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14. ABSTRACT Our primary objective was to identify the issues that are of greatest concern to women in each of three treatment stages: newly diagnosed with ovarian cancer, in-treatment, and post-treatment. The CARES-SF and FACT-O questionnaires were administered to participants following diagnosis and prior to chemotherapy (baseline), during chemotherapy, following chemotherapy, and after recurrence. Data for the study was collected through mailed questionnaires and telephone follow-up from women treated at the Wake Forest University Baptist Medical Center (WFUBMC) and Forsyth Medical Center (FMC). A total of 89 women participated in the study. Quality of life was worse at baseline and improved over time. Physical problems were the greatest problem area and were highest at baseline and improved during treatment. Data collection for the study will last 28 months (patient accrual will last 25 months and follow-up will continue an additional 3 months).					
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PART I - INTRODUCTION

This study focuses on quality of life among women with ovarian cancer. The primary objective is to identify the issues that are of greatest concern to women in each of three treatment stages: newly diagnosed with ovarian cancer, in-treatment, and post-treatment. A combined cross-sectional and longitudinal, repeated measures design is being used to assess problem areas and quality of life from diagnosis to recurrence among women newly diagnosed with ovarian cancer. The CARES-SF and FACT-O questionnaires are administered to participants following diagnosis and prior to chemotherapy, during chemotherapy, following chemotherapy, and after recurrence.

Data for the study are collected through in-person interviews, and mailed questionnaires from women treated at the Wake Forest University Baptist Medical Center (WFUBMC) and Forsyth Medical Center (FMC).

Secondary objectives are of the study: 1) to assess changes in quality of life (as quantified by the FACT-O questionnaire) across the different stages of care, 2) to determine which patient characteristics are predictive of quality of life at each treatment stage, 3) to determine which patient characteristics are predictive of changes in quality of life across the different treatment stages, and 4) to obtain pilot data on problems and quality of life issues for women who experience a recurrence.

PART II – BODY: STATEMENT OF WORK

The primary activities during the first year of the study were to obtain Human Subjects Protection approval from the Department of Defense, finalize study forms, and pilot the study. In August 2002 study recruitment began, but we quickly realized that we needed to change the procedure for questionnaire administration. We realized that instead of having patients complete baseline questionnaires while they were still in the hospital, it would be better to have these questionnaires mailed to patients after their discharge. A request to change the protocol was submitted to HSRRB in September 2002, but we did not receive approval for this change until May 16, 2003. Therefore, much of the time during previous reporting periods was spent waiting for approval from HSRRB for our change in protocol. This delay had a significant impact on our recruitment and ability to conduct the study within the specified timeframe.

During the time we were waiting for the above approval, it also became clear that we needed to add an additional study site. We contacted Forsyth Medical Center (FMC) and they were agreeable to becoming a site. The protocol amendment to request this additional site was submitted to the Office of Human Subjects Protection on 3/14/03, but was not approved until February 2004.

Because we were still concerned about recruiting sufficient numbers of patients to the study, we sought approval to revise our recruitment strategy. We sought to expand the time frame to allow recruitment of women with newly diagnosed ovarian cancer to be recruited up to a month past discharge from the hospital. This request was submitted to the Office of Human Subjects Protection on May 25, 2006 but was not approved until December 28, 2006.

The tasks described in the original statement of work have not changed. However, time involved in obtaining Human Subjects approval from the Department of Defense was not included as part of the original timeline. These approvals took an enormous amount of time and essentially moved the timeline back over almost two years.

Task 1: Develop research protocol (months 1-2)

- a. Compile open-ended questions, relevant questionnaires, and sociodemographics in an interview format
- b. Train study interviewer
- c. Pilot test interview with patients

- d. Finalize questionnaire based on pilot

The above tasks have all been completed

Task 2: Develop data management system (months 1-2)

- a. Develop data management requirements
- b. Develop reporting requirements
- c. Develop contact record
- d. Train research staff to use DMS

The above tasks have all been completed.

Task 3: Identify, recruit, and interview patients who meet eligibility criteria (months 3-40)

- a. Identify eligible patients
- b. Recruit and interview patients
- c. Conduct quality control of interviews
- d. Develop data entry system
- e. Transcribe and code open-ended interviews
- f. Abstract clinical data from charts
- g. Data entry of questionnaires

The above tasks have all been completed

Task 4: Ongoing Follow-up of Patients (months 6-40)

- a. Track women previously interviewed
- b. Interview women at appropriate treatment stages
- c. Interview recurrent cases

The above tasks have all been completed.

Task 5: Data analysis and report writing (months 41-48)

- a. Transfer data into SAS
- b. Clean data and generate codebooks
- c. Analyze data from interviews
- d. Present results at professional meeting
- e. Prepare initial manuscripts

Tasks a and b have been completed. We are currently working on tasks c-e.

Task 6: Develop interventions that can be tested in future research (month 36)

- a. Review findings and develop ideas for interventions
- b. Plan interventions for future trials

We are still working on this task

PART III - KEY RESEARCH ACCOMPLISHMENTS

- Finalization of study forms
- Obtaining human subjects protection approval
- Recruitment of study participants
- Initial data analysis

PART IV - REPORTABLE OUTCOMES

Sample

Seventy-two women with stage 1-4 ovarian cancer, accrued between 6/03 and 4/07 completed questionnaires at baseline (within 3 months of diagnosis), during treatment (between 3 and 7 months following diagnosis), early post treatment (between 7 months and 2 years post-diagnosis), and/or late post-treatment (more than 2 years post-diagnosis). Four of these women only provided data at recurrence and are excluded from the analysis, leaving 68 women in the analysis. These women completed 38 baseline, 29 in-treatment, 22 early post-treatment, and 14 late post-treatment questionnaires.

Characteristics of the 68 women are shown in Table 1. Ages ranged from 30 to 86 with a median of 59 years. The majority (88%) of women were white, 57% were married or living in a married-like relationship, 50% had at least some college education, and 42% found it hard to pay for the basic necessities. Almost half of the women had hypertension and between 15% and 26% had pulmonary, psychiatric, arthritis, or cardiac conditions; 71% had at least one medical condition at baseline. Eighty-four percent of the women were stage 3 or 4, and most received two or more chemotherapy drugs.

Measures

Outcomes

Quality of Life. Quality of Life was measured by the Functional Assessment of Cancer Therapy for Ovarian Cancer (FACT-O) scale. The FACT-O consists of a generic core questionnaire called the FACT that is a 27-item compilation of general questions divided into four primary QOL domains: Physical Well-Being (PWB), Social/Family Well-Being (SWB), Emotional Well-Being (EWB), and Functional Well-Being (FWB). The FACT is considered appropriate for use with patients with any form of cancer. An additional subscale, called "Ovarian Additional Concerns" (OAC) contains 12 items that address issues specific to ovarian cancer. The FACT-O yields five subscale scores and an overall quality of life score (FACT-O).

Problem areas. Current problem areas were assessed with the Cancer Rehabilitation Evaluation System Short Form. The CARES-SF is a multidimensional self-administered instrument where patients rate each problem statement on a 5-pt. scale where 0 represents "not at all" to 4 representing "very much" The following problem areas were assessed: (1) Physical: the physical changes and disruption of daily activities caused by the disease or treatment; (2) Pain; (3) Medical Interaction: problems interacting and communicating with the medical team; (4) Marital: problems associated with a significant marital-type relationship; and (5) Psychosocial: psychosocial issues, communication, and relationship problems (other than partner's problems).

Covariates

Social Support. The RAND Social Support Scale was used to measure respondents' evaluation of the functions and resources provided by their social network. The scale is based on four categories of support: emotional support, tangible support, informational support, and appraisal support.

Optimism. The Life Orientation Scale was used to measure optimistic outlook.

Medical History. Chart reviews were conducted on all patients. Data collected included comorbidities, date of diagnosis, cancer stage, type of chemotherapy, type of surgery, and CA125 levels.

Sociodemographics included questions on age, race, education, marital/partner status, and ability to pay for basics.

Analyses

Mixed models for longitudinal repeated measures were used to assess changes in quality of life over time and to assess the effect of patient covariates on change. Age is included in all models. The four time periods (baseline, in-treatment, early post, and late post) were treated categorically and an unstructured covariance matrix was used to model the within patient correlation over time.

Results

Quality of Life

Quality of life over time. Predicted means, adjusted for age, for the FACT at each timepoint are shown in Table 2. As can be seen in this table, all domains except social functioning improved significantly as time from diagnosis increased. Of particular note, the FACT-OAC increased by approximately 26 points between baseline and late post treatment (25% improvement compared to baseline). The time period between diagnosis and treatment showed the greatest improvement.

Impact of covariates. Table 3 summarizes the associations between patient covariates and quality of life. There were main effects for age, difficulty paying for basics, social support and optimism. Social support was significantly associated with better QOL on all domains and optimism was positively related to all domains except social well-being. Not having trouble paying for basics was related to better QOL on all domains except PWB. Age was positively related to better PWB, ovarian-specific concerns, and overall FACT-O.

Table 4 shows the interactions between each covariate and time. The most notable interaction was number of comorbidities and time such that women with none or only one comorbidity showed improvement over time from diagnosis, while those with more (2+) comorbidities improved initially and then leveled off (Figure 1). Other interactions of note are shown in Figures 2 and 3. The emotional well-being of patients with more education (at least some college) improved faster than those with less education (high school graduate or less). Both groups ended up with similar emotional well being scores after two years. Those with high social support were doing better at late post treatment (Figure 3).

Problems

Problems over time. Table 5 shows the number of problems over time, as measured by the CARES. At the time of diagnosis, physical problems were the greatest, followed by psychosocial problems. Interacting with medical professionals were the least problematic. All problem areas, except interacting with medical professionals, significantly decreased over time, with the time from baseline to in treatment showing the greatest decline. Of note, the number of physical problems decreased from 1.78 at baseline to 0.76 during the late follow-up period, a 57% decrease. Interacting with medical professionals was the only problem area that showed a slight increase among women at late post treatment.

Impact of covariates. Table 6 shows the main effect of each covariates and problem area. Social support and optimism were significantly related to problems with greater social support and optimism associated with fewer problems. Older women reported fewer physical, pain, and psychosocial problems while women with

more comorbidities reported more physical and pain problems. Patients who did not have trouble paying for basics had fewer problems with pain, medical interactions, and psychosocial problems

Table 7 shows the interactions between each covariate and time for each problem area. Patients who had problems paying for basics had more marital problems at baseline and beyond two years of follow-up than those who have no problems paying for the basics. However, during treatment and early follow-up, marital problems are similar for the two groups (figure 4).

Table 1. Summary of patient characteristics for patients with QOL data at baseline, in treatment, early follow-up, or late follow-up (n=68)

Characteristic	(%)	N
Age – Median (Range)	30- 86	(59)
Race		
White	88	(60)
Asian/Pacific Islander	1	(1)
Black	9	(6)
Hispanic	1	(1)
Marital Status		
Widowed	19	(13)
Never married	9	(6)
Presently married	50	(34)
Marriage-like relationship	7	(5)
Divorced/Separate	15	(10)
Education		
High school graduate or less	50	(31)
> HS graduate, < College graduate	29	(18)
College graduate or beyond	21	(13)
Pay for Basics		
Very hard	18	(11)
Somewhat hard	23	(14)
Not very hard at all	58	(35)
Medical Problems		
Hypertension	46	(31)
Cardiac	2	(18)
Arthritis	16	(11)
Psychiatric	15	(10)
Pulmonary	15	(10)
Thyroid	13	(9)
Diabetes	9	(6)
Number of Comorbidities		
0	29	(20)
1	29	(20)
2	24	(16)
3+	17	(12)
Cancer Stage		
1	12	(8)
2	4	(3)
3	75	(51)
4	9	(6)
Chemotherapy Agent		
Carboplatin	81	(55)
Taxol	72	(49)
Gemzar	9	(6)
Topotecan	3	(2)
Doxil	1	(1)
Other	32	(22)
Number of Chemotherapy Agents		
0	3	(2)
1	18	(12)
2	57	(39)
3+	22	(15)

Table 2. FACT-O least squares means and standard errors from mixed model ANOVA. All Models include age.

	Baseline	In Treatment	Early Post	Late Post	Time Effect p-value	Contrast p-values*
PWB	16.3 (1.1)	19.0 (1.1)	21.2 (1.2)	23.8 (1.5)	.001 (a,b,c,e)	.011 / <.001
SWB	24.0 (0.7)	24.4 (0.5)	25.2 (0.5)	24.3 (1.6)	.118	.638 / .522
EWB	16.8 (0.7)	18.4 (0.6)	18.6 (0.8)	20.5 (1.1)	.005 (a,b,c)	.132 / .007
FWB	15.6 (0.8)	18.7 (1.0)	20.0 (1.2)	23.1 (1.5)	<.001 (a,b,c,e)	.029 / <.001
FACT	72.4 (2.6)	80.0 (2.5)	84.8 (3.1)	91.8 (4.8)	.001 (a,b,c,e)	.018 / <.001
OAC	30.6 (1.3)	36.0 (0.9)	37.7 (1.1)	39.1 (1.8)	<.001 (a,b,c)	.072 / <.001
FACT-OAC	102.8 (3.7)	116.0 (3.2)	122.7 (4.0)	130.8 (6.5)	<.001 (a,b,c,e)	.023 / <.001

a – baseline vs in treatment; b – baseline vs early post 3; c – baseline vs late post; d – in treatment vs early post; e – in treatment vs late post; f – early post vs late post

* Contrasts – early + late vs in treatment / early + late vs in treatment + baseline

Table 3. Main effect of Covariates on FACT scores.

Covariate	PWB	SWB	EWB	FWB	FACT	OAC	FACT-OAC
Age	.004+	.080	.063	.082	.007+	.006+	.006+
Marry	.718	.786	.938	.157	.508	.683	.443
Education	.446	.424	.470	.906	.893	.454	.843
Pay Basic	.372	<.001+	.020+	<.001+	.002+	.023+	.003+
# comorbidities	.001-	.096	.785	.147	.052	.005-	.012
Stage	.198	.552	.632	.204	.228	.435	.259
# Chemo Agents	.907	.421	.766	.502	.965	.364	.864
CA125 > 22	.223	.227	.358	.555	.872	.544	.980
Social Support	<.001+	.004+	.002+	.001+	<.001+	.001+	<.001+
Optimism	.003+	.550	<.001+	.001+	<.001+	.004+	<.001+

A '+' beside the p-value indicates higher levels of the covariate are associated with larger outcomes (good or bad); a '-' beside the p-value indicates higher levels of the covariate are associated with worse outcomes. All models include age as a covariate.

Table 4. Interaction between each covariate and time by FACT domain.

Covariate	PWB	SWB	EWB	FWB	FACT	OAC	FACT-OAC
Age	.934	.040	.388	.613	.854	.924	.956
Married	.299	.839	.042	.088	.081	.597	.163
Education	.823	.234	.012	.298	.202	.960	.474
Pay Basics	.189	.498	.707	.387	.457	.337	.336
# comorbidities	.010	.384	.195	.100	.033	.018	.034
Stage	.311	.714	.228	.719	.425	.897	.539
# Chemo Agents	.938	.624	.233	.731	.914	.921	.861
CA125 > 22	.201	.067	.293	.109	.123	.085	.082
Social Support	.001	.224	.379	.328	.056	.303	.089
Optimism	.058	.275	.893	.622	.652	.838	.698

P-values for testing the time*covariate interaction (i.e., does the recovery over time depend on the covariate). All models include age as a covariate.

Table 5. CARES least squares means and standard errors from mixed model ANOVA. All Models include age.

Measure	Baseline	In Treatment	Early Post	Late Post	Time Effect p-value	Contrast p-values*
Physical	1.79 (0.15)	1.31 (0.14)	0.99 (0.14)	0.72 (0.18)	<.001 (a,b,c,e)	.010 / <.001
Pain	1.03 (0.14)	0.66 (0.13)	0.56 (0.13)	0.44 (0.19)	.010 (a,b,c)	.320 / .010
Med Interactions	0.63 (0.12)	0.34 (0.08)	0.28 (0.09)	0.53 (0.28)	.064	.689 / .486
Marital	0.96 (0.16)	0.51 (0.12)	0.62 (0.13)	0.75 (0.34)	.020 (a,b)	.395 / .804
Psychosocial	1.23 (0.12)	0.98 (0.11)	0.98 (0.13)	0.63 (0.20)	.018 (a,c)	.198 / .032

a – baseline vs in treatment; b – baseline vs early post 3; c – baseline vs late post; d – in treatment vs early post; e – in treatment vs late post; f – early post vs late post

* Contrasts – early + late vs in treatment / early + late vs in treatment + baseline

Table 6. Main Effect of Covariates on CARES Scores.

Covariate	Physical	Pain	Med Interactions	Marital	Psycho Social
Age	.042-	.001-	.486	.611	.034-
Married	.601	.813	.939	.370	.506
Education	.570	.901	.839	.129	.577
Pay Basics	.180	.007-	.004-	.147	.008-
# Comorbidities	<.001+	.003+	.240	.152	.124
Cancer Stage	.077	.102	.732	.616	.064
# Chemo Agents	.465	.574	.980	.234	.224
CA125 > 22	.404	.345	.303	.867	.279
Social Support	.048-	.087	.008-	.040-	.018-
Optimism	.051-	.035-	.070	.013-	<.001-

A '+' beside the p-value indicates higher levels of the covariate are associated with larger outcomes (good or bad); a '-' beside the p-value indicates higher levels of the covariate are associated with worse outcomes. All models include age as a covariate.

Table 7. Interaction of each covariate and time on CARES problems.

Covariate	Physical	Pain	Med Interact	Marital	Psycho Social
Age	.829	.426	.827	.891	.780
Married	.423	.960	.302	.849	.013
Education	.995	.118	.184	.466	.262
Pay Basic	.001	.064	.721	<.001	.367
# Comorbidities	.082	.203	.614	.079	.176
Cancer Stage	.925	.090	.419	.892	.959
# Chemo Agents	.927	.690	.034	.150	.914
CA125 > 22	.041	.218	.491	.877	.380
Social Support	.238	.544	.104	.284	.279
Optimism	.210	.205	.335	.018	.966

P-values for testing the time*covariate interaction (i.e., does the recovery over time depend on the covariate). All models include age as a covariate.

Figure 1. Interaction between number of medical problems and time since diagnosis for FACT-OAC. Patients with fewer (0-1) medical problems continued to improve over time while those with more (2+) medical problems improved initially and then leveled off.

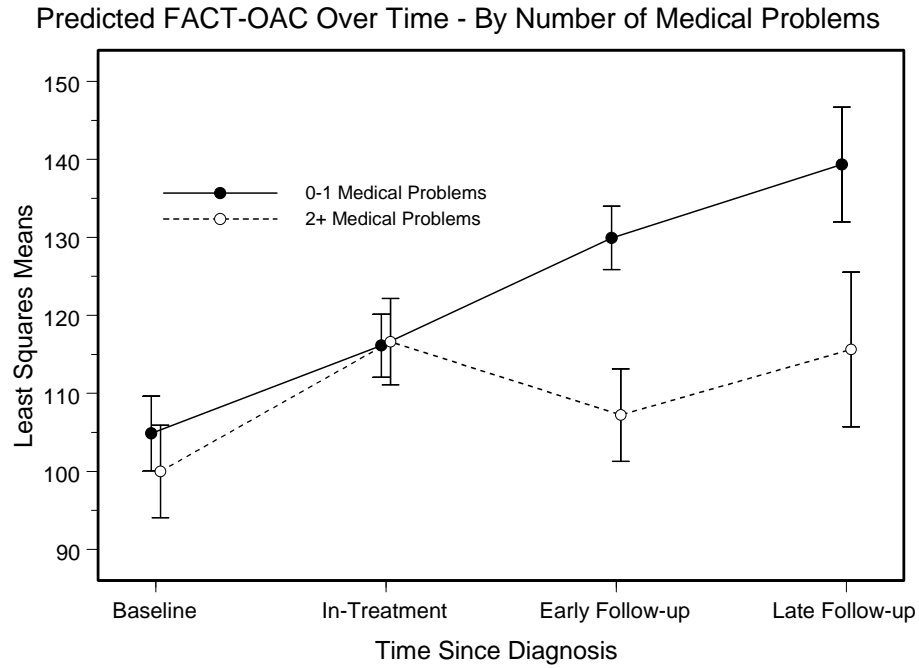


Figure 2. Interaction between education and time since diagnosis for FACT-EWB. Patients with more education (at least some college) improved faster than those with less education (high school graduate or less). Both groups ended up with similar emotional well being scores after two years.

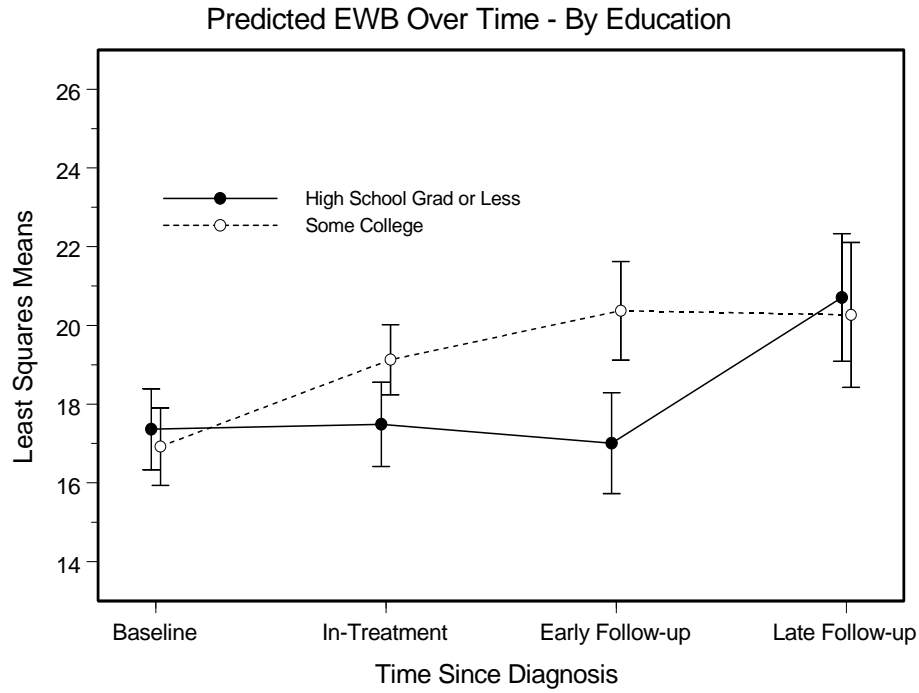


Figure 3. Interaction between social support and time since diagnosis for FACT-EWB. Patients with more social support showed greater PWB at late follow-up.

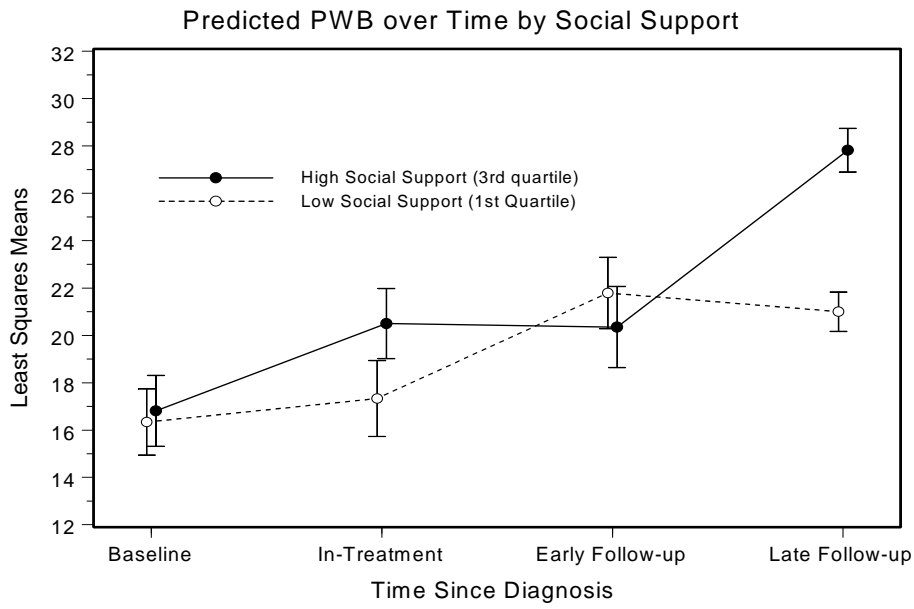
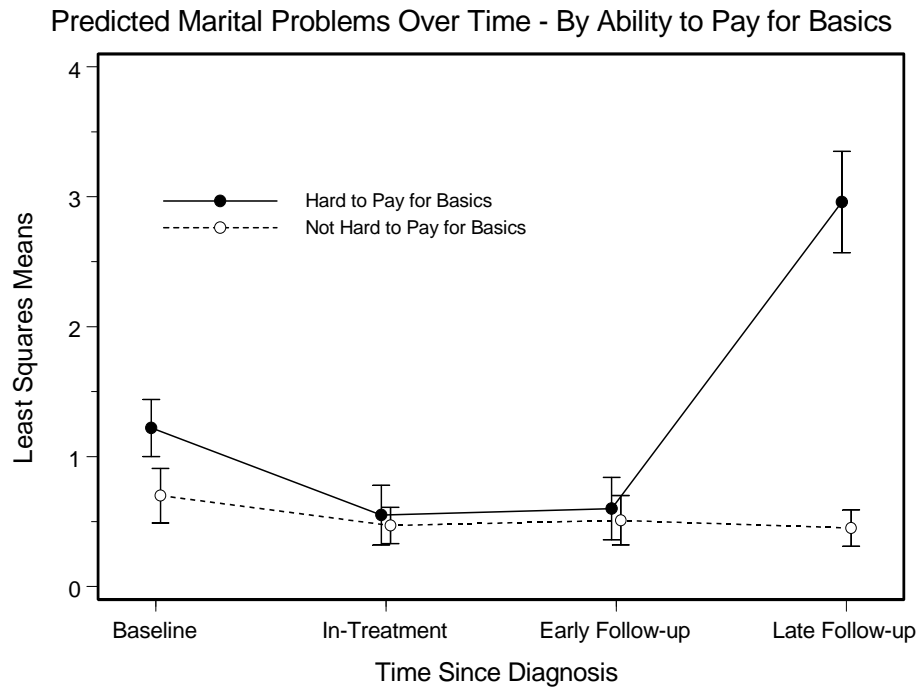


Figure 4. Interaction between pay basics and time since diagnosis for marital problems. Patients who have problems paying for the basics have more marital problems at baseline and beyond two years of follow-up than those who have no problems paying for the basics. However, during treatment and early follow-up, marital problems are similar for the two groups.



PART V - CONCLUSIONS

Interventions to improve QOL among women with ovarian cancer would best be targeted to the time period immediately following diagnosis. Women who have 2 or more comorbidities are at greatest risk for lower QOL and should be targeted for interventions. Social support serves as a protective factor for better QOL and fewer problems

PART VI - REFERENCES

Not applicable