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Clinician Perceptions of Care Difficulty, Quality of Life, and Symptom Reports for Lung Cancer Patients: An Analysis from ECOG E2Z02 (Symptom Outcomes and Practice Patterns; SOAPP)

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Abstract

Introduction—Despite recent therapeutic advances, lung cancer is a difficult disease to manage. This study assessed clinicians' perceptions of care difficulty, quality of life (QOL), and symptom reports for their lung cancer patients compared to their patients with breast, prostate and colon cancer.

Materials and Methods—This report focused on secondary analyses from the ECOG Symptom Outcomes and Practice Patterns (SOAPP) study (E2Z02); outcome measures included clinician ratings of 3106 solid tumor patients. Univariate analyses focused on patterns of disease-specific perceptions; multivariable analyses examined whether disease-specific differences persisted after covariate inclusion.

Results—In univariate comparisons, clinicians rated lung cancer patients as more difficult to treat than other solid tumor patients, with poorer QOL and higher symptom reports. After adjusting for covariates, odds of clinicians perceiving lower QOL for their lung cancer patients were 3.6 times larger than for patients with other solid tumors (OR = 3.6 [95% CI, 2.0 to 6.6], p < 0.0001). Clinicians also perceived weight difficulties 3.2 times more for lung cancer patients (OR = 3.2 [95% CI, 1.7 to 6.0], p = 0.0004). No other outcome showed significant lung versus other differences in multivariable models.

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A portion of these data were presented at the American Society of Clinical Oncology (ASCO) annual meeting in 2010.

Discussion—Clinicians were more pessimistic about the well-being of their lung cancer patients compared to patients with other solid tumors. Differences remained for clinician perceptions of patient QOL and weight difficulty, even after controlling for such variables as stage, performance status, and patient-reported outcomes. These continuing disparities suggest possible perception bias. More research is needed to confirm this disparity and explore the underpinnings.

Introduction

Despite recent advances in early diagnosis and treatment (e.g., CT-based screening, molecular testing, increased efficacy of multimodal therapies), lung cancer remains a difficult disease to manage. Clinicians who treat lung cancer often encounter late stage diagnoses, poor outcomes, treatment toxicities, multiple comorbidities, behavioral risk factors, and complicated symptom burdens.^{1–3} Based on this complexity, clinicians might consider their individual lung patients to be more difficult to treat, have poorer quality of life (QOL), and have more troubling symptoms compared to their patients with other solid tumors. However, little empirical work has actually compared clinician assessments across disease sites; it is unclear how clinicians perceive their lung cancer patients compared to other patient groups.

If clinicians indeed have more pessimistic views of lung cancer patients, do these perceptions accurately reflect their patients' well-being or might perception bias play a role? In other words, might these negative perceptions over-generalize so that clinicians anticipate treatment difficulty, poor OOL, and higher symptom reports for individual lung cancer patients? The concept of "therapeutic nihilism" has described this phenomenon and been used to explain variations in management of lung cancer patients.^{4,5} In addition to the impact on clinician perceptions of lung cancer patients, nihilistic attitudes may bias treatment decisions, limit patient access to evidence-based medicine, and reduce offers of clinical trials.^{6–10} Despite commentaries and indirect links with data, nihilistic attitudes in lung cancer have only been sparsely addressed in empirical research.¹¹ To truly demonstrate the possibility of nihilism specific to lung cancer, it is useful to compare across different cancers and show that perception and treatment disparities remain in absence of clinical differences. One approach involves vignette studies that present identically staged case scenarios to clinicians. For example, a study of referral decisions among primary care physicians compared responses to identically staged case scenarios of breast and lung cancer.¹² Results indicated that primary care physicians were less likely to refer the advanced stage lung cancer patient for further treatment and were also less likely to closely monitor her for uncontrolled pain. It was suggested that these findings may have been driven by physician nihilism and perceptions of lung cancer as an untreatable disease.

Despite preliminary evidence of perception disparities from commentaries and vignette studies, we are unaware of assessments for potential bias and nihilism that include clinicians' views of cancer patients under their care. Such assessments within actual care settings are more difficult to interpret, based on diversity of patient presentations within and across disease types. However, the ability to statistically control for explanatory variables, such as cancer stage, performance status (PS), and patient-reported QOL and symptom reports, allows greater understanding of potential perception differences and serves the

foundation of the present analyses. Specifically, the goal of the current study was to assess clinician responses to their lung cancer patients compared to their patients with breast, prostate and colon cancer. In particular we assessed clinicians' perceptions of: 1) care difficulty, 2) quality of life, and 3) symptom reports for patients under their care. We first examined overall patterns of disease-specific perceptions, to assess whether lung cancer patients were judged differently by their clinicians than patients with other solid tumors. We hypothesized that clinicians would report their lung cancer patients were more difficult to care for, had worse quality of life, and had more symptom difficulties than patients with other solid tumors. To further investigate the possibility of nihilism and perception bias, we explored whether disease-specific differences persisted after the inclusion of other explanatory covariates (including stage, PS, and patient reports).

Materials and Methods

Information about ECOG SOAPP study (E2Z02)

This report focuses on secondary analysis of data from the ECOG Symptom Outcomes and Practice Patterns (SOAPP) study (E2Z02). In this study, patients with breast, colorectal, prostate, or lung cancer were enrolled from outpatient oncology clinics at any point in their care. The primary objective of the SOAPP study was to use cancer patient and clinician reports to describe the prevalence, severity, and interference of symptoms. This study was conducted in 38 institutions and enrolled 3123 patients between March 2006 and May 2008. Further study details can be found on the study website (www.ecogsoapp.com) and from the initial published manuscript.¹³

Measures

Although many variables in the SOAPP study were measured twice (at Initial and 4–5 week Follow-up visits), primary data analysis only included assessments from the initial visit. All outcome measures were from forms completed at the initial assessment by each patient's treating clinician (Clinician Forms). Covariates were collected from both Clinician and Patient Forms administered at the initial visit. Study aims focused on clinician-rated items that assessed 1) care difficulty, 2) quality of life, and 3) symptom reports (problems related to comorbidities, cancer, treatment, medication, weight change; see Table 1). Post-hoc analyses from the follow-up assessment were conducted only for variables that had significant effects in the multivariable analysis at the initial visit.

Statistical Analysis

Frequency and percentages were reported for each variable. Differences in patient and disease characteristics among groups were compared using Chi-square tests. All outcome variables were assessed on a 5-point ordinal scale. Univariate and multivariable cumulative logit models were fitted using generalized estimating equations to test the disease site effect for each outcome variable, with the worse ratings of each outcome variable being modeled. The main independent variable of disease site was fitted into the model with four levels, with a prior contrast on lung vs. the other 3 (breast, colorectal, prostate) combined. If the disease site effect was significant, a post-hoc comparison with family-wise error rate at 0.05 (using the Bonferroni correction, 0.05/6) was further conducted. For each outcome variable,

the covariates included age, sex, race/ethnicity, current status of disease, current stage of disease, metastatic sites, ECOG performance status (PS), weight loss in previous 6 months, currently receiving cancer treatment, prior chemotherapy/immunotherapy/hormonal therapy, current radiation therapy, prior radiation therapy, institution type, clinic practice type, clinician type, and symptom burden (including the number of moderate/severe symptoms, and the number of moderate/severe interference items as measured by MDASI-ECOG). When available, patient reports of each outcome measure (e.g., QOL, symptom reports) were also model covariates. All covariates were treated as discrete variables (Tables 2, 3).

For each outcome variable, only significant covariates (p < 0.10) in univariate models were further fitted into a multivariable model. Except for the covariate of race/ethnicity, patients with missing values on any of the variables in the analysis model were excluded from data analysis. All p values are two sided. A level of 5% was considered statistically significant except specified otherwise. SAS 9.2 (SAS Institute) was used for all data analyses.

Results

Patient, Site, and Clinician Rater Characteristics by Disease Site

Table 2 presents characteristics by disease site for all 3106 analyzable patients: breast (50%), colorectal (23%), prostate (10%), and lung (17%). The median age of patients was 61 years (range 18 to 93). The majority of patients were female (70%) with ECOG PS 0 (57%). Approximate one fourth (24%) were minority patients. In most cases (67%), clinician ratings were conducted by the patient's attending physician; other clinician raters included residents, fellows, advanced practice nurses, and physician assistants. Significant differences were observed across disease sites on all variables listed in Table 2 (all p < 0.0001).

Table 3 includes patient-rated assessments of the corresponding dependent variables (except for care difficulty, which did not have a patient rating). The majority (71%) of patients reported "Good" or "Excellent" quality of life. Most patients reported minimal (defined by "Not at all" or "A little bit") difficulties related to comorbidities (67%), disease (51%), treatment (52%), medications (69%) and weight (66%). Among the patient-reported outcomes listed in Table 3, significant differences were observed among all of them across disease site overall and lung cancer v. others specifically (all p < 0.01). Lung cancer patients had significantly higher odds of reporting worse QOL (odds ratio (OR) = 8.4 (95% CI, 5.0–14.0), p < 0.0001) and more severe symptoms across all included domains (OR ranging from 2.2 to 6.6, all p < 0.01).

Clinician Perceptions of Patient Care Difficulty, QOL, and Symptom Reports

Table 4 lists frequency and percentage of clinician ratings for various outcome variables at the initial visit. Table 5 summarizes odds ratios and significance for both the disease site effect and the planned comparison between lung and others for each outcome variable. Detailed descriptions for each item are described in the following sections.

Care Difficulty—The first study aim focused on clinician perceptions of care difficulty for lung cancer patients compared to breast, prostate, and colon cancer patients. Results from

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the univariate logistic model indicated a significant disease site effect (p = 0.0009) on the distribution of clinicians' care difficulty ratings. In the planned comparison between lung and others, the odds of clinicians reporting more care difficulty ratings for patients with lung cancer were approximately 5 times higher than for those with other diseases (OR = 5.1 (95% CI, 2.5–10.4), p < 0.0001). Conclusions from the univariate model did not hold after adjusting for other explanatory variables. The contrast (lung vs. others) indicated that the odds of clinicians reporting more care difficulty ratings for patients with lung cancer were comparable to those with other diseases (OR = 1.5, 95% CI, 0.8–2.9), p = 0.23), and there was no difference in the distribution of care difficulty ratings among the four disease sites after controlling for other explanatory variables (p = 0.60).

Quality of Life—The second study aim focused on comparing lung v. others in clinicians' perceptions of patient QOL. In addition to demographic and clinical variables, patient's QOL rating at the initial visit was also a covariate in the multivariable model. A significant disease site effect (p < 0.0001) on the distribution of clinicians' QOL ratings was found in the univariate logistic analysis. The prior comparison in QOL ratings indicated a significant difference (OR (lung vs. others) = 17.9 (95% CI, 11.2–28.5), p < 0.0001). These conclusions remained even when the covariates were fitted into the multivariable model; the odds of clinicians reporting poorer QOL ratings for patients with lung cancer were about 3.6 times as large as for patients with other diseases (OR = 3.6 (95% CI, 2.0–6.6), p < 0.0001), supporting the expectation that clinicians would report a worse QOL rating for lung cancer patients. Disease site effect was further evaluated by post-hoc pairwise comparisons. As noted in the top half of Table 6, the odds of clinicians' perceiving a poorer QOL for patients with breast and colorectal were significantly lower than for patients with lung cancer. No statistically significant difference was observed between the other pairwise groups.

Post-hoc analyses focused on clinician assessments of patient QOL at the follow-up visit. Results indicated that after adjusting for confounding factors, the odds of clinicians perceiving lower QOL for their lung cancer patients were still 3.2 times larger than for those with other solid tumors in the follow-up visit (OR = 3.2 (95% CI, 1.2-9.0), p=0.04). The overall disease site effect was no longer significant in the multivariable model.

Symptom Reports—The third study aim focused on comparing clinicians' symptom reports for lung cancer patients with other patient groups. Several items related to this aim (symptom difficulties related to comorbidity, disease, treatment, medication, weight) were analyzed separately to evaluate our hypotheses. For each of these clinician-reported items, patients' symptom reports on the exact same item were included in the model as a covariate (in addition to covariates noted earlier).

Comorbidities: Results from the univariate logistic model showed a significant disease site effect (p = 0.0002) on the distribution of clinicians' reports of patient comorbidity. The planned comparison in comorbidity reports also indicated significant difference, i.e., the odds of clinicians reporting more bothersome comorbidity reports for lung cancer patients were approaching 4 times as high as for those with other disease (OR (lung vs. others) = 3.7 (95% CI, 2.1–6.6), p < 0.0001). However, such a difference no longer existed in clinicians' comorbidity reports among the four disease sites (p = 0.07) and between lung and others (p

= 0.09) after adjusting for other covariates (including patients' responses on the same item) in the multivariable model.

Disease: Results from the univariate logistic model indicated a significant disease site effect (p < 0.0001) on clinicians' reports of disease difficulty, with a significant difference between lung and other cancers. Specifically, the odds of clinicians reporting more disease-related difficulties for lung cancer patients were almost 9 times as high as for those with other cancers (OR (lung vs. others) = 8.7 (95% CI, 4.6–16.3), p < 0.0001). This difference did not hold in clinicians' reports of disease difficulty among the four disease sites (p = 0.17) and between lung and others (p = 0.10) after controlling for other covariates (including patient's response on the same item) in the multivariable model.

Disease Treatment: A significant disease site effect was observed for clinicians' reports of difficulty related to disease treatment (p = 0.0004) using a univariate analysis. The planned comparison between lung and others found significant difference in ratings related to treatment difficulties (OR for lung vs. others = 3.4 [95% CI, 1.9 to 5.9], p < 0.0001). However, after adjusting for other covariates (including patients' responses on the same item), no difference was found between clinicians' reports of lung and others (p=0.089). However, the overall disease site effect still reached significance (p = 0.008). As noted on the bottom half of Table 6, the odds of clinicians reporting more bothersome treatment difficulties for patients with colorectal cancer were significantly higher than for those with prostate and breast disease sites (both adjusted p < 0.05). No statistically significant difference in odds was observed between the other pairwise groups.

Side Effects from Medication: Disease site effect was not significant in the distribution of clinicians' reports of medication side effects, either in the univariate or the multivariable analysis models (p = 0.14 and p = 0.82, respectively). Nor was there any difference for clinician reports of medication side effects between lung cancer patients and patients with other disease (p=0.06 in the univariate analysis and p=0.56 in the multivariable analysis).

Weight Loss or Gain: A significant disease site effect on clinicians' reports of bothersome weight loss or gain weight was observed (p = 0.003) in the univariate logistic regression analysis. Results from the planned comparison between lung and others found that the odds of clinicians reporting more weight-related difficulties for patients with lung cancer were about 5 times as large as for patients with other disease (OR (lung vs. others) = 5.1 (95% CI, 2.6–10.2), p < 0.0001). After adjusting for other covariates (including patient's response on the same item), the same difference pattern was found between clinicians' reports between lung and others (OR lung vs. others = 3.2 [95% CI, 1.7 to 6.0], p = 0.0004). The disease site effect also remained significant (p = 0.009), primarily because the odds of having more bothersome clinician weight ratings for patients with lung cancer were significantly higher than for those with prostate cancer (OR = 1.7, 95% CI, 1.4–2.5, adjusted p < 0.05). No statistically significant difference in odds was observed between the other pairwise groups. No parallel analysis for the follow-up clinician form.

Discussion

This study represents a novel attempt to compare clinician perceptions of care difficulty, QOL, and symptom reports for patients with lung cancer to those with other solid tumors. Analyses focused on both univariate comparisons and multivariable comparisons that controlled for a comprehensive array of patient, disease, and setting variables.

Overall, clinicians had more pessimistic attitudes about their lung cancer patients. In the univariate comparisons, clinicians rated their lung cancer patients as more difficult to treat, with poorer QOL, and higher symptom reports (inclusive of difficulties related to cancer, comorbidities, treatment, and weight change). Despite the general findings, analyses intended to isolate potential perception bias and nihilism demonstrated mixed findings. For most of the outcome variables, the inclusion of patient reports, clinical factors (e.g., cancer stage, PS), and other explanatory covariates negated differences in clinician perceptions of lung cancer versus other patient groups. However, clinicians continued to perceive their lung cancer patients as having a poorer QOL (at both baseline and follow-up assessments) and more difficulties related to weight, even after controlling for these explanatory factors (including patient reports of the outcome variables).

The findings of this study suggest that certain clinician judgments (i.e., QOL and weight problems) may have been influenced by preexisting ideas (e.g., nihilism) about lung cancer patients and their treatment options. In essence, even if their lung cancer patients were sicker than their other solid tumor patients, clinicians perceived their QOL to be lower and weight difficulties as more burdensome after controlling for how sick they were. In the case of QOL, these perceptions were consistent over time; both baseline and follow-up assessments revealed this difference. Lung cancer patients are sick and difficult to treat; our data show that clinicians are well aware of these complexities. However, the data also suggest that this complexity perhaps provides a smokescreen to hide a subtle, but potentially real, underlying bias and nihilism.

Associations between smoking and lung cancer may affect clinicians' views, both through possible perceptions of blame and anticipated treatment non-adherence associated with behavioral risk factors.^{11,12} Given that a subset of findings suggests that features of nihilism do persist, further exploration of this issue is needed. Fortunately, the current landscape surrounding lung cancer care looks very different than it did as little as a decade ago. Recent evidence from the National Lung Screening Trial suggests promise in CT-based screening for early detection and reduced mortality associated with lung cancer.¹⁴ Molecular characterization of lung cancer (such as testing tumors for EGFR and ALK mutations) has enabled oncologists to identify subsets of patients who are amenable to specific and effective treatments other than (or in addition to) standard chemotherapy.^{15–20} There are not only new therapeutics and extended expected survival times, but also more favorable toxicity profiles for many of the new treatments. Such advances have led to suggestions of the "end of the era of therapeutic nihilism" as it relates to lung cancer.⁷ This may very well be the case; as lung cancer becomes more treatable, perceptions of lung cancer patients and their difficulty of care may also improve. Data from this study indicate that research is needed to fully understand the breadth and depth of nihilism and consequences to treatment

decisions and clinician-patient communication (including the potential relationship between clinician nihilism and patient perceptions of lung cancer stigma).²¹ Although certain studies suggest a tendency to under-treat lung cancer patients specifically (i.e., not adhere to evidence-based guidelines for first and second line therapies^{12,22,23}) other data describe potential overtreatment, especially for advanced cancer patients.^{24,25} Low accrual to lung cancer clinical trials is a clear concern²⁶ and emerging evidence identifies provider factors associated with clinical trial involvement and referrals.^{27,28} However, the extent to which provider nihilism may affect how clinical trials are offered to lung cancer patients is unclear and in need of further investigation. Any potential relationship between nihilism and treatment decisions, including decisions to offer clinical trials to patients, is likely to be complex. As more information is gathered about clinician views of lung cancer patients and their treatment outcomes, it is important to consider educational interventions for all health professionals who influence the patient experience of dealing with lung cancer.

Overall, it is very difficult to prove that perception bias and nihilism are the only factors or main factors contributing to our study findings related to clinician perceptions of QOL and weight difficulties. Even with comprehensive covariates, there may be unmeasured factors that are disproportionately present in lung cancer patients and contribute to demonstrated differences in clinician perceptions. Perhaps clinicians are not nihilistic about QOL and weight concerns in patients with lung cancer, but are instead able to incorporate subtle factors elusive to the usual summaries of patients, disease, and treatment. However, these findings suggesting a subtle, potentially real, underlying bias and nihilism are provocative and should be further investigated in order to confirm the findings and explore their underpinnings.

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Table 1

Clinician ratings of care difficulty, quality of life, and symptom reports

Domain	Item		Scoring
Care Difficulty	Relative to difficulty	o other patients with same stage of disease, how would you categorize the degree of in caring for this patient's physical/psychological symptoms?	1=Very difficult 2=Difficult 3=Average 4=Easier than average 5=Much easier than average
Quality of Life	How wou	ld you rate this patient's overall quality of life at this time?	1=Very poor 2=Poor 3=Fair 4=Good 5=Excellent
Symptom Reports	Overall, h	ow much do you think this patient is bothered by (a-e) ?	0=Not at all
	a.	(difficulties related to comorbidities other than cancer)	1=A little bit 2=Moderately
	b.	(difficulties related directly to the cancer)	3=Quite a bit 4=Extremely
	c.	(difficulties related to treatment of cancer)	
	d.	(side effects from medications used to treat pain or other symptoms)	
	e.	(weight gain or loss)	

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	Z	%	Z	%	Z	%	Z	%	Z	%
Number of Patients	1544	50	718	23	320	10	524	17	3106	100
Age										
age < 45	225	15	70	10	1	0	17	3	313	10
45 = < age < 60	652	42	247	34	45	14	140	27	1084	35
60 = < age < 75	537	35	278	39	150	47	266	51	1231	40
75 =< age	130	8	123	17	124	39	101	19	478	15
Sex										
Male	ю	0	372	52	320	100	241	46	936	30
Female	1541	100	346	48	ı	ı	283	54	2170	70
Race/Ethnicity										
Minority	305	21	201	30	81	28	95	20	682	24
White & non-Hispanic	1127	79	475	70	210	72	381	80	2193	76
Unknown	112	ī	42	ı	29	ı	48	ı	231	ï
PS										
0	1048	68	375	52	161	51	171	33	1755	57
1	414	27	299	42	127	40	265	51	1105	36
2-4	73	5	43	9	30	6	85	16	231	7
Unknown	6	ı	1	'	2	'	З	ı	15	ı
Weight Loss										
<5%	1369	90	565	<i>4</i>	286	91	411	79	2631	86
5 - 10%	106	7	87	12	22	٢	64	12	279	6
>=10%	46	ю	60	8	8	3	46	6	160	5
Unknown	23	1	9	1	4	ľ	3	,	36	
Current Status of Disease										
CR	806	53	243	34	45	14	63	12	1157	38
PR	45	б	28	4	26	8	48	6	147	ŝ

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Current Stage of Disease

Unknown

DD

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Total \mathbf{Z}

Lung z

Prostate

Colorectal

Breast

Disease Site

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Local/Regional

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No

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Institution Type

Unknown

Prior Chemo/Immuno/Hormonal Therapy No sites of metastatic disease Local/Regional & Metastatic Prior Radiation Therapy Metastatic Sites Multiple sites Single site Unknown Unknown

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Currently Receiving Cancer Treatment Current Radiation Therapy Yes Yes ů ů

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				Diseas	e Site					
	Brea	ıst	Color	ectal	Pros	tate	Lui	g	Tota	IJ
	Z	%	Z	%	Z	%	Z	%	Z	%
Academic	115	7	65	6	63	20	60	Ξ	303	10
Community	1429	93	653	91	257	80	464	89	2803	90
Clinic Practice Type										
Majority-based	1188	LL	500	70	219	68	417	80	2324	75
Minority-based	356	23	218	30	101	32	107	20	782	25
Clinician										
Attending Physician	1006	66	490	69	198	62	360	69	2054	67
Resident or fellow	78	5	45	9	37	12	33	9	193	9
Advanced practice nurse or nurse practitioner	158	10	58	×	13	4	36	Г	265	6
Physician assistant	59	4	17	7	13	4	27	S	116	4
Other	222	15	101	14	59	18	64	12	446	14
Unknown	21	,	٢		0	1	4	1	32	,
Number of Moderate/Severe Symptoms										
0	614	40	293	41	128	40	127	24	1162	38
1–2	356	23	154	22	75	24	109	21	694	22
3–6	331	22	134	19	LL	24	147	28	689	22
7	237	15	131	18	38	12	140	27	546	18
Unknown	9	'	9	1	7	ï	1		15	ï
Number of Moderate/Severe Interference										
0	1009	66	444	63	195	61	246	47	1894	61
1–2	221	14	119	17	56	18	76	19	493	16
3–6	307	20	147	21	67	21	179	34	700	23
Unknown	7	'	×	'	2	'	0	ı	19	,

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Table 3

Frequency of Care Difficulty, QOL, and Symptom Ratings by Patients (by Disease Site)

			_	Diseas	e Site					
	Bre	ast	Color	ectal	Pros	tate	Lui	5u	Tot	la
	Z	%	Z	%	Z	%	Z	%	Z	%
Quality of Life	a									
Excellent	400	26	136	19	56	18	48	6	640	21
Good	802	52	335	47	149	47	244	47	1530	50
Fair	280	18	198	28	93	29	172	33	743	24
Poor	47	3	40	9	16	5	53	10	156	5
Very Poor	5	0	9	-	4	-	9	-	21	-
Unknown	10	1	33	1	2	,	1	1	16	1
Comorbidity F	Problem	_								
Not at all	533	35	293	41	66	31	158	30	1083	35
A little bit	512	33	216	30	102	32	166	32	966	32
Moderately	315	20	136	19	74	23	113	22	638	21
Quite a bit	146	6	57	8	37	12	75	14	315	10
Extremely	32	7	11	7	9	7	10	7	59	7
Unknown	9	1	5	1	2	1	2	1	15	1
Disease Proble	em									
Not at all	373	24	130	18	88	28	64	12	655	21
A little bit	510	33	208	29	80	25	128	25	926	30
Moderately	363	24	206	29	74	23	160	31	803	26
Quite a bit	227	15	133	19	99	21	131	25	557	18
Extremely	99	'	33	'	×	'	35		142	
Unknown	5	0	8	-	4	-	9	-	23	-
Disease Treati	ment P1	oblen	-							
Not at all	416	27	142	20	115	36	62	15	752	24
A little bit	441	29	193	27	86	27	147	28	867	28
Moderately	379	25	196	28	58	18	156	30	789	26
Quite a bit	219	14	148	21	48	15	109	21	524	17

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			Π	Disease	e Site					
	Bre	ast	Color	ectal	Pros	tate	Lui	gu	Tot	al
	Z	%	Z	%	Z	%	Z	%	Z	%
Extremely	80	S	29	4	6	ю	26	S	144	5
Unknown	6	ı	10	ı	4	,	٢	ŀ	30	ı
Medication Pr	oblem									
Not at all	622	41	298	42	164	52	184	35	1268	41
A little bit	429	28	203	29	74	23	149	29	855	28
Moderately	314	20	119	17	53	17	111	21	597	19
Quite a bit	118	8	74	10	22	Г	67	13	281	6
Extremely	51	3	16	7	б	-	10	7	80	ю
Unknown	10	'	8	1	4	1	3		25	ŀ
Weight Proble	m									
Not at all	523	34	302	42	165	52	196	38	1186	38
A little bit	433	28	206	29	78	25	142	27	859	28
Moderately	298	19	110	15	45	14	84	16	537	17
Quite a bit	202	13	69	10	23	٢	79	15	373	12
Extremely	81	2	27	4	9	7	21	4	135	4
Unknown	7	'	4		3		2		16	

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Table 4

Frequency of Care Difficulty, QOL, and Symptom Ratings by Clinicians (by Disease Site)

				Disease	e Site					
	Brea	ıst	Colore	ectal	Pros	tate	Lui	gu	Tot	le
	Z	%	Z	%	Z	%	Z	%	Z	%
Care Difficulty										
Very difficult	13	1	٢	1	-	0	12	7	33	1
Difficult	127	8	44	9	23	٢	55	11	249	8
Average	634	41	319	45	147	46	271	52	1371	44
Easier than average	482	31	237	33	102	32	141	27	962	31
Much easier than average	275	18	106	15	44	14	42	8	467	15
Unknown	13	'	S	'	3		ю	,	24	ï
Quality of Life										
Very poor	12	-	S	-	'	'	7	-	24	1
Poor	58	4	31	4	16	5	60	12	165	5
Fair	395	26	234	33	102	32	230	4	961	31
Good	760	50	337	47	155	49	196	38	1448	47
Excellent	305	20	106	15	46	14	27	5	484	16
Unknown	14	1	5	1	-	1	4	1	24	'
Comorbidity Problem										
Not at all	701	46	337	47	108	34	162	31	1308	42
A little bit	464	30	239	33	117	37	192	37	1012	33
Moderately	242	16	90	13	61	19	105	20	498	16
Quite a bit	111	Г	41	9	30	6	51	10	233	×
Extremely	12	-	×	-	с	1	11	7	34	1
Unknown	14	·	3	'	1	ı	б	ı	21	,
Disease Problem										
Not at all	615	40	236	33	85	27	76	19	1033	33
A little bit	488	32	224	31	111	35	153	29	976	32
Moderately	289	19	159	22	69	22	159	31	676	22
Quite a bit	109	٢	74	10	45	14	79	15	307	10

Disease Site

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	Brea	st	Color	ectal	Pros	tate	Lui	g	Tot	al
	Z	%	Z	%	Z	%	Z	%	Z	%
Extremely	30	5	22	æ	6	æ	31	9	92	3
Unknown	13	,	с	'	1	'	5	'	22	1
Disease Treatment Problem										
Not at all	468	31	138	19	94	30	96	18	796	26
A little bit	544	36	245	34	130	41	185	36	1104	36
Moderately	360	24	224	31	68	22	164	31	816	26
Quite a bit	133	6	90	13	22	٢	62	12	307	10
Extremely	26	7	16	7	2	-	14	ю	58	7
Unknown	13	1	5	1	4	'	3		25	1
Medication Problem										
Not at all	972	64	438	61	190	60	286	55	1886	61
A little bit	394	26	175	25	91	29	159	31	819	27
Moderately	111	٢	69	10	30	6	56	11	266	6
Quite a bit	40	З	27	4	٢	7	13	ю	87	б
Extremely	11	-	4	-	1	0	5	-	21	-
Unknown	16		5	1	1	'	5		27	
Weight Problem										
Not at all	1011	99	472	99	245	LL	299	57	2027	99
A little bit	328	21	160	22	46	14	134	26	668	22
Moderately	116	8	56	×	18	9	52	10	242	×
Quite a bit	63	4	22	ю	٢	7	33	9	125	4
Extremely	1011	99	472	99	245	LL	299	57	2027	99
Unknown	15	ı	б	ľ	-	'	ю	'	22	'

Table 5

Odds Ratio and Significance of Disease (Dz) Site Effect and the Planned Comparison between Lung and Others for Various Outcome Items

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		Uni	variable M	Inno		IJIMIA	variable M	odel
Items	Z	Dz Site Effect	Lun	g vs. Others	Z	Dz Site Effect	Lung	vs. Others
		Ρ	Ρ	OR (95% CI)		Ρ	Ρ	OR (95% CI)
Care difficulty*	3082	0.0009	<0.0001	5.1 (2.5, 10.4)	3010	0.60	0.23	1.5 (0.8, 2.9)
QOL⁺	3082	<0.0001	<0.0001	17.9 (11.2, 28.5)	3001	0.01	<0.0001	3.6 (2.0, 6.6)
$Comorbidity^{\ddagger}$	3085	0.0002	<0.0001	3.7 (2.1, 6.6)	2971	0.07	0.09	1.6 (0.9, 2.8)
Disease‡	3084	<0.0001	<0.0001	8.7 (4.6, 16.3)	2978	0.17	0.10	1.7 (0.9, 3.2)
Dz Treatment [‡]	3081	0.0004	<0.0001	3.4 (1.9, 5.9)	2962	0.008	0.89	1.0 (0.6, 1.8)
$Medication^{\ddagger}$	3079	0.14	0.06	2.1 (1.0, 4.6)	3017	0.82	0.56	0.8 (0.4, 1.7)
Weight [‡]	3084	0.003	<0.0001	5.1 (2.6, 10.2)	2992	0.009	0.0004	3.2 (1.7, 6.0)

 \sharp The probabilities of having more bothersome ratings was modeled in the analysis model.

Table 6

Odds Ratio of Having Worse Ratings on QOL and Disease (Dz) Treatment in Each Disease Site with Respect to Each Other Site (Row to Column)

$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Item		Breast	Colorectal	Prostate	Lung
$ \begin{array}{c cccc} Colorectal & 1 & 1 & 0.6 \\ Prostate & 0.8-1.5) & 0.6.5 \\ Prostate & 1 & 0.6.6 \\ Lung & 1 & 0.7 \\ Lung & 1 & 0.7 \\ O(2-0.9) & 0.7-1.7) & 0.9 \\ O(2-1.7) & 0.9 & 1 \\ Colorectal & 1 & 1.7 \\ Prostate & 1 & 0.8 \\ Prostate & 1 & 0.8 \\ Prostat & 1 & 0.8 \\ Prost$	DOL	Breast	1	1.1 (0.8–1.4)	$1.1 \\ (0.7-1.6)$	0.7 (0.5–0.9)*
$ \begin{array}{c} \mbox{Prostate} & 1 & 0.6 \\ \mbox{Lung} & Lung & 1 \\ \mbox{Lung} & Lung & 1 \\ \mbox{Dz Treatment} & Breast & 1 & 0.7^* & 1.1 & 0.9 \\ \mbox{Reast} & 1 & 0.7^{-0.9} & (0.7-1.7) & (0.7-1.7) \\ \mbox{Colorectal} & 1 & 1.7^* & 1.4 \\ \mbox{Colorectal} & 1 & 1.7^* & 1.4 \\ \mbox{Prostate} & 1 & 0.8 \\ \mbox{Prostate} & 1 & 0.8 \\ \mbox{Lung} & 1 & 1.0 \\ \mbox{Lung} & 1 \\ \$		Colorectal		1	$ \begin{array}{c} 1.0 \\ (0.8-1.5) \end{array} $	0.6^{*} (0.5–0.8)
Lung Lung 1 Dz Treatment Breast 1 0.7^* 1.1 0.9 Colorectal 1 $0.5-0.9$ $(0.7-1.7)$ $(0.7-1.7)$ $(0.7-1.7)$ Colorectal 1 1 1.7^* 1.4 Prostate 1 $(1.2-1.4)$ $(1.1-1.1)$ Lung Lung 1 $0.6-1.4$		Prostate			-	$\begin{array}{c} 0.6 \\ (0.4 - 0.9) \end{array}$
$ \begin{array}{c ccccc} Dz \ Treatment & Breast & 1 & 0.7^{*} & 1.1 & 0.9 \\ & & & & & & & & \\ & & & & & & & & \\ Colorectal & 1 & 1.7^{*} & 1.4 & 11.4 \\ & & & & & & & & & \\ Prostate & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & & \\ & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & &$		Lung				1
Colorectal 1 1.7* 1.4 (1.2-1.4) (1.1-1. Prostate 1 0.8 Lung Lung 1	Dz Treatment	Breast	Т	0.7^{*} (0.5–0.9)	$^{1.1}_{(0.7-1.7)}$	0.9 (0.7–1.1)
Prostate 1 0.8 (0.6–1. Lung 1		Colorectal		1	1.7^{*} (1.2–1.4)	1.4 (1.1–1.7)
Lung 1		Prostate			-	$\begin{array}{c} 0.8\\ (0.6{-}1.1)\end{array}$
		Lung				1
	* Adjusted $p < 0$.	.05				
* Adjusted $p < 0.05$						