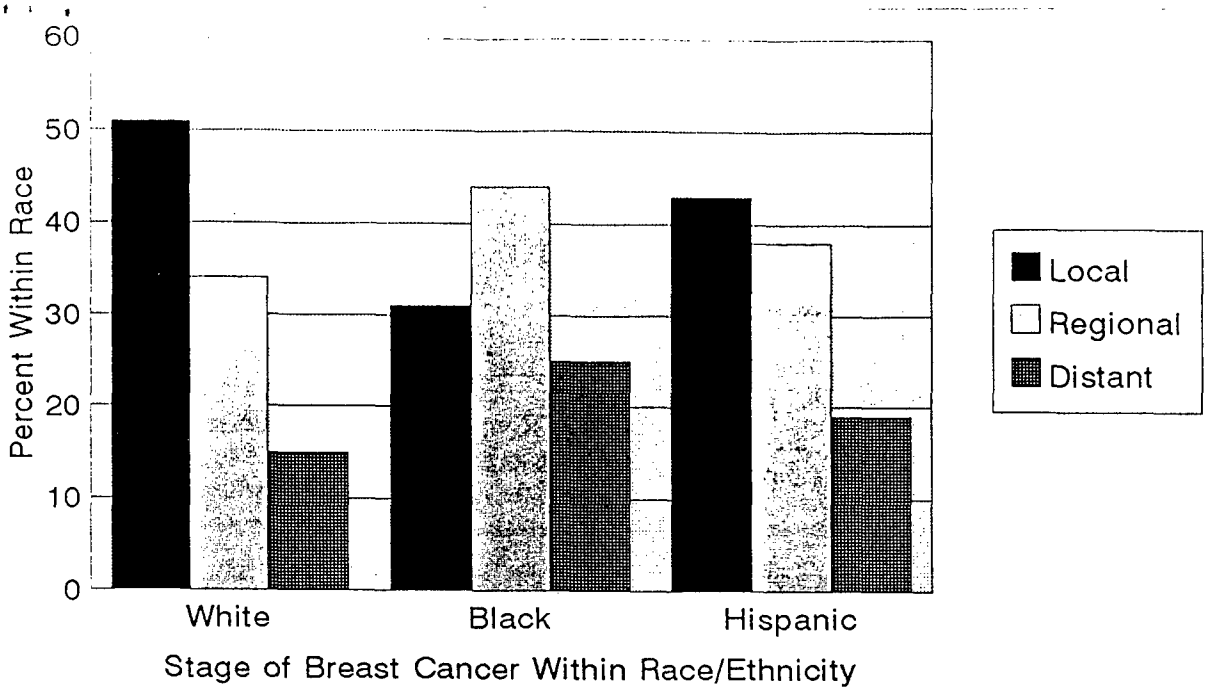


Figure 1. The number of breast cancer cases by race/ethnicity for Dade County from 1981-90. (n=6778)

The mobile mammography unit has reached more than 32,379 women since its inception in 1987. In addition, a total of 143 breast cancer cases have been diagnosed. Table 1 describes the demographics for the Early Detection Program. Women diagnosed with breast cancer are being referred to the Breast Health Center (BHC) at Jackson Memorial Medical Center, a "one stop" facility to provide uniformly high-quality diagnostic services to all patients requesting or requiring them. In addition to screening, the EDP was designed to include follow-up procedures.

All women diagnosed with breast cancer by the EDP are being reported to the tumor registry, FCDS.

The Breast Cancer Early Detection/Prevention Program

With the addition of five research projects and two community outreach programs, the Early Detection Program has expanded into the Breast Cancer Early Detection/Prevention Program (BCEDPP). Figure 2 describes the organizational chart of BCEDPP. The five research projects of Breast Cancer Early Detection Prevention/Program include: Evaluation of a Community-Based Early Detection Pro-

Table 1. Early Detection Program Demographic Characteristics, 1987-1995

CHARACTERISTICS	%
Race/Ethnicity (n=32,379)	
black	39.9
white	6.4
Hispanics	53.6
Other	0.7
Age	
<40	9.3
40-49	30.6
50-64	48.7
65+	11.4
Breast Cancer by Race/Ethnicity (n=143)	
black	47.6
white	6.3
Hispanic	46.1
Breast Cancer by Age	
<40	.7
40-49	19.6
50-64	41.2
65+	38.5

Table 1 describes the demographic characteristics of the EDP population. Since the program's inception, 143 cancers were diagnosed in 140 women (3 women had dual cancers).

FIGURE 2. ORGANIZATION OF THE BREAST CANCER EARLY DETECTION/PREVENTION PROGRAM RESEARCH OUTLINE

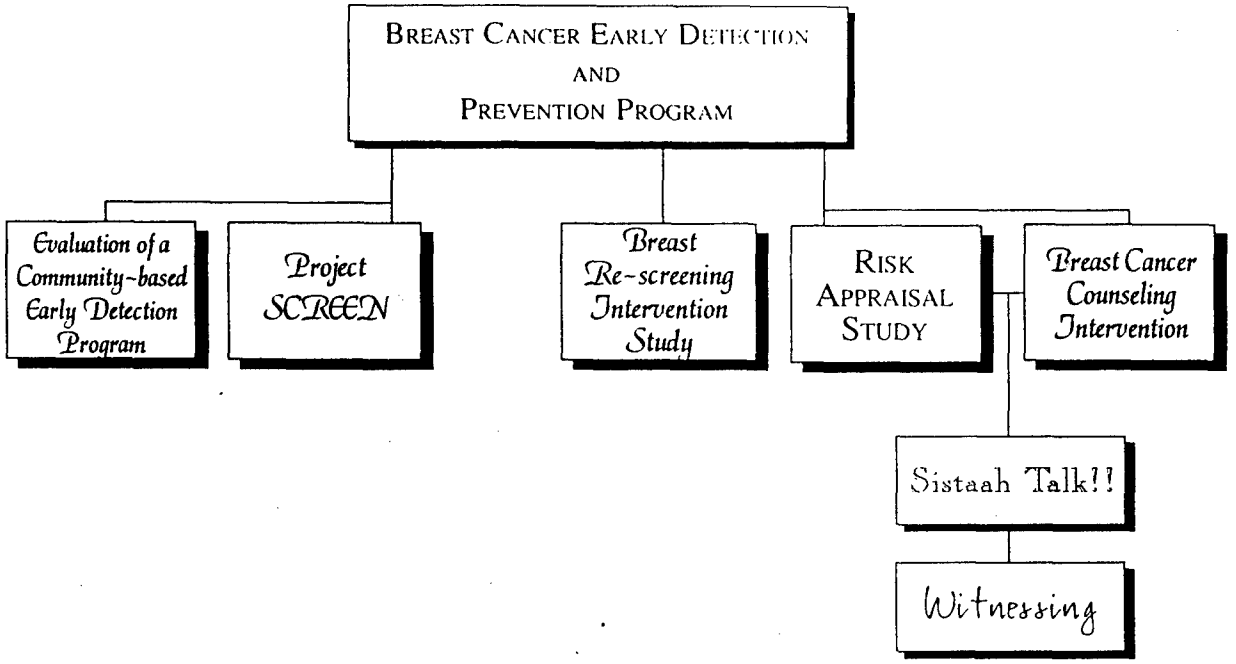
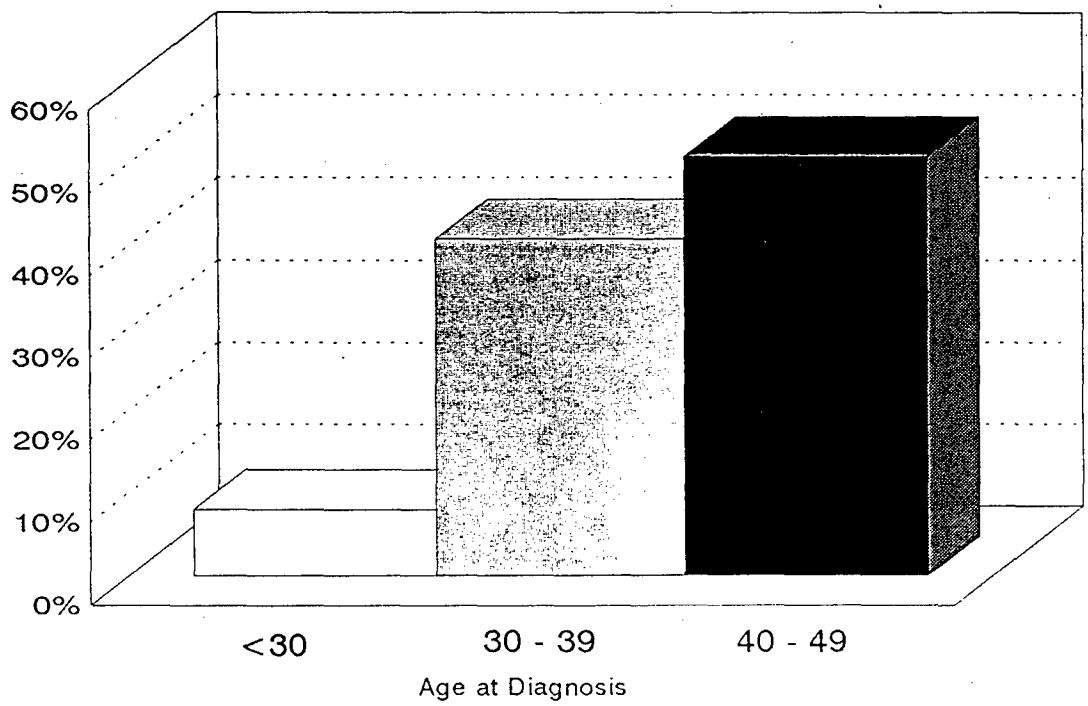


Figure 2



*Source: UM/JMMH Tumor Registry Demographics, (Jan. 1990 - Jul. 1995)
n=143

Figure 3. Distribution by age for African American women diagnosed with breast cancer prior to age 50, UM/JMMC Tumor Registry

gram; Breast Re-Screening in Minority Women; Multigenerational Breast Cancer Risk Factors in African American Women (Risk Appraisal Project/RAP); Breast Cancer Counseling in African American Women; and Screening for Cancer: Referral, Education and Evaluation Network (Project SCREEN). Furthermore, the program is expanding with the addition of a second mammography van donated to BCEDPP by the Health Foundation of South Florida.

Most of the Breast Cancer Early Detection Prevention/Program research projects, such as the Risk Appraisal Project, have used tumor registries. In addition to Florida Cancer Data System, the University of Miami/Jackson Memorial Medical Center Tumor Registry (UM/JMMC TR) has been used for recruitment purposes. The UM/JMMC TR records information about cancer staging, pathology features with known prognostic relevance, hormone receptor data and clinical follow-up for all JMMC patients, including patients screened on the mobile mammography unit receiving diagnostic services at the Breast Health Center. Figure 3 demonstrates the distribution by age for African American women diagnosed with breast cancer under the age of 50 from the University of Miami/Jackson Memorial Medical Center Tumor Registry.

Evaluation of a Community-Based Early Detection Program, a four year research project, assesses and evaluates the effectiveness of the Early Detection Program and determines its generalizability as a model for technology transfer. Factors examined include utilization variables and continuity of care issues (including time elapsed), and patient satisfaction. It is estimated that data on over 45,000 screenings and more than 300 cancers, as well as comparable controls, will be available by the end of the evaluation period. Specifically, the study will compare random samples of screenees and non-screenees. The impact of the Early Detection Program is measured relative to screening and biopsy rates, cancers detected, shifts in staging, survival and mortality. Therefore, analyses are being conducted to compare stage in the EDP to staging of other populations within the county and the state among different subgroups. These measurements of shifts compare EDP to county by county shifts and state shifts utilizing the Florida Cancer Data System data. Comparisons with all breast cancer cases at the University of Miami/Jackson Memorial Medical Center that cover the years of the project are also being made utilizing its tumor registry.

Multigenerational Breast Cancer Risk Factors in African American Women/Risk Appraisal Project (RAP) Data

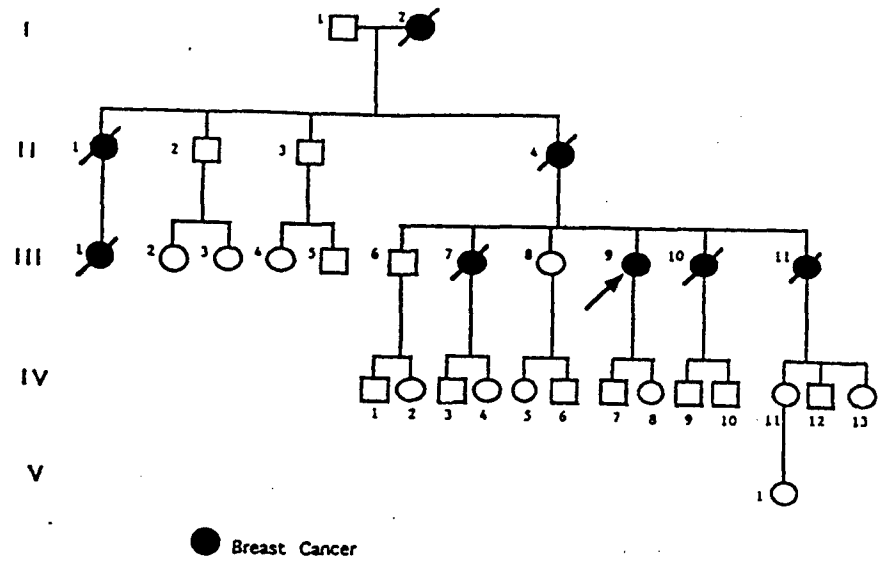


Figure 4. Pedigree for case study 2

The literature has reported an increased rate of breast cancer among African American women under 50 years of age.[13,14] The Multigenerational Breast Cancer Risk Factors in African American Women (Risk Appraisal Project/RAP) was developed to study multigenerational breast cancer risk factors, such as reproductive and lifestyle factors, in African American women under the age of 50 by identifying genetic and environmental influences in the etiology of breast cancer in cases and their family relatives. In addition to the breast cancer case, primary female relatives (PFRs) (mother, sister(s) and female offspring) are screened for risk factors. The study will enroll 200 breast cancer cases and at least two of their PFRs. Participants are identified and recruited primarily from the Jackson Memorial Medical Center/Tumor Registry and the Florida Cancer Data System. Other sources of recruitment include DETECT, Breast Health Center, Cedars Hospital, and South Miami Hospital tumor registries. The general design is a population-based, cohort study with a nested case-control investigation conducted in four phases. The breast cancer cases will be compared to 200 controls screened on the mobile mammography unit, matched by age (within 10 years) and ethnicity. The Risk Appraisal Project has captured data on a total of 51 families to date (Total n= 151). Assessment of family history, pedigree drawing and blood collection for DNA extraction are being conducted.

Using the Canvas computer-based program, pedigrees have being drawn for some of the 51 cases. The pedigree for Case Study 2 is shown in Figure 4. The first generation, represented in tier(I), shows the maternal grandparents of the breast cancer case. The second generation, represented in tier (II), displays the mother and sisters. The breast cancer case (#9) and her siblings are displayed in the third tier. The fourth and fifth tiers shows the daughters, nieces and great nieces. Case #9 developed breast cancer at 32 years of age. Her first degree relatives developed breast cancer before the age of 30 and all died of breast cancer in their early thirties. The breast cancer case's mother and grandmother died of breast cancer at the age of 29. There are eight breast cancer cases within three generations in this family. Families with three or more affected relatives were investigated regarding the presence of mutations in BRCA1 gene. DNA sequencing results for Case Study 2 indicate a 2 base pair deletion at nucleotide position 3888

Table 2. Focus Group Results - Barriers
Breast Cancer Re-Screening in Minority Women Data

CHARACTERISTIC	HAITIAN	AFRICAN AMERICAN	HISPANIC
Benefits or dangers from getting mammogram	benefits	benefits; can detect it early	benefits; danger: too much radiation
Reasons why women don't get mammograms	fear of finding out they have cancer	afraid to find something wrong	afraid that it is going to hurt; fear to know
Reasons why women don't come back for another mammogram	first mammogram was ok; no need for a second one; don't receive a comeback letter; nothing wrong with breasts; don't invite them back; afraid to come back; waiting for a letter of return; procrastination; too painful first time	forget about it; don't understand it is important to do it yearly; nothing wrong first time	one mammogram once a lifetime; squeezes too much first time; uncomfortable; unconcerned; afraid of pain; don't care about health; think they are healthy
Time convenient	yes	yes; better if come earlier	yes
Distance travel convenient	convenient; not a problem	convenient; appreciate service being close by; Jackson very far; traffic terrible; "if I have to go a long way, won't go"	"I don't know"; I think so
Influence to get mammogram	physicians	physician; to know and stop it before it takes over their life	Physician
Frequency of mammograms	every year; "I don't know"; more than 4 times a year	once a year	once a year; once or twice a year depending on the person
How to encourage women to come back	more education	provide them with more information; have someone explaining meaning and importance of yearly mammogram to them; meet with them; have doctor remind them	advertise more; explain the importance of a mammogram; distribute flyers and pamphlets; provide or pay transportation for women

(3888delGA) in exon 11 (codon 1257) of the BRCA1 gene. This mutation causes an in-frame terminator codon (TAG) to appear at codon position 1265. This mutation, though not yet reported in the literature, is predicted to result in a truncated protein. DNA sequencing results and genetic counseling was provided to the family. Case Study 2's family fits the pattern of autosomal dominance. Offspring of the affected persons have 50% of inheriting the gene since the BRCA1 gene mutation is present in this family, (3888delGA) in exon 11. This mutation will be checked in each of the available first degree relatives, above the age of 18, who want to be tested. A special session will be held for family members to explain the meaning of these findings and to educate them about their options, should they test positive or negative for the BRCA1 gene mutation.

Despite the widespread emergence of breast cancer risk counseling programs, there has been a salient absence of systematic attempts to evaluate the impact of providing individualized breast cancer risk information.[15] Subtle changes in how risk information is presented can have marked effects on decision making related to breast health.[16] Based upon preliminary data from the Risk Appraisal Project, the Breast Cancer Counseling in African American women study was developed. The project tests the feasibility of breast cancer risk counseling intervention among African American women. Fifty African American women are being randomly recruited from RAP to participate in two interventions: a multi-component intervention focusing on breast cancer early detection practices, and an enhanced intervention focusing on the multi-component intervention plus personalized lifestyle counseling. The counseling steps are from Johns Hopkins Hospital's Breast Surveillance Service model.[16] Changes in modifiable risk factor behaviors and the effectiveness of the enhanced intervention will be analyzed. Results from this study will assist in the formulation of culturally sensitive counseling materials for women at high risk of developing breast cancer.

The following two studies, Breast Re-screening in Minority Women and Project SCREEN, are not using tumor registry; however, they are an outgrowth of the Early Detection Program, which was created due to analysis of a tumor registry, Florida Cancer Data System. In addition, participants diagnosed as having breast cancer in these studies are being reported to FCDS. Therefore, they are contributing to the tumor registry.

Although many studies have focused on barriers to mammography, little attention has been given to repeat periodic screenings among women completing baseline mammograms. Yet it is among second or later screens that the earliest cancers will be found.[12] Analysis of the Early Detection Program data revealed that many women do not return for periodic screening after completing a baseline mammogram. Re-screening rates are uniformly poor for all women, regardless of race or ethnicity. The Breast Re-screening in Minority Women study was designed to develop intervention strategies that enhance participant re-screening and follow-up rates and determine breast cancer risk factors for the targeted population. This study will enroll approximately 2,900 asymptomatic women who have been screened through the EDP. Of these, 2,000 women are expected to have "negative" mammograms at their first screening, while 900 will have "suspicious" findings. It tests the hypothesis that community "peer counselors" can improve

re-screening rates among women over age 50 more than intervention programs that simply use follow-up letters to remind women of their appointments. The peer counselors are working with screenees to stress the importance of repeat mammography and breast self-examination, as well as to empower them with the skills and knowledge needed to obtain these medical services for themselves. Outcomes include re-screening rates, as well as changes in attitudes and knowledge about cancer re-screening. Focus Groups have been conducted to identify systems and cultural barriers that potentially impede appropriate utilization and continuity of health care services. Each focus group is composed of women screened on the mobile mammovan the previous year. Preliminary focus group results are represented in Table 2. The successful completion of this study will have direct implications on the mammography screening programs in minority populations and can serve as the foundation of minority programs for other diseases.

In addition to screening mammography, Project SCREEN, a community based program, will also increase the rate of usage of cervical cancer screening in uninsured and underserved low income minority women in Dade County. The program allows an expansion of the present program to cover several health care centers that are not currently covered. The extended Dade County Public Health Unit Family Program and Sexually Transmitted Disease Programs provide cervical cancer screening to women of reproductive age. Targeting the older population will encourage use of primary care by low income women, and increase breast and cervical screenings in the population with the highest incidence of breast and cervical cancers and the highest death rate from both types of cancer. Furthermore, culturally competent non-traditional outreach interventions are addressing the needs of the county's multicultural population with the absolute highest number of breast and cervical cancer cases of all counties in the state of Florida.

Two community outreach programs have been initiated by the BCEDPP research team: SISTAAH TALK!! and WITNESSING. These outreach programs are an outgrowth of the Risk Appraisal Project, which has used several tumor registries to identify and recruit participants. Studies have shown that the hope of receiving and giving emotional support and of obtaining increased information were the largest single reasons why women attend breast cancer support groups. The perceived benefits of attending one are also important to attendance.[17] The Breast Cancer Early Detection Prevention Program research team initiated a support group for RAP's breast cancer survivors, SISTAAH TALK!!. SISTAAH TALK!! is a support group for women of color at risk for breast cancer. Issues important to black women with breast cancer—food, hair, skin color, financial stress—which may be difficult to discuss in mixed race support groups, are covered in SISTAAH TALK!!. In addition, they learn about the latest medical procedures, early detection, and lifestyles related to this disease. The support group has been successful. To date, there have been three meetings with an average of 20 women per meeting.

Witnessing is a program designed to increase cancer prevention awareness in the African American community. Through the Witnessing video series and accompanying newsletters, this program is teaching the black community throughout the state of Florida about early detection and prevention practices. Video inserts, recipe preparations by an international chef and demonstrations by professional fitness trainers, all contribute to a practical and entertaining program designed for viewer appeal. Health Departments throughout Florida are participating in this program.

Future Use of Tumor Registry

The breast Cancer Early Detection Prevention Program will continue to use tumor registry data as a key source to collect specific breast cancer information related to diagnosis, treatment, stages, and follow-up care. The data collected from tumor registries will assist projects within BCEDPP in maintaining accurate and current information regarding future and long-term follow-up patient care and medical status. Tumor registries will also be used in developing future BCEDPP research projects.

Acknowledgement

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(Author making presentation)

Name and title Selina A. Smith, Ph.D.

Address 1550 N. W. 10 Avenue , Suite 100 (D4-11)

City Miami **State** FL **Zip** 33136

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Presenter's FAX (305) 243-4754

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Are the appropriate number of original abstracts, blind review copies and author ID forms enclosed (see section requirements)? ● Yes ○ No

Genetic Investigation of African American Families with Breast Cancer. **Selina A. Smith, PhD, J. Fernando Arena, MD, Robert Duncan, PhD, Stephen Richman, MD, LaDora Bankston, CNA, Lennox Scope, BS. University of Miami School of Medicine Sylvester Comprehensive Cancer Center**

Inherited mutations in the BRCA1 gene are associated with a high risk of breast (82%), ovarian (44%), prostate (8%) and colon (6%) cancer in some families. This population-based, cohort study seeks to determine the extent of multigenerational breast cancer cases as well as the presence of other cancers, such as ovarian, prostate and colon cancer, within African American breast cancer cases' family groups. Family history data, including self reported family history of cancers, was collected on 51 breast cancer cases and their primary female relatives (n=151). Family pedigrees were drawn using the Canvas computer-based program. Breast cancer cases reported that 34 of their female relatives developed breast cancer. In addition, they reported that 3 of their family members developed ovarian cancer, 5 prostate cancer while 3 had colon cancer. Other cancers were reported including: cervical (1), brain (1), bone (2), stomach (2), lung (6), throat (3), uterine (1), spinal (1), rectal (1), sarcoma (leg) (1), gland (1), head/neck (1), and unknown types of cancer (1). Of the 51 families, three families (n=24) had three or more affected relatives with breast cancer. They were investigated regarding the presence of mutations in BRCA1 gene. DNA has been extracted from the blood samples of all participants for further investigation. They all presented a mutation in exon 11 being two cases of 2 base pair deletion leading to stop codons and one case of a ten base pair insertion also leading to a stop codon. These mutations have not been previously described in the literature.

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Dietary Intake Patterns of Breast Cancer Cases and Their Primary Female Relatives. **Selina A. Smith, PhD, LaDora Bankston, CNA, Robert Duncan, PhD, Amelie Jean-Francois, MPH, Stephanie A. Lojko, BA. University of Miami School of Medicine Sylvester Comprehensive Cancer Center**

Various aspects of diet have been linked to breast cancer etiology. Studies have shown little or no association between dietary fat and breast cancer. Intake of vitamin A, C and E have been hypothesized to be protective factors for breast cancer. This population-based, cohort study compares dietary intake of African American women diagnosed with breast cancer to diets of their primary female relatives (PFRs). Several questionnaires related to dietary intake were administered to 51 breast cancer cases and their PFRs (Total N= 151). Results showed that participants had an average vitamin A intake of >5,000 IU, which is above the recommended dietary allowance (RDA) of 4,000 (IU). The Cases 'average vitamin A intake (6152 IU) was lower than their siblings (6666 IU) and mothers (8146 IU); but higher than their daughters and nieces (5270 IU). All participants exceeded the RDA for vitamin C (60 mg). Cases and their sisters were similar in their intake of vitamin C (139 mg); however, daughters and mothers' average intake was much higher, 144 mg and 225 mg, respectively. Cases and sisters had the lowest intake of vitamin E (6 mg), which is slightly below the RDA (8 mg). Daughters, nieces and cousins met the RDA for vitamin E (8 mg and 7 mg respectively). The percent of calories from fat, excluding alcohol, was tabulated. The results showed that all members, excluding mothers, have diets higher in fat than is recommended. The Cases' mean fat intake was 36% compared to the mothers' fat intake of 30%. Sisters, daughters, nieces and cousins' fat intake was similar to the cases. These preliminary findings suggest that breast cancer cases and their PFRs have similar dietary intake. These findings are important in developing interventions aimed at modifying dietary intake of African American women and their families at risk for breast cancer.

8. Abstract

Title: \bold {BRCA1 Mutations in African-American Women}
Author(s): \underline {J. F. Arena$^{1}, S. Smith$^{1}, M. Plewinska$^{1}, L. Gayol$^{1}, E. Perera$^{1}, P. Murphy$^{2} and H. Lubs$^{1}}
Institution(s): $^{1}University of Miami School of Medicine, Miami Florida. $^{2}OncorMed Inc., Gaithersburg, Maryland.
Text:
Breast cancer in African-Americans is associated with a poorer prognosis than in Caucasians. African-American women tend to present at an earlier age with larger tumors and a more advanced stage disease. Studies designed to detect a possible molecular basis for this difference have not been reported. As part of a pilot project investigating the presence of BRCA1 mutations in the South Florida population, 3 African- American patients with a strong family history of breast cancer were investigated. Mutations were found in all three cases and all were previously unreported mutations in exon 11 (943 ins 10bp, 3888 del GA and 4160 del AG). Because of these findings, we investigated forty-two additional African-American patients with early onset breast cancer for the presence of mutations in exon 11 of BRCA1. Eight patients (19\%) had a positive family history for breast/ovarian cancer with at least one more affected relative. All others cases (81\%) were sporadic. Our search, using four sets of PCR primers, was directed to the regions in exon 11 surrounding these mutations. Only one mutation was found, a second 943 ins 10bp mutation in an unrelated family. However, we found a previously undescribed polymorphism in exon 11(A3557G), which was present in 4 of 100 chromosomes from African-American controls and in none of 46 chromosomes of White controls. We conclude that, at least in our series, African-Americans with early onset breast cancer and strongly positive family histories may carry BRCA1 mutations different from other ethnic groups and that further studies are urgently needed to elucidate the possible role of genetics in producing a worse breast cancer prognosis in this ethnic group.


FASEB Home Page

Appendix B
Budget Justification

Personnel:

Lola Douglas, Data Entry Ms. Douglas has replaced Myrna Welcome to facilitate data acquisition.

Luis Gayol has been hired for the **Laboratory Technician** position.

ALL OTHER PERSONNEL APPROVED AS IN THE ORIGINAL APPLICATION.

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y)

1 JUN 2001

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports. Request the limited distribution statement for reports on the enclosed list be changed to "Approved for public release; distribution unlimited." These reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

PHYLLIS M. RINEHART
Deputy Chief of Staff for
Information Management

Encl

Reports to be changed to "Approved for public release; distribution unlimited"

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