

Pain Medicine 2010; 11: 1525–1536 Wiley Periodicals, Inc.



# PALLIATIVE CARE SECTION

# Original Research Article Cancer Pain: An Age-Based Analysis

Carmen R. Green, MD,\*<sup>†‡</sup> and Tamera Hart-Johnson, MS\*

Departments of \*Anesthesiology and

<sup>†</sup>Obstetrics and Gynecology, University of Michigan Medical School, Ann Arbor, Michigan;

<sup>‡</sup>Department of Health Management and Policy, University of Michigan School of Public Health, Ann Arbor, Michigan, USA

Reprint requests to: Carmen R. Green, MD, Professor of Anesthesiology, Obstetrics and Gynecology, and Health Management and Policy, University of Michigan, Department of Anesthesiology, 1H247 University Hospital, 1500 East Medical Center Drive SPC 5048, Ann Arbor, MI 48109-5048, USA. Tel: 734-936-4240; Fax: 734-936-9091; E-mail: carmeng@med.umich.edu.

### Abstract

Objective. Although cancer pain (consistent and breakthrough pain [BTP; pain flares interrupting well-controlled baseline pain]) is common among cancer patients, its characteristics, etiology, and impact on health-related quality of life (HRQOL) across the lifespan are poorly understood.

Design. This longitudinal study examines agebased differences and pain-related interference in young and old patients with cancer-related pain over 6 months. Patients in the community with stage III or IV breast, prostate, colorectal, or lung cancer, or stage II–IV multiple myeloma with BTP completed surveys (upon initial assessment, 3 and 6 months) assessing consistent pain, BTP, depressed affect, active coping ability, and HRQOL using previously validated measures.

Results. Respondents (N = 96) were 70% white and 66% female, with a mean age of 57  $\pm$  10 years. There were no significant differences in pain severity based upon age. However, the younger group experienced more pain flares with greater frequency (*P* = 0.05). The oldest group had better emotional functioning at baseline but worse physical function-

ing at 6 months. Younger groups also had worse cognitive functioning at 6 months (P = 0.03). Pain interference was independent of age.

Conclusions. These data provide evidence for the significant toll of cancer pain on overall health and well-being of young and old adults alike but demonstrate an increased toll for younger adults (especially financially). Beyond race and gender disparities, further health care disparities in the cancer and cancer pain were identified by age, illustrating the need for additional research across the lifespan in diverse cancer survivors.

Key Words. Pain; Age-Based Differences and Disparities; Quality of Care; Health-Related Quality of Life; Physician Variability; Cancer

## Introduction

Globally, both cancer and pain are significant public health problems that are increasing in prevalence [1–5]. Despite national efforts such as the Joint Commission on Accreditation of Hospitals and Healthcare Organizations and the Agency for Healthcare Research and Quality, and despite global efforts such as the World Health Organization and the International Association for the Study of Pain designed to improve both cancer and pain care, nearly 70% of people dying from cancer experience unrelieved pain [6-9]. Cancer pain, such as pain associated with cancer or its treatment, exacts a significant individual and societal toll and is increasing, especially among those with advanced cancer [10-17]. Green and Montague showed that cancer pain, including breakthrough pain (BTP), significantly decreases health and guality of life (QOL; physical, social, and emotional health). As age is positively associated with increasing comorbidities, it follows that cancer, chronic pain, i.e., noncancer, nonmalignant, or benign pain, lasting >6 months, and cancer pain will have a greater impact on an aging U.S. population [18].

Unfortunately, the literature also suggests that the pain complaints of the elderly, women, and minorities receive less attention and treatment when compared with other segments of the population [19]. Regardless of cancer stage, racial or ethnic origin, gender, and age, when pain accompanies cancer it significantly impacts health and QOL [20]. The expected increases in the prevalence of cancer and pain will yield increases in the potential negative health sequelae associated with all types of pain,

especially cancer pain. This is an important consideration, as significant demographic changes are expected as the baby boomers (i.e., those born between 1946 and 1964) age. By 2030, there will be an estimated 71.5 million people >65 years old, 137 million minorities, and 185 million females in the United States [21–24]. A National Institute on Aging exploratory workshop (6/2008) emphasized the critical need for research focusing on pain across the lifespan [25]. Despite these efforts, the elderly, minorities, and women continue to remain disadvantaged on major health indices, and pain is a major threat to their overall health [14,26–29].

All in all, pain assessment and treatment remains problematic despite the many therapeutic modalities available to alleviate pain and suffering [30]. Both patient and physician factors contribute to variability in pain assessment and treatment [31–35]. For instance, cancer patients may be reluctant to discuss their pain complaints due to fears that this conversation may distract their physician from treating their cancer. They may also fear that pain is a sign that the cancer is getting worse. In addition, Bernabei et al. showed important clinician variability where older minority patients with cancer were less likely to have their pain score recorded [19]. Even when their pain score was recorded, minorities received less pain medication when compared with whites. Overall, minorities report decreased access and less satisfaction with pain care [31]. They are also more likely to receive suboptimal analgesic therapy to manage their pain complaints when compared with non-Hispanic whites [36]. Even when their pain is assessed and treatment is prescribed, minorities and low-income people experience additional barriers, with pharmacies in minority neighborhoods less likely to maintain adequate opioid analgesic supplies than pharmacies in predominantly white communities [37,38]. Few studies have sought to examine age-based differences in patient attitudes or physician treatment for cancer pain.

Both consistent pain and BTP (a transitory flare of moderate to severe pain interrupting mild background pain that is being controlled by a stable analgesic regimen such as opioid analgesics) are common among cancer patients. Their presence may indicate more severe pain syndromes or an inadequate response to analgesic therapy [39-45]. Although most studies failed to report on potential variations in BTP [46-54], studies in advanced cancer by Green and Montague revealed that minorities experience more consistent pain and BTP while having decreased QOL compared with whites. Moreover, although the literature reveals variability and differences in pain, cancer, and cancer pain based upon both physician and patient factors, it is unclear whether there are reductions in QOL associated with pain, cancer, and cancer pain [32-34,55]. Also unclear is whether potential reductions in QOL associated with pain, cancer, and cancer pain are similar across the lifespan [56]. The cancer pain literature reveals an association between pain and QOL. However, the literature is relatively silent on age-based differences in consistent and breakthrough cancer pain in racially and ethnically diverse men and women. Thus, a prospective

1526

6-month survey study was designed to 1) investigate whether there are age-based differences in cancer pain and 2) examine pain-related interference in young and old adults with advanced cancer.

# Methods

#### Participants and Recruitment

Institutional Review Board approval was obtained from the University of Michigan Health System and four community cancer clinics for this 6-month survey study. Englishspeaking adults, 18-75 years, with stage III or IV breast, colorectal, prostate, or lung cancer or stage II-IV multiple myeloma from four community cancer clinics in Michigan and the University of Michigan (UM) cancer registry, experiencing BTP and receiving analgesics around the clock, were identified by clinic or research staff. They were then recruited to participate, face to face in the case of the four clinics or by letter in the case of the registry. Age 75 years was defined as the upper boundary based on the high prevalence of pain from other sources in people greater than 75 years old. Clinical and research staff identified potential subjects for screening based on diagnosis, pain medication status, and Eastern Cooperative Oncology Group Performance Status of  $\leq 2$  (no more than 50%) of the day spent in bed) while those without pain or not receiving pain medication were excluded. Upon enro-Ilment, written informed consent was obtained. The participants completed questions from a battery of wellvalidated survey instruments upon initial assessment, 3 months, and 6 months. After recruitment, the sample was stratified by age into three groups: 1) Group 1:  $\leq$ 40 years; 2) Group 2: 41–59 years; and 3) Group 3:  $\geq$ 60 years.

## Measures

Validated survey instruments were given to each participant to assess pain characteristics, severity, and quality as well as pain management attitudes, depression, active coping skills, and QOL. Sociodemographic data such as age, race, gender, marital status, education, employment, and household income were also obtained. In addition, cancer type, cancer stage, and comorbidities (using a checklist of 19 different conditions using an instrument adapted from Priccirillo et al. [57]) were also collected.

The Brief Pain Inventory (BPI) assessed pain characteristics, severity, and interference with normal physical and emotional functioning [58]. Both consistent pain and BTP were assessed using four items: pain (least, average, right now, and its worst in the past 24 hours) rated by pain severity (0 = no pain; 10 = worst pain you can imagine). A scale was calculated for each pain type from the mean of the four items. The mean for seven other BPI items was used to determine pain-related interference subscale (0 = no interference; 10 = complete interference) for consistent pain only. Internal reliability for the BPI Severity subscale ranged  $\alpha = 0.89-0.94$  for consistent pain and  $\alpha = 0.83-0.87$  for BTP, and for the BTP Interference subscale ranged  $\alpha = 0.93-0.95$  for the three data waves. The BPI also includes items about pain characteristics (timing, duration, quality, and cause), medication, pain medication effectiveness, and an open-ended item regarding what actions relieved pain. Pain characteristics, pain medication effectiveness (0–100%), and a dummy variable for any activity effectively alleviating some portion of pain (0 = nothing helps; 1 = something can be done to lessen pain) were used for the analyses.

Current medications were collected and classified into 38 classes with near unanimous (99,5%) agreement among knowledgeable health professionals. A distinction was made in the question between consistent pain medications, typically taken on a regular regimen, and BTP medications, prescribed "as needed." The 38 classes of drugs were collapsed into four groups based on their analgesic function with the strongest medication used by the subject for pain relief classified to yield the drug potency variable. The pain at worst score was collapsed into four categories: 0 = absence of pain; 1 = mild pain; 2 = moderate pain; and 3 = severe pain. The treatment analgesic potency was combined with the patient's severity scores at worst during the past week to create the Pain Management Index (PMI; the difference between the analgesic potency and the categorized pain level [ranging from -3 and +3]) [59]. This ordinal variable was also used in its categorical form with 0 = inadequate analgesic therapy (PMI = -3 to -1) and 1 = adequate analgesic therapy (PMI = 0 to +3).

The Center for Epidemiological Studies Depression Scale (CES-D) measured depressed affect. The four positively worded items from the original 20-item survey were dropped as factor analysis showed that the items did not accurately predict negative affect when reversed, and a literature review confirmed this in a cancer population [60,61]. The ordinal values for the remaining 16 items were summed and weighted to calculate an overall score comparable with the published scale range (0–60); scores >15 indicated severe psychological distress and depression. Internal consistency for the 16-item CES-D ranged  $\alpha = 0.81-0.92$ , consistent with published values [60], although the 6-month reliability of 0.81 could be improved to 0.92 if the item "everything I did was an effort" was dropped.

The John Henryism Active Coping Scale (JHACS) evaluated active coping strategies at baseline. John Henryism is a high output coping strategy characterized by protracted struggles against seemingly insurmountable obstacles. The construct was first reported among aging African Americans and is correlated with hypertension and bodily pain. The sum score of 12 Likert-type items was calculated (1 = completely false; 5 = completely true; 60 = maximum active coping score) with higher scores related to greater use of high-effort coping. Internal consistency of the JHACS was  $\alpha = 0.87$ , higher than previously published values [62]; as John Henryism is considered a trait, it was only measured at baseline.

The Barriers Questionnaire (BQ-II) assessed barriers in patient attitudes toward pain assessment and treatment. The BQ-II questionnaire has four separate subscales:

physiological effects, fatalism, communication, and harmful effects [63]. Mean scores were calculated for each Likert-type subscale, and fatalism items were reverse scored before analysis; higher scores were related to greater endorsement for that type of barrier. The internal consistency of BQ-II subscales ranged from  $\alpha = 0.60-0.91$  for the three waves. Although the fatalism subscale at baseline and communication barriers at 3 months had a reliability value below previously published values [63], in this sample, the reliabilities were above the threshold of  $\alpha = 0.60$  and so were considered adequate. The small, diverse sample and low number of questions on these subscales may account for differences in reliabilities.

The European Organization for the Research and Treatment of Cancer survey (EORTC QLQ-C30) assessed health-related QOL [64]. Five QOL functioning domains were assessed: physical, role, cognitive, emotional, and social. In addition, eight symptom-control domains fatigue, pain, nausea and vomiting, dyspnea, anorexia, diarrhea, and constipation—were evaluated for their contribution to QOL. Each symptom control domain surveyed patients for the frequency of a given symptom during the past week. An additional measure assessed financial concerns, and another measured global health and overall QOL. Scores were linearly transformed to a 0–100 scale. Internal consistency of the EORTC subscales ranged from  $\alpha = 0.71-0.91$ , higher than previously published results [64].

#### Statistical Analysis

Descriptive statistics were calculated using SPSS 16.0. Analysis of variance (ANOVA) and chi-square analysis were used to determine differences between race, gender, and age groups on sociodemographics, pain characteristics, and experiences, and for each QOL measure examined. ANOVA is relatively robust in terms of assumptions of normality. Repeated measures of ANOVA were then performed to test whether consistent pain, BTP, depression, or QOL changed significantly over waves, with least significance difference tests performed post hoc to examine paired comparisons. Repeated measures of ANOVA with age group as a comparison (controlling by average pain) was used to test whether changes over time differed by age group. Finally, hierarchical regression was used to test whether pain interference at baseline predicted QOL, comorbidities, and coping at 6 months (although John Henryism active coping was only available at baseline) after controlling for age, race, and gender. In a final block, a term for the interaction between age and interference was added to test whether effects of pain interference are different by age.

#### Results

#### Demographics

One hundred twenty-four participants provided written informed consent. Thirty consenting participants died prior to the study's conclusion or within 6 months from

	Baseline (n)	3-Month Survey (n)	6-Month Survey	After 6 Months	Total
Consented initially (N)	124	103	94	_	
Surveys collected	96 (93%)	66 (81%)	46 (54%)	_	
Nonresponse/still consented (N)	7	15	39	_	
Declined/left study (N)	12	8	3	0	23
Deceased/exited (N)	9	14	6	1	30

original consent. Table 1 summarizes study retention over the three waves of data collection. Nonwhites were more likely than whites to decline after initial consent (21% vs 7%, P = 0.05). Participants who consented and then declined most often responded that they were no longer feeling well enough to complete their surveys. For the sample completing the baseline survey (N = 96), 29%were nonwhite (N = 28; 20 black, 4 Native American, 3 Hispanic, 2 Arabic, and 1 black/Native American). The sample was primarily in the middle age group (41-59 years). The majority (66%) were women, and they were aged from 57  $\pm$  10 years (mean  $\pm$  SD). More than onethird of the sample reported difficulty paying for health care; the youngest group reported significantly more difficulty paying for health care than the older group. The youngest age group had higher minority representation and was less likely to fall in the highest-income group. The most frequent morbidities for the group were arthritis or rheumatism (42.7%), high blood pressure (37.5%), and depression or anxiety (34.4%). Although Group 1 (younger people) had significantly fewer comorbidities (F = 3.30, P = 0.04) at study initiation, these differences disappeared at 3 and 6 months (Figure 1). Employment differed by age group but appears to be largely explained by high retirement status among the oldest group. Additional demographic information is provided in Table 2 and can be found in previously published studies [10,11].

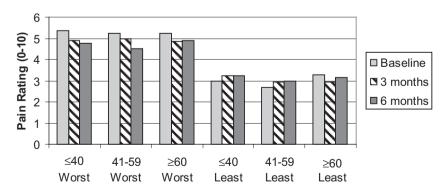
#### Cancer Diagnosis

Breast cancer was the most common diagnosis (32%) followed by lung cancer (28%), multiple myeloma (21%), colorectal cancer (15%), and prostate cancer (3%). There were no significant differences between whites and non-whites in primary cancer diagnosis location or cancer stage. Women were more likely to have breast cancer ( $\chi^2 = 44.2$ , P < 0.001). There are age group differences in cancer diagnosis, particularly the relatively higher frequency of breast and colorectal cancer in the youngest group (P = 0.03). Table 2 provides additional sociodemographic information for the sample.

### Pain Differences

#### Location

The most common pain locations were nonmidline back (36%), spine (31%), and legs (28%). Although there were no significant differences in the number of pain locations at baseline, at 6 months, or at 3 months, there was a trend toward the youngest group having more pain locations (4.5 vs 2.3 and 2.2, P = 0.10). There were also a few differences in pain prevalence at specific location. Pain in low midline back, and arm at 3 months and shoulder pain at 6 months are significantly more prevalent for the young-



**Figure 1** Consistent pain at worst and least by age group. Consistent pain (worst and least) in the last week is measured on a 10-point scale (0 = no pain; 10 = worst pain imaginable) at baseline, 3 months, and 6 months. The participants were further categorized by their age (<40, 41–59, and  $\geq$ 60 years). The figure shows pain at worst dropped at trend level over time (*P* = 0.08).

	Overall	<40 years (n = 8)	41–59 years (n = 50)	>60 years (n = 38)	Difference Statistic* (P)
Age range M $\pm$ SD	56.8 ± 10.1	$35.2\pm5.2$	52.8 ± 4.7	66.1 ± 4.2	244.5 (<0.001)
Race					
% Nonwhite	29.2%	62.5%	24.0%	27.0%	5.08 (0.08)
Gender (% female)	62.9%	60.0%	68.3%	56.0%	1.82 (0.40)
Education					12.35 (0.14)
<12 years	14.6%	0.0%	16.0%	16.2%	
High school	33.3%	0.0%	34.0%	40.5%	
College	52.1%	50.0%	50.0%	43.2%	
Marital status	61.7%	25.0%	62.5%	70.3%	19.45 (0.003)
Personal income					. ,
<\$10,000	12.9%	25.0%	14.3%	8.6%	12.12 (0.06)
\$10,000-30,000	34.4%	62.5%	22.4%	42.9%	. ,
\$30,001-99,999	45.2%	0.0%	53.1%	45.7%	
≥\$100,000	7.5%	12.5%	10.2%	2.9%	
Employed (% Y)	12.6%	20.0%	31.9%	8.6%	32.71 (<0.001)
Alive at 6 months (%)	75.8%	100.0%	71.4%	76.0%	3.83 (0.15)
Trouble paying for health care (%)	40.0%	75.0%	38.8%	35.1%	8.33 (0.08)
Comorbidities (%)	$\textbf{2.23} \pm \textbf{1.94}$	$0.63\pm0.74$	$2.30\pm1.94$	$2.51 \pm 1.99$	3.30 (0.04)
Cancer diagnosis					
Breast	33.3%	50%	41.3%	20.0%	17.41 (0.03)
Colorectal	13.8%	40.0%	11.1%	12.0%	. ,
Lung	30.1%	0.0%	30.2%	36.0%	
Multiple myeloma	17.9%	10.0%	14.3%	24.0%	
Prostate	4.9%	0.0%	3.2%	8.0%	

 Table 2
 Descriptive characteristics of the sample upon recruitment

\*  $\chi^2$  (df = 2) for percentages, *F* for group differences.

est group. Arm, shoulder, and abdominal pain at baseline and spinal pain at 6 months were higher for the youngest group at trend level. Spinal pain at baseline was more common in the middle-age group at trend level.

## Pain Severity and Treatment and Interference

There were no significant differences in consistent or BTP levels at worst or least between the age groups. The changes in the mean scores on the four consistent pain measures over the study's duration are shown in Figure 1. The mean PMI of -1.01 suggests that most participants were prescribed adequate pain medications (range = -3to +3; negative numbers reflecting medication stronger than pain strength and positive numbers reflecting pain stronger than medication). When the PMI was examined as a continuous variable, there were no age differences in medication strength or subject-reported consistent pain relief received from medication (62%, 56%, and 60% over the three waves). Nor were there differences on examining the dummy variable for "adequate" vs "inadequate" medication. However, pain interference was a significant issue for participants. The mean interference at baseline ranged from 3.6 for relationships to 5.5 for work (0 = no interference; 10 = maximal interference). There was significantly greater interference in mood and relationships for the youngest group at baseline, although these differences did not persist over time (Table 3).

## **BTP** Characteristics

Although BTP history was required for study inclusion, there was variability in BTP characteristics. On average, participants experienced BTP for 619 days at baseline, and BTP duration ranged from 0 to 168 months. There were no age differences in BTP duration or length of BTP episodes experienced on average per week, but the youngest group experiences pain flares with significantly greater frequency (62 vs 18 and 12, P = 0.05). Participants attributed the precipitating event for BTP to several causes (e.g., movement, end of a course of pain medication). Although there was great variability within each group, there were no significant differences in the ability to predict BTP onset. Most subjects (79%) reported that BTP could be at least partially palliated. The most common method for relieving BTP was medications (62%). There were no significant ethnic or gender differences in BTP placability, strategies, or effectiveness for BTP relief. Figure 2 shows changes in BTP means over the study course.

# Comorbidities, Depression, Coping Strategies, and QOL

Depression (via CES-D), coping strategies as defined by the BQ-II and the JHACS, and QOL and symptoms as measured by the EORTC are included in Table 3. The

Table 3	Differences	by age	group	in	pain	variables	over time

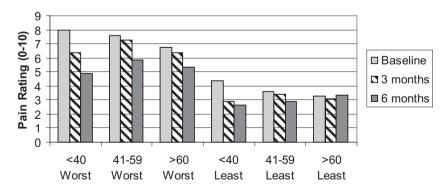
	Initiation				3 Months				6 Months			
Group	I	II	III	Ρ	I	II	III	Ρ	I	II	Ш	Ρ
Pain interference												
General activity	6.67	4.62	4.47	0.29	4.00	4.14	4.66	0.73	3.86	4.00	4.69	0.55
Mood*	8.14	4.35	4.14	0.01	6.43	4.08	3.89	0.18	6.14	4.00	4.39	0.30
Walking ability*	6.57	3.96	4.49	0.17	4.43	3.84	5.23	0.19	4.57	3.86	5.42	0.12
Work (in and out of home)	6.71	5.11	5.74	0.43	5.67	4.54	5.71	0.31	5.83	4.63	5.83	0.27
Relationships	6.43	3.69	2.86	0.02	5.43	3.92	2.88	0.10	5.29	3.74	3.28	0.31
Sleep	7.14	5.08	5.46	0.30	4.29	4.86	4.71	0.90	3.71	4.60	4.94	0.64
Enjoyment of life	7.00	5.06	5.43	0.37	5.57	4.51	5.03	0.65	5.29	4.30	5.31	0.37
EORTC functioning												
General health	43.8	55.4	49.8	0.37	44.8	56.5	51.4	0.30	45.8	55.9	48.6	0.25
Physical	67.5	63.1	54.3	0.17	69.2	62.5	52.5	0.11	62.5	63.2	49.3	0.05
Role <sup>∆</sup> *	47.9	46.9	46.2	0.99	50.0	51.3	43.8	0.55	35.4	52.4	41.9	0.19
Emotional <sup>▲</sup>	54.2	55.0	68.8	0.06	54.2	60.7	70.2	0.16	44.8	60.2	65.7	0.17
Cognition	60.4	63.7	68.6	0.61	50.0	63.0	67.6	0.21	43.8	62.3	69.9	0.03
Social	31.3	51.0	50.5	0.25	37.5	54.6	50.9	0.33	41.7	54.9	47.7	0.39
EORTC symptoms <sup>∆</sup> **	44.5	41.5	44.2	0.78	36.8	39.5	43.5	0.56	44.6	37.7	44.9	0.20
Barriers	1.92	1.73	2.05	0.46	2.28	1.58	1.88	0.20	2.32	1.58	1.98	0.12
Physiological	1.25	1.59	1.17	0.18	2.17	1.69	1.47	0.35	2.25	1.51	1.15	0.04
Fatalism** communication	1.23	1.10	1.16	0.94	1.00	0.87	1.02	0.80	1.15	0.95	1.22	0.53
Harmful effects	2.17	1.91	2.36	0.30	1.93	1.68	1.92	0.68	1.90	1.73	2.06	0.57
CES-D <sup>▲</sup> **	26.1	24.2	20.3	0.34	31.8	23.0	20.8	0.17	35.7	23.1	21.4	0.06

<sup> $\triangle$ </sup> Variables that change over time (**A** P < 0.05,  $\triangle P < 0.10$ ).

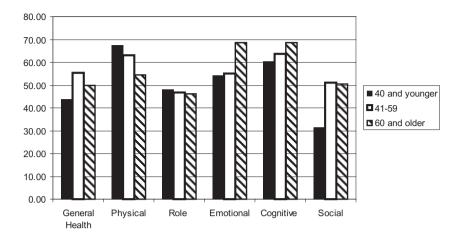
\* Variable for which the slope of change is different by age group (\*\* P < 0.05, \* P < 0.10).

Group 1 = <40 years old. Group 2 = 41–59 years old. Group 3 =  $\geq$ 60 years old.

subjects experienced significant psychological distress and depression when measured with the CES-D (mean baseline =  $22.7 \pm 13.6$ ; maximum score = 60 with scores >16 indicating depression). The CES-D scores did not have significant initial age differences. However, by 6 months, there were trend-level differences in the CESD, with the younger group showing more depressive symptoms. The subscales of the BQ-II also did not differ by age, with the exception of the youngest group having the highest fatalism scores at 6 months (F = 3.33, P = 0.04). All participants scored highly on the JHACS (mean = 47.6, maximum score = 60), but scores did not differ by age.



**Figure 2** Breakthrough pain (BTP) at worst and least by age group. BTP (worst and least) in the last week is measured on a 10-point scale (0 = no pain; 10 = worst pain imaginable) at baseline, 3 months, and 6 months. The participants were further categorized by their age (<40, 41–59, and  $\geq$ 60 years). The figure shows no difference in pain at worst or least over time (*P* = 0.08).



**Figure 3** Functioning by age group via EORTC. The different subscales on the EORTC are shown by age group at baseline. The figure shows that the oldest group tended to have better emotional functioning at baseline (P = 0.06) and had significantly worse physical functioning at 6 months (P = 0.05) while the youngest group had significantly worse cognitive functioning at 6 months (P = 0.03).

Regardless of age group, similarities were found on both the EORTC, Functioning and Symptom Control Scales (Figure 3). The oldest group tended to have better emotional functioning at baseline (F = 2.95, P = 0.06) and had significantly worse physical functioning at 6 months (F = 3.08, P = 0.05) while the youngest group had significantly worse cognitive functioning at 6 months (F = 3.80, P = 0.03).

#### Interactions, Age over Time

Over time, there was a trend-level reduction in pain at its worst (F[2,36] = 2.79, P = 0.08). Other measures did not change. As summarized in Table 3, repeated measures ANOVA with age group as a comparison and controlling for the consistent pain mean found that emotional functioning (EORTC) (F[2,81] = 5.92, P = 0.004) and depression (CES-D) were worse over time (F[2,86] = 8.59, P < 0.001) and CES-D changed differently by group (F[4, 174] = 3.11,P = 0.02), reducing for emotional functioning and increasing for depression. At a trend level, physical functioning (EORTC) (F[2,81] = 2.54, P = 0.09) and symptoms (F[2,83] = 2.45, P = 0.09) both changed. Additionally, there were three significant and four trend-level interactions where the slope of change over time differed by age group. Table 3 details change statistics over time and interactions for the age groups.

# Pain Interference and QOL, Comorbidities, and Coping

# QOL

Demographic variables had limited predictive power related to QOL, with male gender predicting better general health ( $\beta = 0.23$ , P = 0.04). Age predicts better emotional ( $\beta = 0.23$ , P = 0.04) and cognitive ( $\beta = 0.24$ , P = 0.03)

functioning. Pain interference, however, played a much stronger role, significantly predicting worse outcomes for all six functioning scales and symptoms (P < 0.001). After the entry of pain interference, race also becomes significantly ( $\beta = 0.23$ , P = 0.03) associated with physical functioning, where it was not at block of entry, suggesting that were it not for pain interference, minority group members would be physically functioning better than nonminorities. There were no interactions between age and interferences, indicating that pain interference is independent of age.

#### Comorbidities

Other than a trend for pain interference relating to more comorbidities ( $\beta = 0.20$ , P = 0.08), there were no significant relationships in this regression.

## Coping

John Henryism active coping is higher for males at a trend level (P = 0.08) and not related to any other variables. Barriers to treatment, on the other hand, are higher for racial minorities: communication and harmful effects significantly, and physiological effects and fatalism at trend level. When pain interference is added to the regression, this significance disappears for all but harmful effects, suggesting that the racial relationship for the other coping styles is due to the greater pain interference. Finally, at a trend level, all barriers but fatalism have interactions between age and interference, such that older people with more pain perceive greater barriers to pain treatment than younger people or those with less interference.

#### Discussion

The prevalence of both cancer and pain is increasing. Unfortunately, cancer and its treatment are often associ-

ated with pain. Most cancer pain research has focused on single cancer types or treatment modalities. Although disparities in pain care based upon race, ethnicity, and gender are well described, few studies have examined age-based differences in consistent pain and BTP among diverse populations [56,65,66]. Overall, we demonstrated high consistent pain severity (with a slight reduction at its worst over time) as well as high BTP severity over time. Our previously published results identified important ethnic disparities in cancer pain with nonwhites impacted more than whites [10,11]. Although Portenov brought national attention to BTP's impact on QOL, Green and Montague provided important new insights into racial, ethnic, and gender variations in BTP in our previous study [10,11,41,65,67]. Older people are less likely to have their pain assessed and treated and are at risk for increased pain severity and the negative health outcomes associated with pain. However, to our knowledge, the literature has not specifically examined age-based disparities in cancer pain [14,19]. We did not identify any significant differences in consistent pain or BTP at worst or least by age group, although the youngest group did trend toward a higher number of pain locations.

Overall, patient sociodemographic characteristics often influence access and quality of pain care. In fact, the literature consistently reveals an unequal burden of pain and physician variability in pain management decision making based upon social determinants [14,68]. For instance, women have a higher prevalence for many chronically painful syndromes than non-Hispanic whites [14,69]. Women, minorities, and the elderly are also at risk for suboptimal pain assessment and treatment. Thus, it was not surprising for us to find that the younger group had fewer (P < 0.05) comorbidities than the older group at baseline. However, we were surprised to find that these changes disappeared over time. It is plausible that this may be due to survival effects. Patient preferences and attitudes about cancer and pain may also play a significant role in their willingness to report pain and to seek treatment [31,36,70]. Thus, while the etiology remains unclear, the ethnic and gender differences observed in this study are consistent with our previous findings [10,68,69]. Physician variability in assessing and treating pain, as well as structural barriers to accessing quality pain care, may lead to suboptimal cancer pain management, thereby increasing pain severity [35,37,71,72]. Future studies should attempt to determine how patient age influences patient preferences and attitudes about cancer pain management in diverse populations across the lifespan.

Overall, the entire sample experienced clinically important depressive symptoms and psychological distress. When psychological impairment (via the CES-D) was examined, no significant ethnic or gender differences were found. Although there were no age differences at baseline and depressive symptoms for all groups increased over time, the slope significantly differed by age group with the youngest group reporting increasing depressive symptoms over time more than the change in the other age groups (reaching a trend-level difference by 6 months). Younger people also reported significantly (P < 0.05) more interference with their mood and relationships at baseline (differences that disappeared over time), although the relationship slopes were not different by age. As observed in our sample, the literature provides overwhelming evidence for the high prevalence of depression in cancer and chronic pain populations [73–76], although the exact mechanism remains unclear. In addition, the literature reveals increased depression and posttraumatic stress disorder in minorities with chronic pain [31,69]. As both groups were equally depressed, future studies should attempt to disentangle cancer pain's impact on emotional health using structural equation modeling in an ethnically diverse population across the life span.

Maladaptive coping strategies diminish QOL and the ability to cope with significant illnesses. James et al. introduced the concept of John Henryism and its strong association with African Americans [62]. We found John Henryism was prevalent in the entire sample but did not reveal racial or age differences. Attitudes and barriers to care may influence access to care. We did not identify any differences in the physiological, communication, or harmful effects scales, by age group, but fatalism, except at baseline, sloped differently by age group and was significantly higher for the youngest group by 6 months.

All in all, this study provides many significant implications for improving health and QOL in cancer patients. However, there are potential limitations. First, the small sample size used for data analysis may have limited the potential-observed differences between groups, particularly the small number in the <40 years of age group. Related to this, the youngest sample was more likely to be minority than the older two groups, and when considering the small sample size for this group, there may be some confounding of race and age issues. We believe that this racial difference, however, may also indicate cancer disparities, with minorities being more likely to get cancer early and less likely to survive their cancer [15,16]. This is also important, as those >75 years old were originally excluded from the study, and our effects could have potentially been more robust if this population was included. The sample is potentially quite diverse with respect to the length of time since cancer diagnosis, thus making follow-up assessment more difficult to interpret. Due to the unpredictable nature of cancer, participant retention was difficult but comparable with other longitudinal cancer studies [50]. Although differences in survival rates were not significant by age group, it is plausible that some changes over time might have been affected by survival effect, with the healthiest surviving through all three waves of data collection. Future studies should attempt to increase the sample size to perform subgroup analysis. Second, we used the last measured value of a variable to allow for analysis, and this procedure may minimize any changes that may happen over time. Third, self-report and nonresponse bias must be considered, although the surveys were completed privately and kept confidential. Next, participating in this study may have increased both patient and physician attention to pain, thereby enhancing pain care. As subjects were recruited through cancer care facilities, our results may only reflect those with access to care. Finally, outcome variables were frequently correlated. Normally, this would be countered by the use of a multivariate analysis technique, such as MANCOVA, but in looking at the same measure over time, we opted for repeated measures ANCOVA. This means that results include a higher likelihood of type I error, due to running multiple analyses.

In conclusion, to our knowledge, this is the first prospective study examining both consistent pain and BTP over time in a diverse population across the life span. We showed important and distinct differences in the impact of cancer pain based upon the patient's age over time. More specifically, the youngest group initially had the greatest pain interference but improved over time. They did not look different mentally or emotionally at baseline, although both cognitive functioning and depression worsened by 6 months. The oldest group at baseline had better emotional functioning than the other two groups, but by 6 months has significantly worse physical functioning. Overall, these results suggest that the youngest group is having the most difficulty coping with cancer, pain, or both in spite of potentially better survival odds. We also identified important financial difficulties for cancer patients, especially for younger adults, with critically important implications for health care and health policy.

## Acknowledgments

The authors thank the Blue Cross/Blue Shield Foundation of Michigan for funding this research. We also thank Sam Silver, MD, the University of Michigan Cancer Center Network, Ms. Melanie Grierson, Ms. Deena Loeffler, and Ms. Susan Sessions for their ongoing support. We also thank Marcus A. Hatter for his inspiration. This article was presented at the Gerontological Society of America (GSA) 61st Annual Scientific Meeting, National Harbor, Maryland on November 22, 2008.

#### References

- 1 Soyannwo OA. Cancer pain management in developing countries. IASP Pain Clin Updat 2009;XVII:1–4.
- 2 Anderson KO, Mendoza TR, Payne R, et al. Pain education for underserved minority cancer patients: A randomized controlled trial. J Clin Oncol 2004; 22:4918–25.
- 3 Anderson KO, Mendoza TR, Valero V, et al. Minority cancer patients and their providers: Pain management attitudes and practice. Cancer 2000;88:1929–38.
- 4 Anderson KO, Richman SP, Hurley J, et al. Cancer pain management among underserved minority outpatients: Perceived needs and barriers to optimal control. Cancer 2002;94:2295–304.
- 5 Cleeland C. Research in cancer pain. What we know and what we need to know. Cancer 1991;67:823–7.

- 6 Carr DB, Jacox A, Chapman CR. Acute Pain Management: Operative or Medical Procedures and Trauma: Clinical Practice Guideline No. 1. Rockville, MD: U.S. Public Health Service, Agency for Health Care Policy and Research; 1992.
- 7 Carr DB, Miaskowski C, Dedrick SC, et al. Management of perioperative pain in hospitalized patients: A national survey. J Clin Anesth 1998;10:77–85.
- 8 Carr DB, Reines HD, Schaffer J, Polomano RC, Lande S. The impact of technology on the analgesic gap and quality of acute pain management. Reg Anesth Pain Med 2005;30:286–91.
- 9 Brawley OW, Smith DE, Kirch RA. Taking action to ease suffering: Advancing cancer pain control as a health care priority. CA Cancer J Clin 2009;59:285–9.
- 10 Montague L, Green CR. Cancer and breakthrough pain's impact on a diverse population. Pain Med 2009;10:549–61.
- 11 Green CR, Montague L, Hart-Johnson T. Consistent and breakthrough pain in diverse advanced cancer patients: A longitudinal examination. J Pain Symptom Manage 2009;37:831–47.
- 12 Green CR. Unequal burdens and unheard voices: Whose pain? Whose narratives? In: Carr DB, Loeser JD, Morris DB, eds. Narrative, Pain, and Suffering, Progress in Pain Research and Management. Seattle, WA: IASP Press; 2005:195–214.
- 13 Green CR. The quality of cancer pain management for racial and ethnic minority Americans: Unequal burdens and unheard voices. J Cancer Pain Symptom Palliat 2006;2:19–27.
- 14 Green CR, Anderson KO, Baker TA, et al. The unequal burden of pain: Confronting racial and ethnic disparities in pain. Pain Med 2003;4:277–94.
- 15 Satcher D. The unequal burden of cancer. Cancer 2001;91:205–7.
- 16 Institute of Medicine. The Unequal Burden of Cancer: An Assessment of NIH Research and Programs for Ethnic Minorities and the Medically Underserved. Washington, DC: The National Academies Press; 1999.
- 17 Institute of Medicine. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington, DC: The National Academies Press; 2002.
- National Academy on an Aging Society. Chronic Conditions: A Challenge for the 21st Century. Number 1. Washington, DC: National Academy on an Aging Society; 1999.

- 19 Bernabei R, Gambassi G, Lapane K, et al. Management of pain in elderly patients with cancer. SAGE Study Group. Systematic assessment of geriatric drug use via epidemiology. JAMA 1998;279:1877–82.
- 20 Ludwig-Beymer P, Ryan CJ, Johnson NJ, et al. Using patient perceptions to improve quality care. J Nurs Care Qual 1993;7:42–51.
- 21 U.S. Department of Commerce. Minority Population Growth: 1995 to 2050. Washington, DC: Minority Business Agency; 1999.
- 22 U.S. Census Bureau. U.S. population projections. 2008. Available at: http://www.census.gov/ population/www/projections/projectionsagesex.html (accessed September 2009).
- 23 U.S. Census Bureau. Census Bureau projects tripling of Hispanic and Asian populations in 50 years; non-Hispanic whites may drop to half of total population. 2004. Available at: http://www.census.gov/Press-Release/www/releases/archives/population/ 001720.html (accessed December 2009).
- 24 Burke G, Hsiao K. Older women of color and the challenge of regulating cultural competence. Clearing-house Rev J Poverty Law Policy 2009;43:27–36.
- 25 National Institutes of Health. NIH pain consortium. 2008. Available at: http://painconsortium.nih.gov/ NIAPainWorkshopSummary.html (accessed December 2009).
- 26 Crombie IK, Davies HT, Macrae WA. The epidemiology of chronic pain: Time for new directions. Pain 1994;57:1–3.
- 27 Helme RD, Gibson SJ. The epidemiology of pain in elderly people. Clin Geriatr Med 2001;17:417–31.
- 28 IASP Special Interest Group on Sex, Gender, and Pain. Sex, Gender, and Pain. Siena, Italy: IASP Press; 2000.
- 29 Crombie IK, Croft PR, Linton SJ, LeResche L, VonKorff M. Epidemiology of Pain. Seattle, WA: IASP Press; 1999.
- 30 Green CR. The healthcare bubble through the lens of pain research, practice, and policy: Advice to the new president and congress. J Pain 2008;9:1071–3.
- 31 Green CR, Baker TA, Ndao-Brumblay SK. Patient attitudes regarding healthcare utilization and referral: A descriptive comparison in African- and Caucasian Americans with chronic pain. J Natl Med Assoc 2004; 96:31–42.

- 32 Green CR, Wheeler JR, LaPorte F, Marchant B, Guerrero E. How well is chronic pain managed? Who does it well? Pain Med 2002;3:56–65.
- 33 Green CR, Wheeler JR, Marchant B, LaPorte F, Guerrero E. Analysis of the physician variable in pain management. Pain Med 2001;2:317–27.
- 34 Green CR, Wheeler JR, LaPorte F. Clinical decision making in pain management: Contributions of physician and patient characteristics to variations in practice. J Pain 2003;4:29–39.
- 35 Green CR, Wheeler JR. Physician variability in the management of acute postoperative and cancer pain: A quantitative analysis of the Michigan experience. Pain Med 2003;4:8–20.
- 36 Cleeland CS, Gonin R, Baez L, Loehrer P, Pandya KJ. Pain and treatment of pain in minority patients with cancer. The Eastern Cooperative Oncology Group minority outpatient pain study. Ann Intern Med 1997; 127:813–6.
- 37 Green CR, Ndao-Brumblay SK, West B, Washington T. Differences in prescription opioid analgesic availability: Comparing minority and white pharmacies across Michigan. J Pain 2005;6:689–99.
- 38 Morrison RS, Wallenstein S, Natale DK, Senzel RS, Huang LL. "We don't carry that"–Failure of pharmacies in predominantly nonwhite neighborhoods to stock opioid analgesics. N Engl J Med 2000;342:1023–6.
- 39 Bruera E, MacMillan K, Hanson J, MacDonald RN. The Edmonton Staging System for cancer pain: Preliminary report. Pain 1989;37:203–9.
- 40 Zeppetella G, O'Doherty CA, Collins S. Prevalence and characteristics of breakthrough pain in cancer patients admitted to a hospice. J Pain Symptom Manage 2000;20:87–92.
- 41 Portenoy RK, Payne D, Jacobsen P. Breakthrough pain: Characteristics and impact in patients with cancer pain. Pain 1999;81:129–34.
- 42 Patt RB, Ellison NM. Breakthrough pain in cancer patients: Characteristics, prevalence, and treatment. Oncology (Huntingt) 1998;12:1035–46.
- 43 Bruera E, Kim HN. Cancer pain. JAMA 2003;290: 2476–9.
- 44 Bruera E, Portenoy RK. Cancer Pain: Assessment and Management. Cambridge and New York: Cambridge University Press; 2003.
- 45 Banning A, Sjogren P, Henriksen H. Treatment outcome in a multidisciplinary cancer pain clinic. Pain 1991;47:129–34.

- 46 Coleman EA, Coon SK, Mattox SG, O'Sullivan P. Symptom management and successful outpatient transplantation for patients with multiple myeloma. Cancer Nurs 2002;25:452–60.
- 47 Lin CC, Chou PL, Wu SL, Chang YC, Lai YL. Long-term effectiveness of a patient and family pain education program on overcoming barriers to management of cancer pain. Pain 2006;122: 271–81.
- 48 Lips I, Dehnad H, Kruger AB, et al. Health-related quality of life in patients with locally advanced prostate cancer after 76 GY intensity-modulated radiotherapy vs. 70 GY conformal radiotherapy in a prospective and longitudinal study. Int J Radiat Oncol Biol Phys 2007; 69:656–61.
- 49 McGuire DB. Occurrence of cancer pain. J Natl Cancer Inst Monogr 2004;32:51–6.
- 50 O'Mahony S, Goulet J, Kornblith A, et al. Desire for hastened death, cancer pain and depression: Report of a longitudinal observational study. J Pain Symptom Manage 2005;29:446–57.
- 51 Peng WL, Wu GJ, Sun WZ, Chen JC, Huang AT. Multidisciplinary management of cancer pain: A longitudinal retrospective study on a cohort of end-stage cancer patients. J Pain Symptom Manage 2006;32: 444–52.
- 52 Tishelman C, Petersson LM, Degner LF, Sprangers MA. Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death. J Clin Oncol 2007;25:5381–9.
- 53 Epstein JB, Beaumont JL, Gwede CK, et al. Longitudinal evaluation of the oral mucositis weekly questionnaire-head and neck cancer, a patientreported outcomes questionnaire. Cancer 2007;109: 1914–22.
- 54 Castel LD, Saville BR, Depuy V, et al. Racial differences in pain during 1 years among women with metastatic breast cancer: A hazards analysis of interval-censored data. Cancer 2008;112:162–70.
- 55 Green CR, Tait A. Attitudes of healthcare professionals regarding different modalities used to manage acute postoperative pain. Acute Pain 2002;4:15–21.
- 56 McMillan SC. The relationship between age and intensity of cancer-related symptoms. Oncol Nurs Forum 1989;16:237–41.
- 57 Priccirillo JF, Lacy PD, Basu A, Spitznagel EL. Development of a new health and neck cancer-specific

comorbidity index. Arch Otolaryngol Head Neck Surg 2002;128:1172–8.

- 58 Cleeland CS. Measurement of pain by subjective report. In: Chapman CR, Loeser JD, eds. Issues in Pain Measurement. New York: Raven Press, Ltd.; 1989:391–403.
- 59 Green CR, Hart-Johnson T. The adequacy of chronic pain management prior to presenting at a tertiary care pain center: The role of patient socio-demographic characteristics. J Pain 2010;11:746–54.
- 60 Schroevers MJ, Sanderman R, van Sonderen E, Ranchor AV. The evaluation of the Center for Epidemiologic Studies Depression (CES-D) scale: Depressed and positive affect in cancer patients and healthy reference subjects. Qual Life Res 2000;9: 1015–29.
- 61 Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. Appl Psych Meas 1977;1:385–401.
- 62 James SA, Hartnett SA, Kalsbeek WD. John Henryism and blood pressure differences among black men. J Behav Med 1983;6:259–78.
- 63 Gunnarsdottir S, Donovan HS, Serlin RC, Voge C, Ward S. Patient-related barriers to pain management: The Barriers Questionnaire II (BQ-II). Pain 2002;99: 385–96.
- 64 Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365–76.
- 65 Caraceni A, Portenoy RK. An international survey of cancer pain characteristics and syndromes. IASP task force on cancer pain. International Association for the Study of Pain. Pain 1999;82:263–74.
- 66 Caraceni A, Martini C, Zecca E, et al. Breakthrough pain characteristics and syndromes in patients with cancer pain. An international survey. Palliat Med 2003;18:177–83.
- 67 Brescia FJ, Portenoy RK, Ryan M, Krasnoff L, Gray G. Pain, opioid use, and survival in hospitalized patients with advanced cancer. J Clin Oncol 1992;10:149– 55.
- 68 Green CR, Baker TA, Smith EM, Sato Y. The effect of race in older adults presenting for chronic pain management: A comparative study of black and white Americans. J Pain 2003;4:82–90.
- 69 Green CR, Baker TA, Sato Y, Washington TL, Smith EM. Race and chronic pain: A comparative study of

young black and white Americans presenting for management. J Pain 2003;4:176-83.

- 70 Cleeland CS, Gonin R, Hatfield AK, et al. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 1994;330:592–6.
- 71 Hamann J, Langer B, Leucht S, Busch R, Kissling W. Medical decision making in antipsychotic drug choice for schizophrenia. Am J Psychiatry 2004;161: 1301–4.
- 72 Fuentes M, Hart-Johnson T, Green CR. The association among neighborhood socioeconmic status, race and chronic pain in black and white older adults. J Natl Med Assoc 2007;99:1160–9.

- 73 Bekelman DB, Dy SM, Becker DM, et al. Spiritual well-being and depression in patients with heart failure. J Gen Intern Med 2007;22:470–7.
- 74 Block SD. Psychological issues in end-of-life care. J Palliat Med 2006;9:751–72.
- 75 Portenoy RK, Thaler HT, Kornblith AB, et al. Symptom prevalence, characteristics and distress in a cancer population. Qual Life Res 1994;3:183–9.
- 76 Reich M, Lesur A, Perdrizet-Chevallier C. Depression, quality of life and breast cancer: A review of the literature. Breast Cancer Res Treat 2008;110: 9–17.