FINAL PROGRESS REPORT
PSYCHOSOCIAL FACTORS ASSOCIATED WITH DELAY IN DIAGNOSIS AMONG LOCALLY ADVANCED BREAST CANCER PATIENTS – A PILOT STUDY

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A. Background and Specific Aims

Early diagnosis and treatment of breast cancer reduces mortality,[1] and delay in presentation of symptomatic disease is associated with poorer survival.[2] Development of strategies to encourage women to promptly seek evaluation of breast symptoms requires better understanding of factors that are associated with patient delays. Although a few informative literature reviews have been published on studies that looked at demographic factors associated with delay in patient presentation with breast disease,[3-5] little research has been published about women's own reasons for delay in diagnosis. To address this issue, we plan to submit a grant application (R01) to the National Cancer Institute for a population-based study of reasons for delay in diagnosis among women with locally advanced breast cancer (LABC) using data from the Iowa Surveillance, Epidemiology and End Results (SEER) program. The proposed R01 also will assess differences in psychosocial and demographic variables between LABC (stages IIB, III, and IV) and non-LABC (stages I and IIA) patients, because we expect these two groups of patients to differ on many of the variables of interest. Results from the R01 should be helpful in developing interventions to encourage earlier detection among women at higher risk for presenting with late-stage breast cancer.

We requested funding from the Longer Life Foundation to conduct a necessary pilot study to strengthen a future R01 application.

The **Specific Aims** of the pilot study were to:

1) test for differences in response (i.e., participation) rates between LABC and non-LABC patients and between two recruitment strategies,

2) test for recall bias by evaluating the correct reporting of mode of detection (abnormal mammogram vs. palpable mass or other breast symptoms), type of surgery (if any), and receipt of radiation therapy, and testing for differences in correct recall between the two recruitment strategies, and

3) pilot the interview measures.

B. Methods

Recruitment. For this pilot study, we recruited women presenting with a breast cancer diagnosis at the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. After we obtained funding from the Longer Life Foundation, the Protocol Review and Monitoring Committee of the Siteman Cancer Center suggested that we increase our sample size from 40 to 60 women. We were fortunate to be able to secure extra funding from the Barnes-Jewish Hospital Foundation to complete the study with the larger sample. We recruited patients for this study from January 2003 until November 2003.

Four groups of women were recruited. Two groups included women with LABC, diagnosed at stages IIB, III, and IV, according to the criteria established by the American Joint Committee on Cancer (AJCC)[6] and women with non-LABC (stages I and IIA breast cancers). Women with prior *in situ* or invasive breast cancers, who were non-English speaking or had cognitive impairments (e.g., from dementia) were excluded. We also compared two recruitment strategies, 4-6 weeks vs. 4-6 months after diagnosis. Thus, one group of LABC patients and one group of non-LABC patients were recruited prospectively and interviewed within 4-6 weeks of being diagnosed. The other two groups of LABC and non-LABC patients were identified from the medical

records, having been diagnosed 4-6 months earlier (which is similar to rapid-reporting system of the Iowa SEER program), and randomly selected for inclusion.

Eligible patients were identified from the Oncology Data Services database (for patients diagnosed 4-6 months ago), the surgical pathology database, or by individual collaborating physicians (for patients diagnosed 4-6 weeks ago). For each patient, regardless of the recruitment strategy being used, the investigators obtained the physician's permission to contact his or her patient prior to mailing a recruitment letter. Thus, recruitment letters signed by the collaborating physician and duplicate Washington University IRB-approved consent documents were sent to prospective participants either 4-6 weeks after diagnosis or 4-6 months after diagnosis. The PI contacted the participating physicians to obtain approval to recruit their patients to the study.

Interviews. Specially trained interviewers obtained informed consent and conducted the telephone interviews using a computer-assisted telephone interview (CaTI) system to interview participants. Participants completed one 45-60 minute telephone interview and were paid $10 for their time.

Questionnaires previously found to be reliable and valid were included in the interviews, such as measures of cognitive impairment to screen women age 65 and over for inclusion,[7] comorbidity,[8]quality of life,[9] depressed mood,[10] state anxiety,[11] trait anxiety,[12] and perceived availability of social support.[13] In addition, we asked participants about demographic characteristics and smoking status using questions from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System (BRFSS), about their cancer treatment and decision making,[14], attitudes toward mammography (perceived barriers and benefits,[15-21] and their experience of physical, sexual, and emotional abuse (available by request), each using scaled-response choices, and about their reasons for seeking evaluation and treatment at the Siteman Cancer Center using open-ended questions. Clinical data, such as AJCC stage and other tumor characteristics, were obtained from patients' medical records and/or Oncology Data Services at Barnes-Jewish Hospital.

Analysis. We used SPSS 12.0 to perform the analyses. A *p*-value at or below 0.05 was considered statistically significant. The distributions of all variables were reviewed to assess the appropriateness of any outliers. Qualitative data (reasons for delay in diagnosis) were analyzed using thematic analysis techniques.[22] Categories of reasons were identified and the frequency of respondents giving reasons fitting into each category was enumerated. The correct reporting of mode of detection, type of surgery, and receipt of radiation therapy (to test recall bias), comparing patient self-report against the medical record, were assessed using the kappa statistic. Kappa coefficients > .80 indicate nearly perfect agreement between raters.[23] Differences in correct reporting between the two recruitment strategies (4-6 weeks vs. 4-6 months after diagnosis) were tested using logistic regression. Response rates were calculated by dividing the number of participants by the number of recruitment letters sent out. Between-groups differences in the psychosocial measures were tested using analysis of variance.

C. Results

We recruited 61 women to participate in this study with an overall participation rate of 59.2%. Response rates were 62.5% for the 4-6 week group, 56.4% for the 4-6 month group, 59.6% for the non-LABC group, and 58.8% for the LABC group. None of the differences in response rates by group were statistically significant.

Among women who participated, 47.5% were married, 65.6% received some college education, 47.5% were employed full or part-time, 23% were unable to work at the time of the interview, 67.2% were white, 32.8% were black, 70.5% had private insurance, and 29.5% had Medicaid. Mean age ± SD of the sample was 54.57 ± 10.23 (range 38 to 89).

There were no statistically significant differences between the women who participated and those who did not participate by recruitment strategy, extent of disease (i.e., LABC vs. non-LABC), race, marital status, or

type of insurance (Table 2). Participants were younger on average compared to non-participants (mean age ± SD 54.57 ± 10.23 vs. 59.64 ± 12.97, respectively; p = .029).

Table 2. Comparison of Participants to Non-participants

	Participants	Non-participants	p
Recruitment strategy [n (%)]			
Prospective group	30 (49.2)	18 (42.9)	.527
4-6 month group	31 (50.8)	24 (57.1)	
Stage of disease			
Early stage	31 (50.8)	21 (50.0)	.935
LABC	30 (49.2)	21 (50.0)	
Marital status			
Married	32 (55.2)	24 (57.1)	.845
Not married	26 (44.8)	18 (42.9)	
Race			
White	41 (67.2)	27 (64.3)	.475
African-American	20 (32.8)	14 (33.3)	
Asian	0	1 (2.4)	
Type of insurance			
Private	43 (70.5)	32 (76.2)	.523
Medicaid/Medicare only	18 (29.5)	10 (23.8)	

Table 3. Participant Characteristics by Recruitment Strategy

	Prospective	4-6 month	p
Age (m ± sd)	54.53 ± 8.62	54.61 ± 11.72	. 976
Employment status			
Not employed	14 (51.9)	14 (46.7)	.696
Employed full or part-time	13 (48.1)	16 (53.3)	
Marital status			
Married	16 (53.3)	13 (41.9)	.373
Not married	14 (46.7)	18 (58.1)	
Race			
White	19 (63.3)	22 (71.0)	.525
African-American	11 (36.7)	9 (29.0)	
Asian	0	0	
Education			
No college	11 (36.7)	10 (32.3)	.717
Some college	19 (63.3)	21 (67.7)	

Among women who participated, there were no statistically significant differences in race, age, marital status, education, or employment status by either recruitment strategy or extent of disease (Tables 3 and 4).

Table 4. Participant Characteristics by Extent of Disease

	Early stage	LABC	p
Age (m ± sd)	54.84 ± 9.98	54.30 ± 10.64	. 839
Employment status			
Not employed	14 (46.7)	14 (51.9)	.696
Employed full or part-time	16 (53.3)	13 (48.1)	
Marital status			
Married	15 (48.4)	14 (46.7)	.893
Not married	16 (51.6)	16 (53.3)	
Race			
White	19 (61.3)	22 (73.3)	.316
African-American	12 (38.7)	8 (26.7)	
Education			
No college	9 (29.0)	12 (40.0)	.367
Some college	22 (71.0)	18 (60.0)	

No statistically significant differences in the psychosocial variables were observed between the two recruitment strategies (Table 5) or the two extent-of-disease groups (Table 6).

Table 5. Differences in Psychosocial Variables by Recruitment Strategy

	Prospective	4-6 month	p
MOS Perceived Social Support	4.42 ± .42	4.17 ± .88	. 161
Beck Anxiety Scale	12.30 ± 8.89	11.06 ± 9.44	.601
STAI Trait Anxiety	35.33 ± 10.68	36.19 ± 13.93	.788
FACT-B	105.07 ± 21.09	103.10 ± 25.03	.741
CES-D	13.10 ± 11.15	11.68 ± 13.20	.651

Table 6. Differences in Psychosocial Variables by Extent of Disease

	Early stage	LABC	p
MOS Perceived Social Support	4.43 ± .57	4.15 ± .80	. 115
Beck Anxiety Scale	11.52 ± 8.86	11.83 ± 9.52	.893
STAI Trait Anxiety	36.58 ± 10.68	34.93 ± 14.00	.606
FACT-B	104.03 ± 20.01	104.10 ± 26.09	.991
CES-D	12.68 ± 11.48	12.07 ± 13.00	.846

No statistically significant differences were found for correct recall of either surgery type or receipt of radiation therapy by recruitment method (Table 7) or extent of disease (Table 8).

Table 7. Correct Recall by Recruitment Method and Extent of Disease

	Correct recall	
	Surgery type	Receipt of radiation
Recruitment method	(p=.144)	(p=.288)
Prospective group	28/30 (93.3%)	30/30 (100%)
4-6 month group	31/31 (100%)	26/27 (96.3%)*

Table 8. Correct Recall by Extent of Disease

	Correct recall	
	Surgery type	Radiation
Extent of Disease	(p = .981)	(p = .288)
Early stage	30/31 (96.8%)	30/30 (100%)
LABC	29/30 (96.7%)	26/27 (96.3%)*

*Responses for 4 of the women were excluded from the recall of radiation analysis because we were not able to get radiation data from their physicians.

Twenty (15.6%) women reported that they received radiation therapy. Among those who did not receive radiation, seven (5.5%) said their doctor recommended against it, six (4.7%) selected an alternative treatment, and 11 (8.6%) had a mastectomy. (Respondents could report more than one reason for not receiving radiation therapy.) Twenty-eight women (21.9%) had not yet started their radiation.

We asked the women their reasons for seeking medical attention when they did. Twenty-four women (39.3%) said it was because they felt a lump, and nine (14.8%) had positive mammograms. Similarly, 16 (26.2%) sought medical attention because they wanted to know what was going on. Seven women (11.5) said it was because they had family history of breast cancer, six (9.8%) said they were encouraged to seek medical attention, four (6.6%) said they were afraid, one (1.6%) said it was because of her children, and one (1.6%) said she could afford to seek treatment at that time. There were no statistically significant differences by recruitment strategy as to whether women sought medical attention because of a lump (p = .674) or because of mammogram results (p = .256). Because of the variety of responses to this question, some omitting crucial information about the history behind their response (e.g., wanting “to know what was going on” or being “afraid” without explaining whether or not they felt a lump or had an abnormal clinical breast exam or screening mammogram), we know that we will have to probe for the responses that are of interest to us in future studies.

When asked if they could have sought medical attention sooner, 23 (37.7%) of the women said yes. The most frequent reasons (each reason reported by six women) for delaying were denial, other life events happening at the same time, and not having symptoms/having negative mammograms. Three women reported lack of money as a reason. Two reported fear, two reported lack of knowledge about what to do, and two reported having fibroids in their breasts as reasons for delaying diagnosis. There were no statistically significant differences by recruitment strategy in whether or not women delayed seeking treatment ($p = .716$).

D. Discussion

Data from the pilot study regarding participation rates will be used to plan our recruitment for the larger study. The pilot study data also helped us determine that we could recruit cancer patients 4-6 months after their diagnosis and have confidence in patients' recall of events pertaining to their care. Since we did not find statistically significant differences in recall between the prospectively recruited patients and the patients recruited 4-6 months after diagnosis, we plan to submit a grant application (R01) to the National Cancer Institute for a population-based study of reasons for delay in diagnosis among women with locally advanced breast cancer (LABC) recruiting cases identified from the Iowa SEER program, using their rapid-case-ascertainment process, which identifies new cases 3 to 6 months after diagnosis. The proposed R01 will assess reasons for delay in diagnosis and predictors of delay in diagnosis in women with LABC (stages IIB, III, and IV) from among psychosocial, clinical, and demographic variables. In addition, we will compare measures of these variables between women with LABC and women with early-stage breast cancer. We are particularly interested in identifying stable psychological (trait) variables that may differ between these two groups of women. Results from the R01 should be helpful in developing interventions to encourage earlier detection among women who we find may be at higher risk of presenting with late-stage breast cancers.

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References

1. Nystrom L, Andersson I, Bjurstam N, Frisell J, Nordenskjold B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. *Lancet* 2002;359:909-919.
2. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999;353:1119-1126.
3. Caplan LS, Helzlsouer KJ. Delay in breast cancer: a review of the literature. *Public Health Reviews* 1992/1993;20:187-214.
4. Facione NC. Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. *Social Science and Medicine* 1993;36:1521-1534.
5. Ramirez AJ, Westcombe AM, Burgess CC, Sutton S, Littlejohns P, Richards MA. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. *Lancet* 1999;353:1127-1131.
6. American Joint Committee on Cancer. *Manual for staging of cancer*. Philadelphia: AJCC/JB Lippincott; 1992.
7. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short Orientation-Memory-Concentration test of cognitive impairment. *American Journal of Psychiatry* 1983;140:734-739.

8. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Medical Care* 1996;34(1):73-84.
9. Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the functional assessment of cancer therapy-breast quality of life instrument. *Journal of Clinical Oncology* 1997;15:974-986.
10. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1:385-401.
11. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology* 1988;56:893-897.
12. Spielberger CD. *Manual for the State-Trait Anxiety Inventory STAI (Form Y)*. Palo Alto, CA: Mind Garden; 1983.
13. Sherbourne C, Stewart A. The MOS social support survey. *Social Science and Medicine* 1991;32:705-714.
14. Andersen MR, Urban N. Involvement in decision-making and breast cancer survivor quality of life. *Annals of Behavioral Medicine* 1999;21:201-209.
15. Aiken LS, West SG, Woodward CK, Reno RR. Health beliefs and compliance with mammography-screening recommendations in asymptomatic women. *Health Psychology* 1994;13:122-129.
16. Champion VL. Instrument development for health belief model constructs. *Advances in Nursing Science* 1984;6:73-85.
17. Champion VL. Instrument refinement for breast cancer screening behaviors. *Nursing Research* 1993;42:139-143.
18. Skinner CS, Arfken CL, Sykes RK. Knowledge, perceptions, and mammography stage of adoption among older urban women. *American Journal of Preventive Medicine* 1998;14:54-63.
19. Skinner CS, Champion VL, Gonin R, Hanna M. Do perceived barriers and benefits vary by mammography stage. *Psychology, Health & Medicine* 1997;2:65-75.
20. Bryant H, Mah Z. Breast cancer screening attitudes and behaviors for rural and urban women. *Preventive Medicine* 1992;21:405-418.
21. Haiart DC, McKenzie L, Henderson J, et al. Mobile breast screening: Factors affecting uptake, efforts to increase response and acceptability. *Public Health* 1990;104:239-247.
22. Miles MB, Huberman AM. *Qualitative data analysis*. Beverly Hills, CA: Sage; 1984.
23. Landis J, Koch G. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159-174.