# Symptom Burden, Perceived Control, and Quality of Life Among Patients Living With Multiple Myeloma

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# ABSTRACT

Background: New therapies for multiple myeloma (MM) have improved survival rates but often expose patients to heightened toxicities and prolonged treatment, leading to increasing complications and side effects. We evaluated the association between symptom burden, perceived control over illness, and quality of life (QoL) among a national sample of patients with MM. Methods: For this observational, cross-sectional study, we used data from the Cancer Experience Registry research initiative to examine symptom- and functioningrelated concerns among 289 patients with MM across the illness trajectory. We applied hierarchical multiple linear regression analyses to explore associations between symptom burden and perceived control over illness with QoL indicators: depression, anxiety, and social satisfaction. Results: In our sample, 73% of participants with MM reported currently receiving treatment; 39% experienced relapse; 56% received 1 to 2 autologous transplants, 10% received  $\geq$ 3 autologous transplants, and 4% received allogeneic and autologous transplants; 30% had not received a stem cell transplant. Average time since diagnosis was 4.4 years. The most highly endorsed concerns included eating and nutrition (61%), physical activity (59%), moving around (56%), fatigue (55%), pain (52%), and sleep (46%). Only 27% believed they had control over their disease, whereas 48% perceived having control over the physical side effects of MM. Approximately one-third of the variance in anxiety and depression and nearly two-thirds of variance in social satisfaction were explained by sociodemographic, clinical, and symptom burden variables. Perceived control over illness significantly predicted depression and anxiety, but not social satisfaction. Our results highlight substantial concern among patients with MM about physical symptoms and function. Additionally, greater symptom burden significantly accounted for poorer QoL, and lower perceived control over illness was linked to depression and anxiety. **Conclusions:** Patients with MM and survivors experience substantive long-term QoL issues. Together, these findings point to the critical need for comprehensive symptom management, integrated palliative care, and enhancement of social and emotional support for individuals with MM.

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## Background

Multiple myeloma (MM), a plasma cell malignancy, is the second most common hematologic cancer in the United States, with an estimated 32,110 new cases occurring in 2019, and an estimated 12,960 deaths.1 Advances in treatment using autologous stem cell transplantation and novel therapies have resulted in significantly improved survival rates in the past 15 years.<sup>2–5</sup> However, despite improved treatment, MM is incurable and progressive, and as such, the overarching aim of treatment-often interspersed with durations of remission with minimal or maintenance treatment<sup>6</sup>—is to control the disease and prolong survival. Although people with MM are living longer, they are doing so with increasing complications of the disease and cumulative side effects from prolonged treatment.7-9 Characteristic features of MM include destructive bone disease, bacterial infections, impaired renal function, anemia, and hypercalcemia.<sup>10</sup> As a result, patients often experience significant adverse effects on quality of life (QoL), including fatigue, pain, breathlessness, muscle weakness, and peripheral neuropathy,<sup>11,12</sup> which can negatively impact work, social, and familial roles.13 Research has shown patients with MM experience greater symptom burden and poorer QoL compared with those with other hematologic cancers.<sup>14</sup> Given the prospect of ongoing complications from treatment-related toxicities across the illness trajectory, patient-reported outcomes have been recognized as an important endpoint in the management of MM.11,15,16

Despite awareness of the importance of patient outcomes in the management of MM, research has largely focused on the physical effects of MM and its treatments; comparatively little is understood about the impact of symptom burden on the psychosocial wellbeing of patients with MM. Research has found that both high symptom burden and mental health symptoms are strong determinants of health-related QoL in patients with MM.<sup>17</sup> For example, in a recent longitudinal study, Ramsenthaler et al<sup>18</sup> reported that symptom level, anxiety, and pain were more likely to predict declining

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health-related QoL than demographic or clinical characteristics. However, although studies have examined the impact of symptom burden on health-related QoL,<sup>12,14,15</sup> limited research has focused on identifying specific symptoms and factors that impact psychosocial wellbeing in patients with MM. Understanding specific factors associated with adverse psychosocial well-being has the potential to guide development of targeted interventions designed to alleviate symptom burden and improve patient QoL.

Furthermore, given the chronic nature of MM, the illness trajectory can be unpredictable, and can result in a perceived sense of loss of control. Perceived control (ie, the capacity to achieve positive and avoid negative outcomes through their own behaviors)19 has been considered an important modifiable factor in psychosocial well-being. Research among people with different cancer types (eg, early-stage breast cancer)<sup>20</sup> has found positive associations between perceived control and psychosocial well-being and QoL. However, few studies have examined the impact of perceived control in managing a chronic disease such as MM. Unpredictability of MM can create burden, and given the substantial risk of recurrence<sup>10</sup> combined with ongoing management of disease and treatment side effects, the potential of a protective factor such as perceived control for psychosocial well-being for patients with MM warrants attention.

As such, the purpose of our study is 2-fold: to identify the most frequently reported areas of distress among individuals living with MM, and to examine how symptom burden and perceived control over the cancer experience are associated with depression, anxiety, and social satisfaction among patients with MM and survivors. To capture the patient experience across the MM illness trajectory, this cross-sectional study included patients with MM regardless of their stage or phase of illness.

# Methods

## Procedure

In 2013, the Cancer Support Community (CSC) launched the Cancer Experience Registry, an online research initiative examining the social and emotional impact of cancer. Individuals diagnosed with MM were invited to answer core registry questions asked of all participants, regardless of their diagnosis, as well as questions specific to living with MM (referred to as the Cancer Experience Registry: Multiple Myeloma). Participants were recruited through CSC and Leukemia & Lymphoma Society (LLS) community-based affiliates/chapters and online communities, CSC's toll-free support helpline and LLS's information resource center, and other advocacy organizations and social media. Participants were invited to complete the survey online. Although surveys were typically completed at home, in some cases completion occurred in clinic on a computer or tablet. Ethical and Independent Review Services (E&I) served as the study Institutional Review Board of record. All procedures performed involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participants provided electronic informed consent prior to participation.

## **Participants**

From March 2013 through December 2016, 598 US residents with a history of MM enrolled in the registry; 441 initiated the web-based survey and 289 answered at least 1 question about emotional and social functioning and symptom burden, constituting the current analysis dataset. The racial composition of the analysis sample (89% white; 6% black or African American; 2% other; 3% preferred not to share) was significantly different (P=.005) from that of nonparticipants (76% white; 15% black or African American; 9% other), but the samples did not differ on other sociodemographic characteristics or cancer history.

# Measures

# Sociodemographic Characteristics and Clinical History Participants provided information about age, sex, race (white, black or African American, or other/multiracial), Hispanic ethnicity, region, annual household income, education (dichotomized as whether the patient graduated from college), and employment status. Participants also reported years since MM diagnosis, history of relapse, history of MM-related kidney disease, MM stage at diagnosis, and number and type of autologous and allogeneic bone marrow transplants. Participants were asked if they were currently receiving treatment of cancer (yes/no) and whether (yes/no) they had ever received chemotherapy, radiation therapy, and biological therapy ("a type of treatment that works with your immune system to help fight cancer or control side effects").

# CancerSupportSource

Participants completed CancerSupportSource, a 25-item distress screening tool that examines physical, social, emotional, and practical concerns and unmet needs.<sup>21</sup> Participants rated their level of concern (0 = not at all; 4 = very seriously) for each item that began with the stem, "Today, how concerned are you about..." (eg, "Today, how concerned are you about feeling lonely or isolated?" and "Today, how concerned are you about pain and/or physical discomfort?"). Top concerns were assessed descriptively by calculating the proportion of respondents who reported moderate to very serious

concern for each item. CancerSupportSource data were collected to describe distress and unmet needs, and not included in multivariate analyses.

## PROMIS-29

Participants completed the Patient-Reported Outcomes Measurement Information System 29 Profile V1.0 (PROMIS-29),<sup>22</sup> a collection of 4-item subscales assessing participant physical and emotional symptoms and functioning. Participants rated each item with reference to the past 7 days; function/satisfaction scales have no time frame. Higher scores represent more of the construct being measured. Scores are converted to standardized T-scores (mean [SD], 50 [10]); normative reference groups are the US general population. Subscale internal consistency reliability ranged from good to excellent (Cronbach  $\alpha$ =0.84–0.96). Physical function and fatigue subscales were used to examine symptom burden and function; depression, anxiety, and social satisfaction subscales were used to examine psychosocial well-being.

## Symptom Interference

Participants rated the extent to which peripheral neuropathy, bone pain, gastrointestinal toxicity, and infection each interfered with daily life in the past 7 days (0 = not at all; 4 = very much); the average of the 4 ratings was calculated to create a symptom interference score (range, 0–4;  $\alpha$ =0.61).

#### Illness Control

For items assessing perceived control, participants rated their perceived control (0 = no control at all; 4 = complete control) over the physical side effects of MM and its treatment, type of follow-up care received, and control over the course of their MM (ie, whether MM will come back or worsen); the average of the 3 ratings was calculated to create a perceived control score (range, 0–4;  $\alpha$ =0.63). For preparedness to manage side effects, participants indicated in a single item the extent (0 = not at all; 4 = very much) to which they felt their healthcare team had prepared them to manage side effects of MM treatment.

#### Analysis

Data analysis was conducted using Stata, version 14 (StataCorp LLP).

## Descriptive Analyses

Descriptive statistics were calculated for all study variables. When reporting descriptive results, scales were collapsed into dichotomous categories for cancer-related distress (0 = not at all, slightly; 1 = moderately, seriously, very seriously), symptom interference (0 = not at all, a little bit, somewhat; 1 = quite a bit, very much), perceived

control (0 = no control, a little; 1 = moderate amount, a great deal, complete), and PROMIS scales (0 = T-scores <1 SD than the national average; 1 = T-scores  $\geq 1$  SD) to facilitate reader interpretation. When used in statistical analysis, original scale responses were retained.

## Hierarchical Multiple Regression Analyses

The dependent variables were PROMIS-29 scores on depression, anxiety, and social satisfaction. Pearson and Spearman correlations and chi-square tests were used to examine bivariate relations between dependent variables and potential covariates/independent variables: sociodemographic (age, sex, education, race, ethnicity, annual household income, employment status, regional location), clinical history (years since diagnosis, history of relapse, MM-related kidney disease, disease stage at diagnosis, stem cell transplant history, currently receiving treatment, and treatment after diagnosis), symptom burden and function (PROMIS-29 physical function, PROMIS-29 fatigue, symptom interference), and illness control variables (perceived control, preparedness to manage side effects). To minimize type I error, these potential covariates were selected for regression models based on a priori hypotheses.

Variables significantly associated with dependent variables in bivariate analyses were included in hierarchical multiple linear regression analyses as follows: step 1, sociodemographic variables; step 2, clinical history variables; step 3, symptom burden and function (symptom interference, fatigue, and physical function); and step 4, illness control (perceived control and preparedness to manage side effects). We performed complete case analysis when fitting regression models.

# Results

## Clinical Description of the Sample

#### Participant Characteristics

A total of 289 participants responded to at least 1 item about emotional and social functioning and symptom burden. Sociodemographic characteristics and cancer history are presented in Table 1. More than half (56%) received 1 to 2 autologous transplants, 10% received  $\geq$ 3 autologous transplants, and 4% received allogeneic and autologous transplants; 30% had not received a stem cell transplant. Most (85%) received chemotherapy, and 73% reported currently receiving treatment; 39% experienced a relapse of MM and 13% indicated they had MM-related kidney disease.

# **Cancer-Related Distress**

The most strongly endorsed concerns (moderate to very serious) among patients with MM were related to physical function and symptom burden: eating and

Table 1. Patient Characteristics (N	=289)
Characteristic	n (%)
Age, mean (SD), y (n=249)	62.6 (9.0)
Women (n=283)	153 (54%)
Race (n=283)	
Black or African American	18 (6%)
White	253 (89%)
Other	5 (2%)
Prefer not to share	7 (3%)
Hispanic or Latino ethnicity (n=283)	6 (2%)
Region (n=263)	
Rural	66 (25%)
Suburban	142 (54%)
Urban	53 (20%)
Do not know	2 (1%)
Education (n=280)	
No college	33 (12%)
Some college	57 (20%)
College degree	114 (41%)
Graduate degree	76 (27%)
Annual household income, \$USD (n=241)	
<\$20,000	19 (8%)
\$20,000–\$39,999	43 (18%)
\$40,000–\$59,999	37 (16%)
\$60,000–\$79,999	22 (9%)
\$80,000–\$99,999	20 (8%)
≥\$100,000	32 (13%)
Don't know/prefer not to share	68 (28%)
Employment status (n=274)	
Full-time	49 (18%)
Part-time	12 (4%)
Not employed, retired	127 (46%)
Not employed, disability	68 (25%)
Not employed, other	18 (7%)
Years since MM diagnosis, mean (SD) (n=283)	4.4 (4.0)
Relapse history (n=259)	102 (39%)
MM-related kidney disease (n=286)	36 (13%)
MM stage at diagnosis (n=285)	
Stage	51 (18%)
Stage II	50 (18%)
Stage III	92 (32%)
Other/Do not know	92 (32%)
Stem cell transplant history ( $n=278$ )	, 2 (32,6)
None	84 (30%)
	154 (54%)
	28 (10%)
	12 (49/)
	12 (4/0)

Table 1. Patient Characteristics	(N=289) (cont.)
Characteristic	n (%)
Currently receiving treatment (n=285)	209 (73%)
Treatment after diagnosis	
Chemotherapy	245 (85%)
Radiation therapy	89 (31%)
Biological therapy	194 (67%)

Abbreviation: MM, multiple myeloma.

nutrition (61%), physical activity (59%), moving around (56%), fatigue (55%), pain (52%), and sleep (46%) (Table 2). Many participants also reported concern about emotional and interpersonal matters (eg, 43% reported worry about the future and what lies ahead, and 32% reported feeling sad or depressed).

# Symptom Burden and Function

Several respondents reported that the following types of symptoms interfered with daily life quite a bit or very much: bone pain (22%), peripheral neuropathy (21%), gastrointestinal toxicity (16%), and infection (3%). A total of 38% of respondents reported physical functioning in ranges suggestive of substantial impairment ( $\geq$ 1 SD than the national average), and 33% reported fatigue in ranges suggestive of impairment.

# Illness Control

Only 27% of participants believed they had control (moderate, a great deal, or complete) over the course of their MM (ie, whether it will come back, get worse, or they will develop a different type of cancer); 48% perceived having control over the physical side effects of MM; and 88% over the type of follow-up care they receive. A total of 57% of participants reported feeling prepared by their healthcare team to manage the side effects of MM treatment.

# Psychosocial Well-Being

Substantial proportions of patients with MM reported psychosocial well-being in ranges suggestive of impairment ( $\geq$ 1 SD than the national average) with respect to depression (17%), anxiety (20%), and social satisfaction (29%).

## **Correlation and Regression Analyses**

Bivariate associations between independent and dependent variables are presented in Table 3, and results from hierarchical multiple linear regression analyses are presented in Table 4. All models were significant at all steps; the greatest proportion of variance in each model was accounted for by symptom burden and physical function variables.

### Table 2. Most Strongly Endorsed Concerns<sup>a</sup> (N=283)

	n (%)
Eating and nutrition	176 (61%)
Exercising and being physically active	168 (59%)
Moving around (walking, climbing, stairs, lifting, etc.)	159 (56%)
Feeling too tired to do the things you need or want to do	157 (55%)
Pain and/or physical discomfort	150 (52%)
Sleep problems	132 (46%)
Health insurance or money worries	131 (46%)
Thinking clearly (eg, "chemo brain," "brain fog")	134 (46%)
Worrying about the future and what lies ahead	125 (43%)
Changes or disruptions in work, school, or home life	121 (42%)
Intimacy, sexual function, and/or fertility	105 (37%)
Managing side effects of treatment (nausea, swelling, etc.)	107 (37%)
Worrying about family, children, and/or friends	107 (37%)
Body image and feelings about how you look	103 (36%)
Making a treatment decision	103 (36%)
Feeling irritable	91 (32%)
Feeling sad or depressed	92 (32%)
Finding meaning or purpose	91 (32%)
Communicating with your doctor	88 (31%)
Recent weight change (gain or loss)	76 (27%)
Feeling lonely or isolated	69 (24%)
Problems in your relationship with your spouse/partner	56 (20%)
Feeling nervous or afraid	56 (19%)
Transportation to treatment and appointments	32 (11%)
Tobacco or substance use—by you or someone in your household	20 (7%)

Sample sizes ranged from 281 to 287.

<sup>a</sup>Participants indicating "moderately" to "very seriously" concerned.

## Depression

Nine predictors explained 36% of the variance in depression (adjusted  $R^2 = 0.36$ , F(10,209) = 13.10; P < .001); in the final model, younger age (semipartial r = -0.11; P = .048), greater symptom interference (semipartial r = 0.11; P = .050), greater fatigue (semipartial r = 0.30; P < .001), lower perceived control over MM side effects (semipartial r = -0.16; P = .005), and lower preparedness to manage side effects (semipartial r = -0.11; P = .037) were associated with significantly greater depression. Lower education and history of MM-related kidney disease were associated with greater depression at steps 1 and 2 of the model, but became nonsignificant after the addition of symptom burden variables.

# Anxiety

Eight predictors explained 33% of the variance in anxiety (adjusted  $R^2 = 0.33$ , F(8,206) = 13.99; P<.001); in the final model, younger age (semipartial r = -0.13, -0.023), greater symptom interference (semipartial r = 0.11; P=.046), greater fatigue (semipartial r = 0.32; P<.001), and lower perceived control over MM side effects (semipartial r = -0.17; P=.002) were associated with greater anxiety. Women reported significantly greater anxiety at steps 1 and 2 of the model, but sex became non-significant after the addition of symptom burden variables.

# Social Satisfaction

Eight predictors explained 62% of the variance in social satisfaction (adjusted  $R^2 = 0.62$ , F(9,207) = 40.31; P < .001); in the final model, poorer physical function (semi-partial r = 0.28; P < .001) and greater fatigue (semi-partial r = -0.31; P < .001) were associated with lower social satisfaction. Lower education, history of relapse, and ever receiving chemotherapy were associated with lower social satisfaction at steps 1 and 2 of the model, but became nonsignificant after the addition of symptom burden variables.

To summarize, results from hierarchical multiple linear regression models predicting depression, anxiety, and social satisfaction indicate that higher symptom burden and lower perceived control are strongly associated with poorer QoL among patients with MM.

# Discussion

Advances in the treatment of MM have extended the life expectancy of patients<sup>1,4,7</sup>; however, as patients with MM live longer, they also spend more time receiving treatments that can be physically and mentally demanding.15 As such, this study explored the physical and psychosocial experiences of illness of patients with MM. Our results highlight 3 primary findings. First, we provide a robust description of distress and unmet needs that impact patients with MM in their daily lives. We also demonstrate that many patients with MM not only report symptom burden and interference with daily functioning but also perceive a lack of control over their lived experiences. And finally, our results highlight the specific contributions of physical factors, such as symptom burden, and psychosocial factors, such as perceived control, on patients' overall psychosocial well-being. Taken together, these results highlight considerable distress, lack of control, and frequent symptom burden and interference among many patients with MM. Furthermore, the findings present opportunities to develop targeted interventions that may improve the lives of patients with MM.

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Table 3. Associations	Between	Quality	of Life	and P	redicto	r Varia	bles										
	Mean (SD) or n (%)	-	5	ю	4	ъ	9	۲	œ	6	6	7	12	13	4	15	16
Dependent variables: quality of lit	e																
1. Depression	49.9 (9.0)																
2. Anxiety	51.6 (9.7)	0.73**															
3. Social satisfaction	46.0 (9.3)	-0.47**	-0.42**														
Sociodemographic																	
4. Age, y	62.6 (9.0)	-0.17**	-0.23**	0.07													
5. College education	190 (68%)	-0.19**	-0.15*	0.15*	0.01												
6. Female sex	153 (54%)	0.13*	0.19**	-0.08	-0.13*	-0.12											
Clinical history																	
7. Years since MM diagnosis	4.4 (4.0)	-0.08	-0.14*	-0.05	0.11	0.06	-0.08										
8. Currently receiving treatment	209 (73%)	0.03	0.07	-0.09	-0.05	-0.11	0.06	-0.11									
9. Ever received chemotherapy	, 245 (85%)	0.06	0.08	-0.24**	-0.19**	-0.04	0.03	0.10	0.01								
10. Ever received biological therapy	194 (67%)	-0.01	0.04	-0.07	-0.02	0.16**	0.05	0.11	0.13*	-0.04							
11. Relapse	102 (39%)	0.08	0.09	-0.17**	-0.01	0.03	-0.01	0.47**	0.16**	0.15*	0.18**						
12. MM-related kidney disease	36 (13%)	0.13*	0.06	-0.09	0.06	-0.01	0.05	-0.02	0.03	0.10	0.04	0.05					
Symptom burden																	
13. Symptom interference	1.0 (0.8)	0.41**	0.38**	-0.50**	-0.16*	-0.27**	0.09	-0.02	0.11	0.14*	-0.01	0.02	0.11				
14. Physical function	43.5 (8.1)	-0.32**	-0.27**	0.68**	0.08	0.12*	-0.09	0.03	-0.07	-0.21**	0.02	-0.04	- 0.03	-0.50**			
15. Fatigue	54.7 (10.8)	0.53**	0.52**	-0.69**	-0.15*	-0.16**	0.09	-0.04	0.20**	0.13*	0.05	0.13*	0.08	0.50**	-0.57**		
Illness control																	
16. Perceived control	1.7 (0.8)	-0.35**	-0.32**	0.33**	0.09	-0.01	-0.18**	0.03	0.08	-0.07	-0.06	-0.13*	-0.03	-0.25**	0.23**	-0.26**	
17. Prepared to manage side effects	2.6 (1.2)	-0.18**	-0.09	0.13*	-0.03	-0.04	-0.12	-0.02	0.08	0.11	-0.01	-0.02	-0.11	-0.09	0.10	-0.11	0.22**
Numbers in table denote Pearson Abbreviation: MM, multiple myelc *P<.05; **P<.01.	correlation co ma.	pefficients.															

# Table 4. Hierarchical Multiple Regression Analyses Predicting Depression, Anxiety, and Social Satisfaction

	Predictor Variablesª (∆ Adjusted R²)	Model Statistics at Final Step			
Dependent Variable		Model-Adjusted <i>R</i> <sup>2</sup>	Significant Predictors	Parameter Estimate <sup>b</sup>	Part <i>r</i> ⁴
Model 1: depression (n=220)	Step 1: Education, age, sex (0.06)	.36***	Age, y*	-0.11	-0.11
	Step 2: MM-related kidney disease (0.02*) Step 3: Symptom interference, physical		Symptom interference*	1.37	0.11
	function, fatigue (0.23***)		Fatigue***	0.32	0.30
	manage side effects (0.05***)		Perceived control**	-1.91	-0.16
			Prepared to manage side effects*	-0.89	-0.11
Model 2: anxiety (n=215)	Step 1: Education, age, sex (0.08)	.33***	Age, y*	-0.14	-0.13
	Step 2: Years since MM diagnosis (0.01) Step 3: Symptom interference, physical		Symptom interference*	1.52	0.11
	function, fatigue (0.21***)		Fatigue***	0.36	0.32
	Step 4. Ferceived control (0.05 <sup>m</sup> )		Perceived control**	-2.25	-0.17
Model 3: social satisfaction (n=217)	Step 1: Education (0.02) Step 2: Relapse, ever received chemotherapy (0.06***) Step 3: Symptom interference, physical function, fatigue (0.53***) Step 4: Perceived control, prepared to manage side effects (0.01)	.62***	Physical function***	0.45	0.28
			Fatigue***	-0.36	-0.31

Abbreviation: MM, multiple myeloma.

<sup>a</sup>Variables significantly associated with response variable in bivariate analysis.

<sup>b</sup>The parameter estimates (β coefficients) are the average change in the response variable associated with a unit change in the predictor, assuming other predictors are held constant.

<sup>c</sup>Semipartial correlation.

\**P*<.05; \*\**P*<.01; \*\*\**P*<.001.

Consistent with prior research,<sup>15,23</sup> we found that patients with MM commonly reported concerns and cancer-related distress related to symptoms and side effects. For example, >50% were distressed by fatigue, pain, and limited physical function, and nearly 50% were distressed by sleep difficulties. In contrast to prior studies,<sup>15,23</sup> we also examined concerns about eating and nutrition, and found, notably, that this was the greatest concern in the current sample, with 61% of respondents reporting being moderately to very concerned about eating and nutrition. Unfortunately, interventions for these symptoms often present a challenge. Appetite stimulants yield marginal results, and most pharmacologic approaches to cancer cachexia do not vield improvements in lean body mass or physical function.<sup>24–26</sup> Similarly, fatigue management requires multimodal intervention, and many patients do not have access to evidence-based approaches because of cost and limited insurance coverage.27,28 Regarding sleep difficulties, although sometimes managed in the short term with medications, they are best addressed using behavioral interventions, such as cognitive behavioral therapy.<sup>29,30</sup> These concerns, which have meaningful life impact, are unlikely to be addressed adequately through standard cancer care pathways. Our findings suggest the need for more targeted attention and intervention related to appetite and nutrition, fatigue management, and physical function in patients with MM.

Building upon these results, we also found that patients with MM perceived a lack of control over their lived experiences of illness, which had a small but significant association with greater depression and anxiety, even after controlling for the role of physical symptom burden. This is concerning, and perhaps reflective of inadequate attention to symptom assessment and management in routine cancer care. Studies of early integrated palliative care during active cancer treatment show that attending to symptoms improves patients' overall QoL<sup>31-33</sup> and may lead to prolonged survival.<sup>34</sup> Our findings suggest that routine cancer care for MM does not address distress adequately, and that targeted efforts to improve symptom management have the potential to yield improved illness experiences for patients with MM. However, research has shown that palliative care services are underutilized among patients with hematologic malignancies, and most trials of integrated palliative care have excluded hematology patients.<sup>35</sup> Thus, efforts are needed to facilitate the early integration of palliative care as part of MM management. In addition, assessing symptom burden and QoL outcomes throughout the illness trajectory as part of routine care has the potential to identify areas of concern accurately, and enable tailoring of services, care, and interventions to meet patient needs effectively.

Last, we found that physical function and symptom burden among patients with MM are associated with depression, anxiety, and social satisfaction. Although these constructs are complex, the pattern is consistent and clear. As such, these analyses support the notion that targeted attention to symptom burden and physical function of patients with MM has the potential to yield dividends in improving patients' overall lived experiences of MM. More research is needed in this area, along with the development of targeted interventions specifically for patients with MM.

Our study has limitations. Clinical history was provided by participants and we did not ask about specific therapeutic agents; given the complexity of MM, selfreported medical history (including relapse, history of MM-related kidney disease, and disease stage) may not be fully accurate, and we are not able to differentiate between active versus maintenance therapy. In addition, we do not have data on nonparticipants; patients with MM who participate in online research may differ from the overall population of patients with MM and survivors. In this instance, we believe it is of note that the physical, emotional, and practical burden of living with MM remains substantive even in a sample that may overrepresent higher-functioning patients. Furthermore, structural barriers, including limited access to the internet or restricted time for completion, may select more socioeconomically advantaged patients with MM into our sample. In this study, we were able to compare those who began the website-based survey but stopped prematurely and those who completed most or all of the survey, including items pertinent to the present study. Although we did not find differences in many sociodemographic characteristics and clinical variables, we did observe a significant difference in racial distribution. This suggests there may be underrepresentation of underserved groups. The study was cross-sectional in nature and included a heterogenous population comprising patients with MM receiving treatment, long-term survivors, and

patients with newly diagnosed MM. Thus, our analyses can describe associations but cannot attribute causation.

## Conclusions

Patients with MM experience substantive concerns about the physical, emotional, and practical impact of disease. Symptom burden significantly predicted poorer QoL outcomes, including depression, anxiety, and social satisfaction. Moreover, perceived lack of control over illness was associated with greater anxiety and depression among our national sample of patients with MM. As long-term survival for patients with MM improves, the need to address symptom burden, integrate palliative care, and enhance social and emotional support becomes ever more important.

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