Associations of uncertainty with psychological health and quality of life in older adults with advanced cancer

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Abstract

Context: Older adults with advanced cancer face uncertainty related to their disease and treatment.

Objective: To evaluate the associations of uncertainty with psychological health and quality of life (QoL) in older adults with advanced cancer.

Methods: Secondary cross-sectional analysis of baseline data from a national clustered geriatric assessment trial. Patients 70 years with advanced cancer considering a new line of chemotherapy were recruited. We measured uncertainty using the modified 9-item Mishel Uncertainty in Illness Scale. Dependent variables included anxiety (Generalized Anxiety Disorder-7), depression (Generalized Depression Scale-15), distress (Distress Thermometer), QoL ([Functional Assessment of Cancer Therapy-General (FACT-G)], and emotional well-being (FACT-G subscale). We used multivariate linear regression analyses to evaluate the association of uncertainty with each dependent variable. We conducted a Partial Least Squares (PLS) analysis with a Variable Importance in Projection (VIP) plot to assess the contribution of individual variables to the model. Variables with a VIP <0.8 were considered less influential.

Results: We included 527 patients (median age: 76 years, range 70-96). In multivariate analyses, higher levels of uncertainty were significantly associated with greater anxiety (β=0.11, SE=0.04), depression (β=0.09, SE=0.02), and distress (β=0.12, SE=0.02), and lower QoL (β=−1.08, SE=0.11) and emotional well-being (β=−0.29, SE=0.03); the effect sizes were considered small. Uncertainty items related to disease and treatment were most strongly associated with psychological health and QoL scores (all VIP > 0.8).

Conclusions: Uncertainty among older patients with advanced cancer is associated with worse psychological health and QoL. Tailored uncertainty management strategies are warranted.

Keywords

Uncertainty; psychological health; quality of life; older adults; oncologists

Introduction

Patients with advanced cancer face uncertainties such as whether their disease may progress or recur, or how long they may live. Uncertainty is the cognitive state created when a person cannot adequately structure an event due to insufficient cues. It occurs when the individual is unable to assign definite value to objects or events and/or to accurately predict outcomes.(1) In cancer care, uncertainty may arise from the unknown probability of treatment success, the complexity of information, lack of or poor communication with healthcare personnel, complex processes related to healthcare, or psychosocial and existential consequences of cancer.(2) In older adults, who actually constitute the largest proportion of new patients with

cancer,(3) these issues might be amplified by aging-related concerns, such as the impact of treatment on independent living and cognition.

Uncertainty can negatively affect physical, psychological, and existential outcomes.(4,5) In the general population of patients with cancer, greater uncertainty is associated with increased fatigue, insomnia,(6) emotional distress,(4) anxiety, depression,(7) and lower quality of life (QoL).(8) Uncertainty can also influence psychosocial adjustment to the diagnosis of cancer.(9) Older adults may not seek health information on their own and may have little social support to provide them with such information, both of which may contribute to uncertainty.(10)

In this secondary analysis, we described uncertainty among older adults with advanced cancer and its association with psychological health and QoL. We hypothesized that higher uncertainty was associated with worse psychological health and QoL in this population.

Materials and Methods

Study Design

We performed a cross-sectional analysis of baseline data from a national cluster-randomized trial that evaluated the effect of geriatric assessment (GA) information and GA-driven recommendations on patient satisfaction and communication with oncologists regarding age-related concerns [University of Rochester Cancer Center (URCC) 13070; ClinicalTrials.gov identifier: NCT02107443].(11) This trial was carried out within the URCC National Cancer Institute Community Oncology Research Program (NCORP) and enrolled patients from 31 community oncology practice sites between October 2014 and April 2017. The study was approved by the Research Subjects Review Board at URCC and institutional review boards at all enrolled practice sites. All patients provided informed consent at enrollment.

Participants and Measures

The primary study included patients aged ≥ 70 years, with a stage III or IV solid tumor or lymphoma deemed to be incurable, considering or receiving any line of cancer treatment, and with at least one impaired GA domain (i.e. vulnerable older patients with age-related conditions). After informed consent was provided, demographics and GA were obtained. Assessed GA domains included functional status, physical performance, comorbidity, medications, nutrition, cognition, psychological health, and social support. (12-14) Some GA assessments were completed by the patients and others were administered by clinical research associates (Supplemental Table 1). Patients completed additional measures via self-administered questionnaires at baseline, as described below.

Independent variable - Uncertainty

Uncertainty was evaluated using the Mishel's Uncertainty in Illness Scale (MUIS).(15,16) The original measure consists of 32 questions measuring several aspects of uncertainty (ambiguity, complexity, inconsistency, and unpredictability).(17) MUIS has been validated in patients with cancer.(15,16) For this study, we selected 9 items deemed relevant for patients with advanced cancer based on investigator consensus. Each item is presented in a

Likert scale of 1 to 5, with total scores ranging from 9 to 45 and higher scores indicating greater uncertainty. Cronbach's alpha was 0.72 for the modified 9-item MUIS scale. If participants had <100% of missing data for the uncertainty measure, we imputed missing data by averaging the items. Patients with complete missing of MUIS items were excluded.

Dependent variables - Psychological health and QoL

All measures were assessed using validated instruments: 1) Anxiety [Generalized Anxiety Disorder –7 (GAD-7) scale], 2) Depression [Geriatric Depression Scale-15 (GDS-15)], 3) Distress (Distress Thermometer), 4) QoL [Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire overall score], and 5) Emotional well-being (subscale of the FACT-G; this was reported separately and in addition to FACT-G as we were interested in examining psychological health of patients). GAD-7 consists of 7 questions scored in a scale from 0 (hardly ever) to 3 (nearly every day), with a score of 0-21 and a higher score indicating worse anxiety symptoms.(18) GDS-15 consists of 15 yes/no questions, scored 0 or 1, with higher scores indicating worse depressive symptoms.(19) The Distress Thermometer consists of an 11-point Likert scale (range 0-10), with a higher score indicating higher distress.(20) FACT-G is comprised of 27 questions scored on a 0-4 Likert scale, with a range of 0-108 and higher scores indicating better QoL. Emotional well-being is one of the FACT-G subscales, scored in the same fashion as FACT-G, with a range of 0-24 and higher scores indicating better emotional well-being.(21) Based on prior studies, minimal clinically important differences (MCID) were 3 points, 4-5 points, 2 points, 4-7 points and 1-2 points respectively for GAD-7, GDS-15, Distress Thermometer, FACT-G, and emotional well-being.(22-25)

Covariates

Covariates were identified a priori based on investigator consensus and prior literature. (15,26,27) These included patient demographics, cancer type, and number of impaired GA domains. Patient sociodemographic factors included age, gender, marital status, race, education, and annual household income.

Statistical analyses

Demographics and summary scores for uncertainty, depression, distress, QoL, and emotional well-being were reported using descriptive analyses. We conducted bivariate and multivariate linear regression analyses to evaluate the associations of uncertainty with anxiety, depression, distress, QoL, and emotional well-being. Each dependent variable was evaluated in a separate model, adjusting for covariates. The effect of practice oncology site clusters was tested by likelihood ratio tests linear mixed models with practice site included as random effects and not statistically significant (all p>0.10); therefore, results from the original multivariate models are presented. To account for the potential problem of multiple comparisons, two-sided p values of <0.01 were considered statistically significant.(28)

To provide understanding on which individual MUIS items contributed the most to our dependent variables, we conducted an exploratory Partial Least Squares (PLS) analysis using the 9 MUIS items as independent variables, and psychological health and QoL measures as dependent variables. PLS provides the Variable Importance for Projection (VIP)

statistic, which summarizes the contribution of an individual variable to the PLS model. Variables with a VIP <0.8 were deemed less influential in the model.(29) All analyses were performed using the SAS software package (version 9.4; SAS Institute, Cary, NC), and Stata 15.0 (StataCorp LLC, College Station, TX).

Results

The primary study included 541 patients; we excluded 14 patients with 100% missing data on the uncertainty measure, resulting in a final sample of 527 patients. Fifty-five patients (10.4%) had <50% missing uncertainty data. The mean age of patients was 76.6 years (SD 5.2 years, range 70–96); 51.2% were male, 51.8% completed at least some college education, and 50.6% of patients had an annual household income of >$50,000. Around half of the patients had a gastrointestinal or lung primary tumor. The mean number of impaired GA domains was 4.4 (SD 1.5). Other characteristics are shown in Table 1.

Uncertainty

The mean score for the modified 9-item MUIS was 19.7 (SD 4.8, range 9-33). The distribution of each item is shown in Table 2. The majority of patients agreed or strongly agreed with statements regarding communication with providers: "The doctors and nurses use everyday language so I can understand what they are saying" (93.1%) and "I understand everything explained to me" (74.8%). Half of the patients (50.4%) agreed or strongly agreed with the statement "The treatment I am receiving (or may receive) has a known probability of success." Most patients (73.0%) agreed or strongly agreed with the statement "The seriousness of my prognosis has been determined."

Psychological health and QoL

The average scores were 2.9 (SD 4.0, range 0-21) for GAD-7, 3.1 (SD 2.7, range 0-13) for GDS-15, 2.9 (SD 2.7, range 0-10) for distress, 80.7 (SD 14.7, range 30-108) for FACT-G, and 18.9 (SD 4.0, range 3-24) for emotional well-being respectively. The correlation coefficients among the dependent variables are shown in Table 3.

Multivariate analyses

In multivariate analyses, greater uncertainty was statistically significantly associated with higher levels of anxiety (β=0.10, SE=0.04, p=0.006), depression (β=0.10, SE=0.03, p<0.001), and distress (β=0.11, SE=0.02, p<0.001), as well as worse QoL (β=−1.10, SE=0.11, p<0.001) and emotional well-being (β=−0.29, SE=0.03, p<0.001) (Table 4). In other words, a 1-point increase in the 9-item uncertainty scale was associated with a 0.10 point increase in GAD-7, a 0.10 point increase in GDS, a 0.11 point increase in the Distress Thermometer, a 1.10 point decrease in total FACT-G and 0.29 point decrease in the emotional well-being subscale. The effect sizes were considered small.

Regarding covariates, older age was associated with lower levels of distress as well as better QoL scores. In contrast, a higher number of impaired GA domains was associated with higher levels of anxiety, depression, and distress as well as worse QoL and emotional well-being (Table 4).

Partial Least Squares (PLS) analysis

The VIP resulting from PLS (Figure 1) showed that uncertainty items related to patient-provider communication and those related to treatment options and effectiveness were more influential in the association with psychological health and QoL (all VIP > 0.8). Uncertainty related to trust in nursing personnel (MUIS7) or severity of prognosis (MUIS8) were less influential for determining patient outcomes.

Discussion

In this secondary analysis, we describe uncertainty in a population of vulnerable older adults with advanced cancer. Consistent with our hypotheses, we found that higher levels of uncertainty were associated with poorer psychological health and QoL. Uncertainty items related to patient-provider communication and those related to treatment options and effectiveness were most influential in these associations.

There are no clear validated cut-offs to define levels of uncertainty. The original MUIS scale (32-item) was initially described in multiple cohorts of patients, including those with cancer, with mean scores ranging from 59.8 to 103.7 on a 160-point scale.(17) In a study of older patients with cancer undergoing surgery, a 25-item MUIS scale (125-point scale) was used and mean score was 59.6.(30) In our sample, a 9-item MUIS scale (45-point scale) was used and mean score was 19.7, which was relatively similar to the aforementioned studies.

Cognitive, emotional, and behavioral responses to uncertainty can be both negative (e.g., anxiety, distress, avoidance) and positive (e.g., feelings of hope, information seeking). The balance between these responses is called "uncertainty tolerance", which is an individual characteristic mediated by personal and stimulus-dependent factors, such as education level or the complexity of the disease process.(31) In our study, we examined negative responses to uncertainty in vulnerable older adults with cancer, and found that uncertainty was associated with worse psychological health and QoL scores. However, effect sizes for these relationships were considered small based on previously reported MCID for the respective measures. (22-25) Findings from our study were consistent with previous reports in populations unselected by age. In a cross-sectional study of 30 patients with cancer (median age: 66 years), a higher level of uncertainty was associated with a higher level of anxiety. (32) In another cross-sectional study of 49 patients with lung cancer (mean age: 64 years), a higher level of uncertainty in the form of ambiguity was associated with increased perception of stress and poorer emotional well-being.(15) Furthermore, intolerance of uncertainty was associated with increased perception of stress, more depressive symptoms, and worse emotional well-being.(15) Uncertainty regarding prognosis is also prevalent in hospitalized patients with advanced cancer and can lead to distress and lower QoL.(4) For those with higher uncertainty-related distress, palliative care consultation may be beneficial. (4)

Management of uncertainty in older adults is under studied. Mishel and colleagues performed a randomized trial evaluating an uncertainty management intervention based on cognitive-behavioral strategies in older survivors of breast cancer.(33) At 10 months, the intervention improved cognitive reframing, cancer knowledge, patient-healthcare provider

communication, and coping skills. Uncertainty remained low 20 months after the intervention. In another study, patients with early prostate cancer (mean age: 62) were randomized to an uncertainty management decision-making intervention consisting of provision of information about the disease, communication strategies, and telephone calls performed between the diagnosis of prostate cancer and the first appointment with their physician.(34) Compared to usual care, patients receiving the intervention had improved cancer knowledge, problem-solving skills, and participation in decision-making, with less decisional regret. Importantly, there was no difference in mood or QoL.

Results from our exploratory PLS analysis showed that uncertainty items related to patient-provider communication and those related to treatment options and effectiveness were more influential in the association with psychological health and QoL. This treatment-related uncertainty may be addressed by improving communication. On the other hand, prognosis-related uncertainty was less influential in our model. Physicians may try to reduce uncertainty by providing extensive information but some patients may prefer to remain uncertain about a poor prognosis (35). Most of the patients in our study agreed that the seriousness of their prognosis had been determined. However, we have previously shown that 60% of these patients have different beliefs about their cancer curability compared to their oncologist (36). These patients could have a positive appraisal of prognosis-related uncertainty leading to hope. Attempting to reduce uncertainty by increasing prognostic understanding without addressing their psychological state may instead increase anxiety and lead to worse QoL.

Uncertainty may also arise from irreducible sources, such as existential concerns. Physicians also need to identify other potential causes of uncertainty, such as the potential impact of cancer in daily life and personal relationships. The GA can address some of these areas. Therefore, it is important that physicians first ascertain how much patients wish to know about their disease and prognosis, their preferred role in decision-making, and then assess if they would benefit from any intervention.(37,38) In patients with distress due to information-related uncertainty, improving communication may be an adequate strategy, whereas in those with distress due to irreducible uncertainty, a cognitive reframing of uncertainty might be more useful, so that patients are able to cope with it. (39)

Our study has several strengths. We recruited a large number of patients from community oncology practices where most vulnerable patients are treated. We used several validated instruments to assess psychological health and QoL. There are some limitations to our study. First, we did not inquire about the meaning of uncertainty to the patients. Second, our study sample was mostly non-Hispanic white and relatively well-educated, and therefore our findings may not be generalizable to patients of other ethnicities and races or lower education levels. Third, we adapted the original MUIS into a modified 9-item scale with items selected by the perspectives of the study team in an effort to reduce missing data, which limits comparison to other studies. Data was also imputed in about 10% of patients. In addition, the original MUIS and Mishel's uncertainty model did not assess aspects such as personal relationships or existential concerns.(40) Fourth, we did not collect information on the length of relationships between patients and oncologists, which may potentially affect

uncertainty levels. Finally, we cannot infer causation due to the cross-sectional nature of our study.

Significant gaps remain in knowledge about uncertainty in older adults with advanced cancer. Sources of uncertainty in older adults are not well studied. It is also unknown if all patients benefit from addressing uncertainty. Individual tolerance to uncertainty may differ, and influence the cognitive appraisal and response to an uncertainty-triggering situation, such as the diagnosis of cancer. (31) Future efforts to study uncertainty in older adults should aim to identify sources of uncertainty and the effects of uncertainty on psychological health and QoL in a prospective fashion, as well as other outcomes such as prognostic understanding, treatment decision-making, and treatment adherence.

In conclusion, in a vulnerable population of older patients with advanced cancer, higher uncertainty was associated with poorer psychological health and QoL. Uncertainty management strategies tailored to the needs of older adults with advanced cancer are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement:

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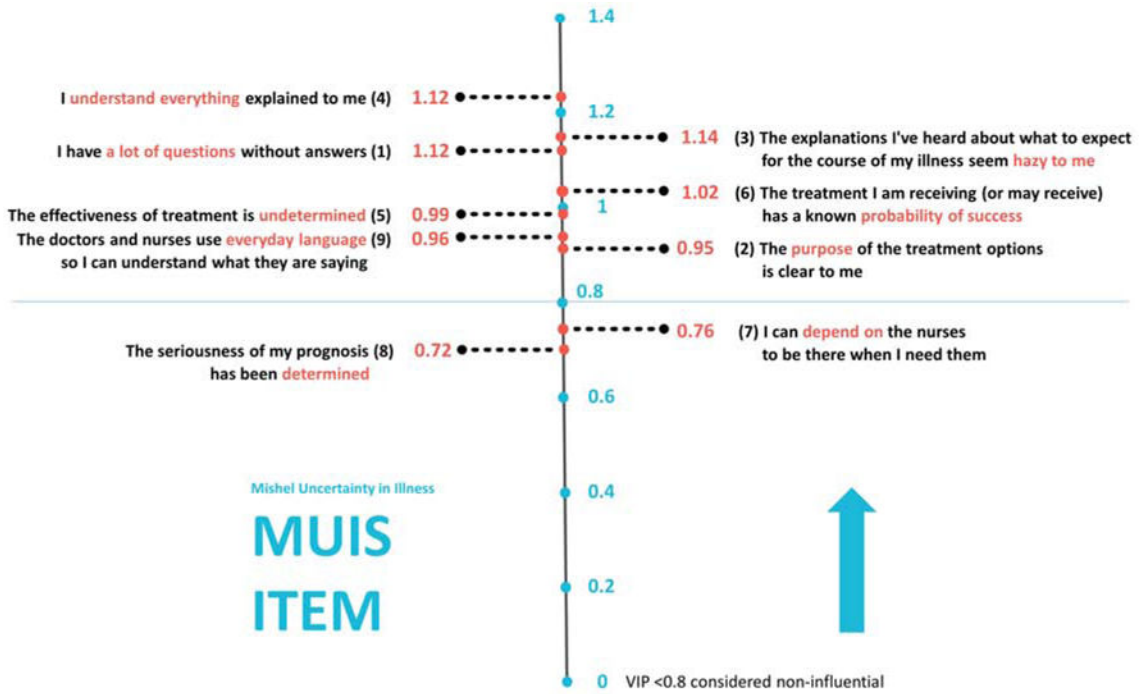**Key message:** This article describes the association of uncertainty with anxiety, depression, distress, and quality of life in an understudied population of older adults with advanced cancer. Our results indicate that a higher level of uncertainty is associated with worse psychological health and quality of life.

Figure 1.
Modified 9-item MUIS Variable Importance for Projection (VIP) plot

Table 1.

Patient characteristics

Characteristics (N=527)		N (%) or mean (SD)
Age, mean (SD)		76.6 (5.2)
Gender, N (%)	Female	257 (48.7)
	Male	270 (51.2)
Marital status, N (%)	Married	339 (64.4)
	Not married	187 (35.5)
Race, N (%)	White Non-Hispanic	471 (89.3)
	Other	56 (10.6)
Education, N (%)	Less than complete high school	63 (11.9)
	Complete high school	191 (36.2)
	Some college or above	273 (51.8)
Annual household income, N (%)	$50,000	259 (49.3)
	>$50,000 or Decline to answer	266 (50.6)
Cancer type, N (%)	Gastrointestinal	136 (25.8)
	Lung	135 (25.6)
	Other	255 (48.4)
Number of impaired GA domains, mean (SD)		4.4 (1.5)
Uncertainty, modified 9-item MUIS, mean (SD)		19.7 (4.8)
Anxiety, GAD-7 , mean (SD)		2.9 (4.0)
Depression, GDS-15, mean (SD)		3.1 (2.7)
Distress thermometer, mean (SD)		2.9 (2.7)
Quality of Life, FACT-G, mean (SD)		80.7 (14.7)
Emotional well-being, mean (SD)		18.9 (4.0)

Abbreviations: SD, standard deviation; GA, geriatric assessment, MUIS, Mishel's Uncertainty in Illness Scale; GAD-7, Generalized Anxiety Disorder −7; GDS-15, Geriatric Depression Scale-15; FACT-G, Functional Assessment of Cancer Therapy-General

Table 2

Distribution of Modified 9-Item Mishel Uncertainty in Illness (data shown prior to imputation)

Mishel Uncertainty in Illness (MUIS) Item	Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
1) I have a lot of questions without answers. [a,b]	4.2%	13.4%	20.2%	35.9%	26.3%
2) The purpose of the treatment options is clear to me. [c]	39.1%	45.5%	10.5%	3.2%	1.7%
3) The explanations I've heard about what to expect for the course of my illness seem hazy to me. [a,d]	4.8%	18.8%	20.2%	32.9%	23.3%
4) I understand everything explained to me.	26.4%	48.4%	16.3%	7.0%	1.9%
5) The effectiveness of treatment is undetermined. [a,b]	13.0%	36.6%	26.5%	16.4%	7.4%
6) The treatment I am receiving (or may receive) has a known probability of success. [b,d]	13.0%	37.4%	33.2%	5.5%	2.9%
7) I can depend on the nurses to be there when I need them. [e]	46.6%	43.2%	7.3%	1.5%	1.4%
8) The seriousness of my prognosis has been determined. [f]	26.6%	46.4%	20.7%	3.8%	2.5%
9) The doctors and nurses use everyday language so I can understand what they are saying. [c]	45.7%	47.4%	5.0%	0.8%	1.1%

[a] Item was reversely scored

[b] 3 missing responses

[c] 2 missing responses

[d] 42 patients (8.0%) selected "not applicable"

[e] 8 missing response

[f] 5 missing response

Table 3.

Correlation between psychological and quality of life measures

Measures	Correlation coefficient (p)				
	FACT-G	**EWB**	**GAD7**	**GDS**	**DT**
FACT-G total (FACT-G)	1	0.72 (<0.001)	−0.44 (<0.001)	−0.59 (<0.001)	−0.47 (<0.001)
Emotional well-being subscale of FACT-G (EWB)	0.72 (<0.001)	1	−0.49 (<0.001)	−0.45 (<0.001)	−0.51 (<0.001)
Anxiety (GAD7)	−0.44 (<0.001)	−0.49 (<0.001)	1	0.43 (<0.001)	0.56 (<0.001)
Depression (GDS)	−0.59 (<0.001)	−0.45 (<0.001)	0.43 (<0.001)	1	0.44 (<0.001)
Distress thermometer (DT)	−0.47 (<0.001)	−0.51 (<0.001)	0.56 (<0.001)	0.44 (<0.001)	1

Table 4

Multivariate analyses evaluating the associations of uncertainty with psychological health and quality of life

Dependent variable	Covariates	B coefficient,[a] standard error (SE)	95% CI	p value
Anxiety, GAD-7 score[b]	Uncertainty, modified 9-item MUIS	0.10 (0.04)	0.03 to 0.17	0.006
	Age	−0.08 (0.03)	−0.14 to −0.01	0.018
	Number of impaired GA domains	0.69 (0.14)	0.42 to 0.95	<0.001
Depression, GDS-15 score[b]	Uncertainty, modified 9-item MUIS	0.10 (0.02)	0.05 to 0.14	<0.001
	Age	−0.05 (0.02)	−0.09 to −0.01	0.019
	Number of impaired GA domains	0.66 (0.09)	0.49 to 0.83	<0.001
Distress thermometer score[b]	Uncertainty, modified 9-item MUIS	0.11 (0.02)	0.06 to 0.16	<0.001
	Age	−0.06 (0.02)	−0.11 to −0.02	0.005
	Number of impaired GA domains	0.43 (0.09)	0.25 to 0.61	<0.001
Quality of Life, FACT-G score[c]	Uncertainty, modified 9-item MUIS	−1.10 (0.11)	−1.33 to −0.88	<0.001
	Age	0.28 (0.10)	0.07 to 0.48	0.009
	Number of impaired GA domains	−3.90 (0.43)	−4.74 to −3.05	<0.001
Emotional well-being subscore[c]	Uncertainty, modified 9-item MUIS	−0.29 (0.03)	−0.36 to −0.22	<0.001
	Age	0.07 (0.03)	0.01 to 0.13	0.031
	Race (non-white vs. white)	1.16 (0.52)	0.14 to 2.18	0.027
	Number of impaired GA domains	−0.52 (0.13)	−0.77 to −0.27	<0.001

[a] Changes in dependent variable scores for every 1 point increment in modified 9-item MUIS, based on separate multivariate linear regression models, adjusting for age, gender, race, education, marital status, income, tumor type, and number of impaired geriatric assessment domains

[b] Higher score indicates a worse outcome

[c] Lower score indicates a worse outcome