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Research Article

QOL and Survival Comparisons by Race in Oncology Clinical Trials

Tan AD[1], Novotny PJ[1]*, Kaur JS[2], Buckner JC[2], Mowat RB[3], Paskett E[4] and Sloan JA[1]

[1]Alliance Statistics and Data Center, Division of Biomedical Statistics Informatics, Mayo Clinic, Rochester, Minnesota, USA
[2]Department of Oncology, Mayo Clinic, Rochester, Minnesota, USA
[3]Bixby Medical Center/Hickman Cancer Center, Sylvania, Ohio, USA
[4]College of Medicine, Ohio State University, Columbus, OH, USA

***Corresponding Author:** Mr. Paul J. Novotny, Alliance Statistics and Data Center, Division of Biomedical Statistics Informatics, Mayo Clinic, Rochester, Minnesota, USA; Tel: 507-284-4186; Fax: 507-266-2477; E-mail: novotny@mayo.edu

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Abstract:

Background: Significant efforts have been made to increase access and accrual to clinical trials for minority cancer patients (MP). This meta-analysis looked for differences in survival and baseline quality of life (QOL) between MP and non-minority cancer patients (NMP).

Materials and Methods: Baseline QOL and overall survival times from 47 clinical trials (6513 patients) conducted at Mayo Clinic Cancer Center/North Central Cancer Treatment Group were utilized. Assessments included Uniscale, Linear Analogue Self Assessment, Symptom Distress Scale (SDS), Profile of Mood States and Functional Assessment of Cancer Therapy - General, each transformed into a 0-100 scale with higher scores indicating better outcomes. This transformation involves subtracting the lowest possible value from the assessment, dividing by the range of the scale (the maximum minus the minimum), and multiplying by 100. Analyses included Fisher's Exact tests, linear regression, Kaplan-Meier curves, and Cox proportional hazards models.

Results: Eight percent of patients self-reported as MP (0.45% American Indian/Alaskan Native, 0.7% Asian, 5% Black/African American, 1.5% Hispanic, 0.1% Native Hawaiian and 0.3% Other). MP had no meaningful deficits relative to non-MP in overall QOL but were slightly worse on FACT-G total score, physical, social/family, functional, and SDS nausea severity. MP with lung, neurological or GI cancers had significantly worse mean scores in nausea (58 vs. 69), sleep problems (34 vs. 54); emotional (53 vs. 74); and social/family (60 vs. 67), respectively. Regression models confirmed these results. After adjusting for disease site, there were no significant differences in survival.

Conclusion: MP on these clinical trials indicated small deficits in physical, social, and emotional subscales at baseline compared to NMP. Within cancer sites, MP experienced large deficits for selected QOL domains that bear further attention.

Introduction: Only 2.5% of all cancer patients enroll on clinical trials [1]. Participation by minority cancer patients has been even smaller with many barriers identified [2-7]. These barriers include issues of 1) awareness: such as the education of the patient and the care givers, 2) opportunity: such as economic issues and not being made aware of opportunities to participate, and 3) acceptance: such as mistrust in clinical trials or the medical profession [8]. Placing high priority clinical trials into centers with larger minority populations and developing trusting partnerships has been crucial to successful recruitment [9-11]. These barriers, while not measured in clinical trials, could skew QOL results for minorities and misrepresent how clinical trial results will generalize to minorities. These barriers could restrict low income, less educated minorities from participating in cancer clinical trials. This study uses a patient-level pooled analysis to determine whether presumed/unmeasured deficits in access and other barriers facing minority patients manifest into quality of life (QOL) differences between minority patients (MP) and non-minority patients (NMP) on clinical trials. This is an exploratory, hypothesis generating study whose results need to be validated in future studies.

Materials and Methods:

Patients: This patient-level pooled analysis includes all 47 studies conducted either at the Mayo Clinic or through the North Central Cancer Treatment Group (NCCTG) which used the health-related quality of life (HRQOL) questionnaires Spitzer Uniscale [12], Linear Analogue Self Assessment (LASA) [13-17], Symptom Distress Scale (SDS) [18,19], Profile of Mood States (POMS-SF) [20] or Functional Assessment of Cancer Therapy – General (FACT-G) [21-23]. These HRQOL questionnaires were included in this study, because they were utilized in a large number of clinical trials, resulting in an adequate number of minority and non-minority patients for comparison. Other more focused, cancer-specific HRQOL forms were not included in this study, because there were not enough clinical trials using those questionnaires to get sufficient numbers of minority patients. Minority status was based on patient self-reported race. Several of the studies did not accrual any minority subjects. These studies are still included in the analyses in order to increase the power of the study and to provide a true picture of minority accrual onto cancer clinical trials. Less than 20% of the patients were from the Mayo Clinic, with the other patients representing a wide spectrum of cancer practice around the United States. A total of 6513 patients, aged 17-95, were entered on these studies between 1995 and 2011. Patients had a median age of 62 (range of 17 to 95), 46% were female, and 47% had gastrointestinal (GI) cancer. All patients provided informed consent on their respective studies. The large proportion of GI studies is due to several very large GI studies. These large studies are common in cancer research. While this cohort is representative of the clinical trial experience, it might not be directly generalizable to a different cohort with an extremely different mix of cancer sites.

Measures: The Spitzer Uniscale is a global measure of overall QOL that has been used in more NCCTG cancer treatment studies than any other measure [24]. Patients were asked to mark the appropriate place within the bar (with lowest quality on one end of the bar and highest quality on the other end of the bar) to indicate their overall QOL during the past week.

LASA is a general measure of global QOL constructs on a 0 to 10 scale. LASA items have been constructed and validated at Mayo Clinic for use in cancer patients [25-26]. This analysis focuses on five LASA items: overall QOL, physical well-being, emotional well-being, spiritual well-being, and mental/intellectual well-being.

SDS is a 13-item scale designed to measure the degree of discomfort associated with the following 11 symptoms as perceived by the patient: nausea, appetite, insomnia, pain, fatigue, bowel pattern, concentration, appearance, outlook, breathing, and cough on a 1-5 scale [18,27]. The SDS total score was calculated by subtracting the average score of 13 items from 5 and multiplying by 25.

POMS is a 37-item scale utilized to assess patients' mood disturbance such as fatigue-inertia, vigor-activity, tension-anxiety, depression-dejection, anger-hostility and confusion-bewilderment [20]. Each subscale score was calculated by summing the corresponding five items and transformed it into 0-100 scale. The POMS total score was calculated by summing the raw scores of the six subscales and transformed it into a 0-100 scale.

FACT-G is a 27-item self-administered cancer-specific HRQOL questionnaire and consists of four subscales: Physical Well-Being (PWB), Social/Family Well-Being (SWB), Emotional Well-Being (EWB) and Functional Well-Being (FWB). Subscale scores are calculated by summing the values of item responses. The 4 subscale scores are summed to calculate a total FACT-G score [21-23].

All of the QOL measures were patient self-reported using validated QOL instruments. The psychometric properties of each QOL measure are available in the references. All item scores were transformed into a 0-100 point scale with higher scores indicating better outcomes.

Statistical methods: We compared patient characteristics, QOL differences at baseline, and overall survival between MP versus NMP for each HRQOL questionnaires. The QOL measurements were all collected prior to starting treatment on the study. Analyses were done overall, by subsets of patients having each HRQOL questionnaire, and by tumor sites.

Statistical methods included Kruskal-Wallis tests for comparing the various QOL scores and Chi-square tests for comparing discrete patient characteristics. A score of $\leq$50 on a 0-100 point scale has consistently been demonstrated to be clinically significant and prognostic for overall survival in multiple settings, cancer sites, and QOL instruments [28-31]. The primary endpoint, proportion of patients experiencing this clinically significant deficit, was compared between MP and NMP using a Fisher's exact test. With 6513 patients and roughly 8% minorities, Fisher's exact test had 80% power to detect differences in the incidence rates of QOL deficit of 6.5% with a two-sided Type I error rate of 5%. Multivariate linear and logistic models were used to adjust for differences in age and disease site. Standard survival analyses were used to account for the censored survival times.

Kaplan-Meier curves were constructed for overall survival data, and log-rank tests were utilized to compare survival times between groups. Cox proportional hazards models stratified by study were used to analyze the combined effects of age, ECOG performance score [32], race, and tumor sites on survival [33]. Proportional hazards assumptions were tested using Schoenfeld residuals. All tests were 2-sided and comparison-wise p-values of less than 0.05 were considered statistically significant. Because of the exploratory nature of this meta-analysis, no adjustments were done to handle multiple testing. Separate analyses were done comparing Black or African American patients to non-minority patients. The results of these analyses are not reported since they were almost identical to the analyses comparing all minorities to non-minorities.

Results:

Overall patient demographics: Supplementary table 1 shows the list of clinical trials included in this study, and patient characteristics are summarized in supplemental table 2. Of the 6513 patients, 8% (531) were classified as minorities (0.45% American Indian or Alaskan Native, 0.7% Asian, 5% Black or African American, 1.5% Hispanic, 0.1% Native Hawaiian and 0.3% Other). MP were about 3 years younger than NMP ($p<0.0001$) and were more likely to be enrolled in GI studies. There were no statistically significant differences in gender, performance score, or overall survival times (median survivals of 1.16 vs. 1.26 years, $p=0.14$, Figure 1) between MP and non-MP cohorts.

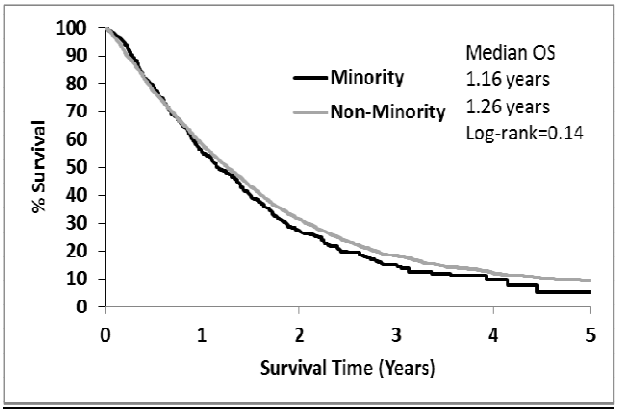

Figure 1: Overall Survival Times by Minority Status

Study No.	Description	Tumor Sites	Study Type	Number of Minority Patients	Number of Non-Minority Patients	QOL Assessments
952053	Thoracic radiation therapy with cisplatin/etoposide	Lung	Adjuvant	2	80	UNISCALE
954651	Phase II trial of oral 776C85 and oral 5-FU	GI	Metastatic	3	76	UNISCALE
959204	Quality of life in hospice patients and their caregivers	Psychosocial	Metastatic	0	58	POMS, UNISCALE
959255	Megace vs. Marinol vs. both for anorexia and cachexia	GI, Lung, Other	Cancer Control	64	421	FACT-G
959257	Flutamide chemoprevension in men with prostatic intraepithelial neoplasia	GI	Cancer Control	0	63	POMS
962451	LU 103793 for advanced NSCLC	Lung	Metastatic	1	16	UNISCALE
969256	Glutamine vs. placebo for preventing acute diarrhea	GI, GU, Gyn, Other	Cancer Control	6	123	UNISCALE
971151	Benefin shark cartilage for advanced cancer	Breast, GI	Cancer Control	2	85	LASA, SDS, UNISCALE
972451	CAI for advanced NSCLC	Lung	Metastatic	5	180	FACT-G, UNISCALE
979202	Dehydroepiandrosterone and Biaxin in monoclonal gammopathy	Other	Adjuvant	0	34	UNISCALE

Study No.	Description	Tumor Sites	Study Type	Number of Minority Patients	Number of Non-Minority Patients	QOL Assessments
979251	Low molecular weight heparin for advanced cancer	Breast, GI, GU, Lung	Cancer Control	0	140	LASA, SDS, UNISCALE
979253	Erythropoietin vs. placebo in anemic patients	Many	Cancer Control	29	315	FACT-G, SDS, UNISCALE
982452	Docetaxel and gemcitabine for stage IIIB/IV NSCLC	Lung	Metastatic	5	100	UNISCALE
983252	Paclitaxel, carboplatin and trastuzumab for metastatic breast cancer	Breast	Adjuvant	7	91	FACT-G
987251	BCNU, cisplatin and oral etoposide in grade 3 astrocytoma	Brain Tumor	Adjuvant	1	28	FACT-G, LASA, POMS, SDS
987252	BCNU, cisplatin and oral etoposide in grade 4 astrocytoma	Brain Tumor	Adjuvant	4	89	FACT-G, LASA, POMS, SDS
987403	Cisplatin for patients with squamous cell carcinoma	Other	Other: Locally advanced	0	19	FACT-G
989251	Imiquimod for chemoprevention of cervical intraepithelial neoplasia (CIN)	Gyn	Cancer Control	1	56	UNISCALE
MC00C6	Citaloprim for hot flashes	Other	Cancer Control	0	25	POMS
MC0115	Patient and caregivers QOL on phase I clinical trials	Many	Metastatic	1	15	LASA
MC0145	Esophageal adenocarcinoma and Barrett's esophagus registry	Many	Cancer Control	8	106	LASA
MC0192	QOL in women with ovarian cancer and their partners	Gyn	Cancer Control	2	169	FACT-G, SDS
MC01C1	Paroxetine for hot flashes in men	GU	Cancer Control	1	25	POMS
MC997C	Multidisciplinary intervention to improve QOL	Many	Metastatic	0	107	LASA, POMS, SDS
MC9991	Social support Assessment	Many	Cancer Control	0	50	SDS, UNISCALE
MC99C2	Glutamine in preventing myalgias and arthralgias	Many	Cancer Control	1	34	LASA, SDS
N0021	Gemcitabine and epirubicin for mesothelioma	Head and Neck	Other: Locally Advanced	9	59	SDS
N0022	Vinorelbine for the treatment of metastatic NSCLC	Lung	Metastatic	3	56	UNISCALE
N0031	Ceramide lipids for cutaneous breast cancer	Breast	Metastatic	1	25	FACT-G
N0044	Preoperative radiation and chemotherapy for locally advanced esophageal cancer	GI	Other: Neoadjuvant	3	50	SDS, UNISCALE
N0048	CPT-11 or 5-FU/CF for metastatic colorectal carcinoma	GI	Metastatic	2	17	SDS, UNISCALE
N0074	ZD 1839 in newly diagnosed glioblastoma	Brain Tumor	Adjuvant	1	96	FACT-G, LASA, POMS, SDS

Study No.	Description	Tumor Sites	Study Type	Number of Minority Patients	Number of Non-Minority Patients	QOL Assessments
N0087	Interleukin-12 and rituximab for non-Hodgkin's lymphoma	Lymphoma	Other	0	58	FACT-G
N00C9	Ginkgo biloba for chemotherapy – related cognitive dysfunction	Breast	Cancer Control	10	152	POMS
N0149	Oxaliplatin and Capecitabine for adenocarcinoma	GI	Cancer Control	2	45	FACT-G
N014C	PS-341 and gemcitabine for pancreatic adenocarcinoma	GI	Metastatic	2	88	FACT-G, SDS, UNISCALE
N01C4	Zinc Sulfate for altered taste in head and neck cancer during radiation	Head and neck	Cancer Control	8	151	LASA
N01C9	Docetaxel and inflixmab/placebo in NSCLC	Lung	Cancer Control	4	58	FACT-G
N0242	Docetaxel and capecitabine for adenocarcinoma	GI	Metastatic	1	42	LASA
N0272	Imatinib mesylate for oligodendroglioma and oligoastrocytoma	Brain Tumor	Other: Locally Advanced	0	19	LASA
N02C2	Erythropoietin in anemic patients	Many	Cancer Control	9	355	SDS
N9741	OXAL, 5-FU, and CPT-11 for adenocarcinoma	GI	Adjuvant	206	1460	SDS, UNISCALE
N9841	CPT-11 versus OXAL/5-FU/.CF for advanced colorectal carcinoma	GI	Metastatic	62	414	SDS, UNISCALE
N9923	Topotecan and paclitaxel limited-stage SCLC	Lung	Adjuvant	0	31	UNISCALE
N9942	Gemcitabine, cisplatin and radiation therapy in advanced pancreatic cancer	GI	Adjuvant	4	44	SDS
N9946	OXAL, 5-FU and CF in metastatic colorectal carcinoma	GI	Metastatic	1	45	SDS, UNISCALE
N99C7	Depomedroxyprogesterone acetate for hot flashes	Breast	Cancer Control	13	212	UNISCALE

Supplementary Table 1: List of Studies Included in Analysis

	Minority (N=531)	Non-Minority (N=5982)	Total (N=6513)	P value
Age				<0.0001
Median (Range)	60 (19-87)	63 (17-95)	62 (17-95)	
Female (%)	46%	46%	46%	0.9988
Performance Score, (%)				0.0855
Missing	27%	25%	25%	
0	26%	31%	31%	
1	42%	39%	39%	
2	5%	5%	5%	
Major Tumor Sites, (%)				<0.0001
GI	67%	46%	47%	
Lung	11%	16%	16%	
Breast	9%	11%	11%	
GU	2%	4%	4%	
Brain Tumor	1%	4%	4%	
Multiple	1%	1%	1%	
Other[1]	9%	16%	16%	
Unknown	1%	2%	2%	
Study Type, (%)				
Adjuvant	47%	33%	34%	<0.0001
Cancer Control	32%	43%	42%	
Metastatic	20%	21%	21%	
Other[2]	2%	3%	3%	

[1]Other Major Tumor Sites include gyn, head and neck, hematologic, lymphatic, musculoskeletal sites, psychosocial, and skin.
[2]Other Study Types include locally advanced and neoadjuvant studies.

Supplementary Table 2: Patient Characteristics

Assessment-specific QOL: HRQOL response rates were similar between minorities and non-minorities on each of the studies. The overall response rates were 85% (451/531) for minorities and 88% (5247/5982) for non-minorities. The results of multivariate models supported each of the following results.

There were 22 studies with 4201 patients (3.4% MP) that used the Uniscale assessment. In the subgroup of patients that reported the Uniscale, there were no significant differences in mean Uniscale QOL between MP and NMP (73 vs. 76) or in their overall survival (median survival times of 1.33 vs. 1.27 years).

LASA assessment was utilized in 12 studies with a total of 946 patients (3.6% MP). In this subset, no differences were reported in age, gender, performance score or median survival time (2.0 vs. 1.17 years, MP vs. NMP, respectively, $p = 0.54$).

There were 18 studies with 3924 patients (9.5% MP) assessed by SDS. No significant differences were reported on median survival times in MP and NMP (1.35 years vs. 1.21 years) or gender between groups. MP were significantly younger than NMP (mean age of 58 vs. 62, $p < 0.001$). There was no meaningful difference in SDS total score between the two groups and also when categorized by disease sites. For individual SDS item comparisons, minorities had significantly better mean appetite (64 vs. 62, $p=0.027$), concentration (72 vs. 68, $p<0.001$) and less fatigue (56 vs. 51, $p<0.001$), cough (70 vs. 68, $p=0.043$), breathing problems (74 vs. 73, $p=0.035$) and less fearful or worried about things (55 vs. 53, $p=0.035$) than non-minorities. But none of these differences were of a magnitude to be considered clinically significant.

The POMS assessment was used in 9 studies with a total of 662 patients (2.9% MP). Minorities were relatively younger (mean age of 49 vs. 58, p = 0.004) and the majority of them were female (74% vs. 49%, p = 0.035). The median survival time was 2 years for minorities and 1.73 years for non-minorities (p = 0.955). The POMS total score for both groups was between 71 and 72 which are about the norm for a healthy population [20]. But, both groups reported a low score in mean vigor activity (45 vs. 42, MP vs. NMP, respectively). Again, none of these scores were significantly different between the two groups.

There were 14 studies with 1805 patients (6.8% MP) that utilized the FACT-G. Minorities were younger than non-minorities (mean age of 59 vs. 63, p = 0.009). Minorities reported lower mean scores on physical well-being (65 vs. 69, p = 0.042), social/family well-being (62 vs. 68, p < 0.001), functional well-being (47 vs. 57, p < 0.001) and FACT-G total score (59 vs. 64, p < 0.001). Minorities had shorter median survival times than non-minorities (0.54 years vs. 0.85 years, respectively, p = 0.001). After stratifying by study and adjusting for site, age, study type and performance score in a Cox Proportional Hazards model, minority status was no longer significant.

Overall, minorities had worse overall FACT-G scores and slightly better overall SDS scores. Similarly, minorities reported slightly better scores on most SDS questions and were worse on the FACT-G subscales (Figure 2). There were no significant differences by minority status on LASA, SDS, POMS, Uniscale and FACT-G within each study type. Table 1 shows differences in the percent of patients having clinical deficiencies between minorities and non-minorities along with a p-value from Fisher's exact test comparing the two groups. These p-values are not adjusted for any other factors. MP had a higher percentage of patients with deficiencies in SDS nausea severity, Fact-G Social Family, and FACT-G Functional Deficits. MP had a lower percentage of patients with SDS Appetite and SDS Fatigue concerns.

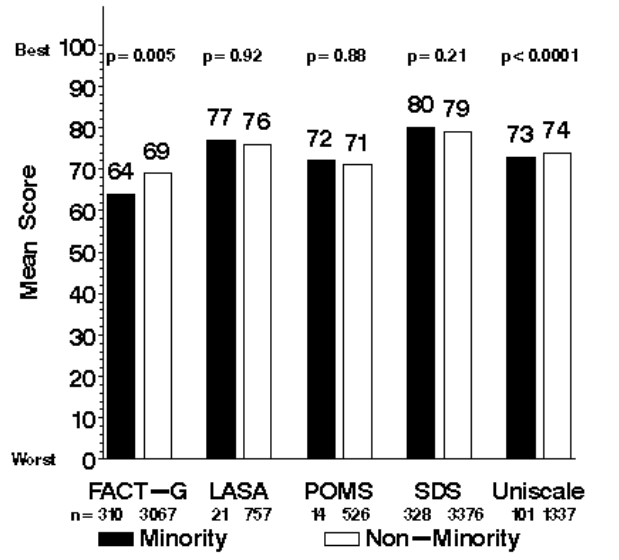

Figure 2: Overall QOL Assessment Scores by Minority Status

Questionnaire	Measure	Minorities	Non-minorities	Fisher's Exact p-value
Uniscale	Overall QOL	54/328 (16.5%)	486/3376 (14.4%)	0.325
LASA	Overall QOL	3/21 (14.3%)	96/757 (12.7%)	0.742
	Physical WB	4/21 (19%)	135/757 (17.8%)	0.779
	Emotional WB	6/21 (28.6%)	109/757 (14.4%)	0.109
	Mental WB	2/21 (9.5%)	87/758 (11.5%)	1.000
	Spiritual WB	3/21 (14.3%)	66/747 (8.8%)	0.425
SDS	Nausea Frequency	22/306 (7.2%)	219/3072 (7.1%)	0.908
	Nausea Severity	43/254 (16.9%)	300/2759 (10.9%)	0.005
	Appetite	72/313 (23%)	873/3085 (28.3%)	0.047
	Insomnia	100/315 (31.7%)	913/3192 (28.6%)	0.241
	Pain Frequency	101/315 (32.1%)	983/3183 (30.9%)	0.655
	Pain Severity	101/315 (32.1%)	983/3183 (30.9%)	0.654
	Fatigue	104/314 (33.1%)	1360/3164 (43%)	0.001
	Bowel	68/307 (22.1%)	650/3049 (21.3%)	0.716
	Concentration	25/314 (8%)	351/3167 (11.1%)	0.104
	Appearance	57/307 (18.6%)	477/3056 (15.6%)	0.190
	Breath	15/307 (4.9%)	194/3068 (6.3%)	0.384
	Outlook	93/310 (30%)	1006/3175 (31.7%)	0.565
	Cough	23/307 (7.5%)	301/3074 (9.8%)	0.222
	Total Score	17/310 (5.5%)	117/3067 (3.8%)	0.167
POMS	Depression-Dejection	0/14 (0%)	45/526 (8.6%)	0.619
	Anger-Hostility	0/14 (0%)	23/526 (4.4%)	1.000
	Confusion-Bewilderment	1/14 (7.1%)	54/526 (10.3%)	1.000
	Tension-Anxiety	1/14 (7.1%)	75/526 (14.3%)	0.704
	Fatigue-Inertia	3/14 (21.4%)	118/526 (22.5%)	1.000
	Vigor Activity	9/14 (64.3%)	359/526 (68.3%)	0.775
	Total Score	1/14 (7.1%)	50/526 (9.5%)	1.000
FACT-G	Physical WB	32/111 (28.8%)	334/1459(22.9%)	0.163
	Social/Family WB	19/104 (18.3%)	122/1371 (8.9%)	0.005
	Functional WB	65/105 (61.9%)	561/1360 (41.3%)	0.0001
	Emotional WB	27/103 (26.2%)	286/1352 (21.2%)	0.262
	Total Score	24/101 (23.8%)	227/1337 (17%)	0.102

QOL = Quality of Life; WB = Well-Being; LASA = Linear Analogue Self Assessment; SDS = Symptom Distress Scale; POMS = Profile of Mood States; FACT-G = Functional Assessment of Cancer Therapy – General

Table 1: Percent of Patients Clinically Deficient (i.e. Scores of 50 or Less Out of 100)

QOL by assessments for each tumor site and study type: QOL differences by minority status for studies categorized by site and study type are summarized in table 2. For Uniscale assessments, patients with lung cancer had lower overall QOL compared to patients with breast, GI and genitourinary (GU) cancer. MP who had breast cancer were significantly younger (mean age of 47 vs. 56, p = 0.0001). The mean LASA scores reported between groups for patients who had GI and Other tumor sites differed by a maximum of 7 points, where MP reported a better score in overall QOL, physical well-being, spiritual well-being and mental/intellectual well-being. There was a significant difference in mean emotional well-being (53 vs. 74, MP vs. NMP, respectively, p = 0.035) reported for patients with brain tumors however only three MP had this tumor site as compared to 206 NMP. There were not enough minorities with breast cancer in our sample to make any claims about QOL differences in this subgroup.

For mean SDS assessments, minority lung cancer patients reported more nausea frequency (58 vs. 69, p=0.028), nausea severity (52 vs. 69, p=0.011), and insomnia (34 vs. 54, p=0.007); but less cough (68 vs. 56, p=0.031) than non-minorities. However, minorities with GI cancer tended to have less fatigue (59 vs. 54, p<0.001), worry less about things (55 vs. 53, p=0.016); and better concentration (73 vs. 71, p=0.009) than non-minorities. On the other hand, minorities with breast tumor site had more insomnia than non-minorities (means of 43 vs. 54, p = 0.033, respectively).

Minorities Worse	Mean Difference	Subgroup	Mean Difference	Minorities Better
Social/Family WB	7.6	GI	4.4	Fatigue
Functional WB	11.8		2.1	Concentration
FACT-G Total Score	6.6		2.5	Outlook
Nausea Frequency/Severity	11.1/16.5	Lung	11.9	Cough
Insomnia	20.3			
Functional WB	7.9			
Insomnia	10.9	Breast	--	N/A
Functional WB	23.9			
FACT-G total Score	11.8			
N/A	--	Brain Tumor	--	N/A
N/A	--	Adjuvant	5	Fatigue
			2.4	Concentration
Nausea Severity	9.9	Cancer Control	--	N/A
Insomnia	7.6			
Pain Frequency	8.8			
Pain Severity	10.3			
Appearance	5.9			
Social/Family WB	4.3			
Functional WB	5.9			
N/A	--	Metastatic	2.9	Concentration
			6.4	Outlook
Nausea Severity	2.9	Overall	2.1	Appetite
Physical WB	3.8		5.9	Fatigue
Social/Family WB	6.4		3.3	Concentration
Functional WB	9.6		1.4	Breathing
FACT-G Total Score	5.3		1.9	Outlook
			1.9	Cough

WB = Well Being; N/A = Not Applicable; FACT-G = Functional Assessment of Cancer Therapy – General

Table 2: Significant QOL Differences Between Minorities and Non-Minorities by Site, Study Type, and Overall

Due to the small number of minorities assessed using POMS, the site subgroup analyses were only done on patients who had brain tumors (34%) or breast (25%) cancer. No significant differences were found in any of the POMS subscales.

For patients reporting a FACT-G, minorities with breast cancer were 12 years younger than non-minorities (mean age of 46 vs. 58, $p<0.001$), but had worse mean functional well-being (44 vs. 68, $p = 0.003$), FACT-G total score (55 vs. 67, $p = 0.029$) and also showed signs of having worse social/family well-being (58 vs. 67, $p = 0.081$). Similarly, minorities with GI cancer were about 3 years younger than non-minorities (mean age of 62 vs. 65, $p = 0.091$), reported a significantly worse social/family well-being (means of 60 vs. 67, $p = 0.002$), functional well-being (means of 44 vs. 56, $p = 0.009$), FACT-G total score (means of 56 vs. 63, $p = 0.009$), and slightly worse physical well-being (means of 58 vs. 66, $p = 0.052$). Further, minority lung cancer patients were about 2 years younger than non-minorities (mean age of 65 vs. 67, $p = 0.132$) with 22% vs. 10% with performance scores of 2, significantly worse functional well-being (means of 48 vs. 56, $p = 0.039$), and somewhat worse social well-being (means of 64 vs. 68, $p=0.064$). On the contrary, minorities with brain tumors were about the same age as non-minorities, with 83% vs. 45% having performance scores of 1, 17% vs. 12% having performance scores of 2, and they had significantly better emotional well-being (83 vs. 67, respectively, $p=0.029$).

Summary of significant results: In total, 115 scores on different QOL-related patient reported outcome assessments were compared between MP and NMP. Of these 115 tests, 16 indicated significant differences. By chance alone 5 or 6 of the 100 tests would be expected to be statistically significant at the 5% level. These differences included social/family well-being, functional well-being, FACT-G total score, fatigue, concentration and outlook assessed among GI cancer patients; nausea (frequency and severity), insomnia, functional well-being and cough assessed among lung cancer patients; insomnia, functional well-being and FACT-G total score assessed among breast cancer patients; and FACT-G/LASA emotional well-being assessed among brain tumor patients.

In terms of survival, there was no overall difference between MP and NMP. A survival difference was observed, however, between MP and NMP in studies that utilized the FACT-G with median survival times of 198 days vs. 310 days, respectively. However, after stratifying by study, the survival differences were no longer significant.

Conclusion: Overall the results of this meta-analysis across 47 studies involving over 6,000 patients indicate that the QOL experience of minority patients entering clinical trials is similar to the non-minority patients. Despite the preponderance of similarities, minority patients did indicate small deficits in physical, social, and emotional subscales relative to non-minority patients. Minority patients experienced larger tumor-specific deficits for a few QOL domains that bear further attention. Specifically, minority patients with lung, neurological or GI cancers had lower QOL scores in terms of emotional and social well-being as well as more problems with nausea and insomnia. There were also some areas where minorities did better than non-minorities, such as fatigue, outlook, and coughing.

These QOL differences indicate that minority patients may benefit from interventions targeted at these deficits. In particular, increasing accessibility to mental health services, social workers, patient advocates, and chaplaincy may address the social and emotional deficits. These services need to be sensitive to racial differences so they will be more likely accessed and utilized.

Because of the low enrollment rates of minorities onto clinical trials, QOL differences between minorities and non-minorities are getting overlooked. These undetected QOL differences could be contributing to the well documented differences in treatment efficacy.

Pooled analyses such as the present study have many inherent limitations. The sample of clinical trials included cannot be considered as being generalizable to all patients in all cancer clinical trials. Rather, the results must be interpreted through the analytic lens from the perception of our group's experience only. The trials included run the gamut of an active cooperative group portfolio and so combining the various eccentricities of 47 different studies into a collective analysis could produce estimates that are influenced by effects of investigators, research teams, and other non-clinical variables beyond the obvious heterogeneity in clinical treatment and outcomes. The 47 studies were selected based on QOL instrumentation from a large database of NCCTG clinical trials, thus, have the potential for biased results. The patients on this study were very heterogeneous, including a wide range of tumor types, tumor stages, and treatment modalities. These differences between studies were handled using subgroup analyses and adjusted survival analyses. Further studies are needed to explore the implications of these findings within specific cancer cohorts. We also hold no illusions that the minority patients participating in our trials represent the total minority population. A study done at Howard University Cancer Center noted that the majority of their African American population treated at their Center could not qualify for cancer treatment trials because of comorbidities [2]. Our findings are relevant to the patient population, both minority and non-minority, who meet clinical trial eligibility criteria. The purpose of our study, however, was to investigate, both in a collective and subset manner, whether systemic differences were so profound so as to be evident in the presence of this heterogeneity. We did indeed observe some such differences, especially within the trial subgroups, that will aid us in designing future studies. These results were based on exploratory subgroup analyses and require validation in other studies. Future studies should also explore subgroups where we did not observe differences between MP and NMP, since some of these subgroups might have been underpowered. The results of this meta-analysis are strongest in the estimation of survival and overall QOL differences. Despite detecting diversities within subgroups, observed differences in QOL and survival were more a function of disease state than differences in minority status. This finding is consistent with prior research showing that cancer survival is mainly related to cancer stage, treatment, and comorbidities [34]. Because this study did not find a significant survival effect, and some research suggests there may be survival issues for minorities in the general population [35], this enhances the idea that minority clinical trial participants are likely very different from the general minority population.

One supplementary analysis was done after excluding the 0.7% of Asian patients from the minority group and a separate analysis compared only Blacks versus non-minorities. These analyses did not result in any noticeable improvement or decline in QOL score at baseline between the two groups.

Underserved populations, especially those in socio-economically challenged situations, are not accruing to oncology clinical trials. Extensive efforts have been undertaken to increase minority participants in clinical trials, but successes have been limited [5]. The NIH Office of Cancer Survivorship is supporting six pilot projects to increase access to clinical trials for underserved populations. Difficulties establishing community partnerships and culturally competent methods for contacting potential participants remain primary barriers to minority and underserved populations' access to quality cancer care and clinical trials [6].

Increasing minority patient access to, eligibility for, and willingness to be involved in trials remains a challenge for all clinical trials groups. If eligibility changes allow more patients with comorbidities, the incidence and severity of many QOL issues might be even greater. Further insights into the needs of minority populations will help us design racially appropriate interventions. More research is needed to find out what underlies the observed differences and to plan intervention studies to reduce the observed deficits in QOL.

Summary: This study suggests that minority patients do have specific QOL deficits relative to non-minority patients that need identification and consideration in offering various treatment and clinical trial alternatives. QOL differences were consistent across the types of trials. Hence, after adjusting for various confounding factors, we found no evidence to suggest that minority patients fare better or worse on different types of trials than non-minority patients. This may be due to a greater socioeconomic homogeneity among clinical trial participants than exists in the community. Marital status and socioeconomic status could also be confounding factors for some of the QOL differences, especially for social/family wellbeing. Unfortunately, these hypotheses could not be explored in this manuscript, because socioeconomic status and marital status were not available for the patients on these clinical trials. Because of socioeconomic and other barriers to minority enrollment in clinical trials, these results might not reflect the situation that exists in the general community.

Implication for practice: It would seem prudent and appropriate to include a simple screening for QOL deficits in clinical practice that could facilitate identification, communication and amelioration of these problems in both minorities and non-minorities. This is an area of intense research activity that will undoubtedly eventually improve the quality of care for all patients.

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