Survival and Cost-Effectiveness of Hospice Care for Metastatic Melanoma Patients

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Objectives

We analyzed the association of hospice use with survival and healthcare costs among patients diagnosed with metastatic melanoma.

Methods

We used the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked databases to identify patients 65 years or older with metastatic melanoma who died between 2000 and 2009. We analyzed claims data to ascertain cancer treatment utilization and costs. Survival, end-of-life costs, and incremental cost-effectiveness ratio were evaluated using propensity score methods. Costs were analyzed from the payer perspective in 2009 dollars.

Results

Of 862 patients, 225 (26%) received no hospice care, 523 (61%) received 1 to 3 days of hospice care, and 114 (13%) received 4 or more days of hospice care. The median survival time was 6.1 months for patients with no hospice care, 6.5 months for patients enrolled in hospice for 1 to 3 days, and 10.2 months for patients enrolled for 4 or more days (P <.001). The hazard ratio for survival among patients with 4 or more days of hospice use was 0.66; 95% confidence interval, 0.54-0.81, P <.0001 in the propensity score–matched model. Patients with 4 or more days of hospice care incurred lower end-of-life costs than the comparison groups ($14,594 vs $22,647 for the 1-to-3-days hospice care, and $28,923 for patients with no hospice care; P <.0001).

Conclusions

Patients diagnosed with metastatic melanoma who enrolled in 4 or more days of hospice care had longer survival than those who had 1 to 3 days of hospice or no hospice care, and this longer overall survival was accompanied by lower end-of-life costs.

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The 5-year survival rate for patients with melanoma detected at the earliest stages is approximately 95%,[1] but falls precipitously to 15% for patients diagnosed with metastatic disease.[2] Melanoma also places a significant economic burden on society and patients.[3] The estimated annual cost of melanoma care in the United States is $249 million and the average lifetime disease-associated cost for a patient from the time of diagnosis with melanoma until death is approximately $28,210.[3] Furthermore, 40% of the annual cost is attributed to stage 4 melanoma, which includes only around 3% of melanoma patients.[3]

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Since stage 4 melanoma is rarely curable, most medical treatment for these patients—including surgery, radiation therapy, chemotherapy, and biologic therapy—is prescribed with limited expectations for long-term survival, and often with palliative intent. Increasingly, hospice care has become an acceptable alternative for patients with metastatic cancer. Hospices provide the necessary care, pain management, and emotional support to provide a comfortable end-of-life experience. The use of hospice also likely results in a decrease in utilization of surgery, radiation therapy, and chemotherapy,[4] thus likely leading to a decrease in medical costs, although this has not been studied among patients with metastatic melanoma. Other investigators have shown that hospice utilization does not result in shortened survival for other terminal illnesses such as advanced lung cancer and pancreatic cancer.[5,6] However, no studies have examined whether survival is reduced when patients elect hospice care for metastatic melanoma. Our goal is to examine the associations of use of hospice care with survival and costs among patients with metastatic melanoma and to analyze the cost-effectiveness for different durations of hospice care in patients with this disease.

METHODS

Data Source and Cohort Definition

We conducted this study using data from the National Cancer Institute's Surveillance, Epidemiology, and End Re-

sults (SEER)-Medicare-linked databases. This database covers 17 geographic areas in the United States and encompasses approximately 28% of the US population.[7] The SEER registries are linked to the Medicare claims databases, which are updated biennially and include 97% of US citizens 65 years and older.[8] All available Medicare claims files were used to obtain information on treatments and costs of care. The Patient Entitlement and Diagnosis Summary File (PEDSF) contains 1 record per person linked via encrypted identifiers to a corresponding file in the SEER database and provides basic information on sociodemographic and tumor characteristics. All data were de-identified such that no protected health information could be linked to individual patients. The institutional review board from the University of Texas MD Anderson Cancer Center, Houston, Texas, and the University of Texas Health Science Center, Houston, Texas, exempted this study.

Take-Away Points

- Patients who enrolled in hospice for 4 or more days showed longer median survival than patients who did not use hospice care or who enrolled in hospice care for only 1 to 3 days after diagnosis with metastatic melanoma.
- Among patients who were enrolled in 4 or more days of hospice care, the end-of-life costs decreased by $14,680 in the model with the original cohort, and by $9576 in the model with the propensity score–matched cohort.
- The incremental cost was $29,426 per life-year gained for patients who received 4 or more days of hospice care.

We identified patients 65 years and older who were diagnosed with pathologically confirmed malignant melanoma (stage 4) between January 1, 2000, and December 31, 2009. Patients were excluded if their death year and month in the SEER data set and Medicare data sets did not match, or if their cancer diagnosis came from either an autopsy or death certificate. Patients were excluded if they did not have continuous coverage through enrollment in Medicare Part A and Part B from the date of melanoma diagnosis until death or if they had health maintenance organization coverage during this time.

Dependent Variables

Overall survival was defined as the time from diagnosis of melanoma to the patient's death due to the melanoma. The costs incurred in the last 3 months were used to estimate the incremental cost-effectiveness ratio, defined as cost per life-year gained.

Independent Variables

Independent variables in the analysis included age at diagnosis, sex, marital status, neighborhood income and education levels, geographic region, comorbidity score, and hospice density. Hospice density, defined as the number of hospice facilities available within each patient's health service area, was obtained from the Area Resource File.[9] The Charlson Comorbidity Index score was calculated from an algorithm developed by Klabunde and colleagues.[10,11] The use of hospice care was identified based on any hospice service date after the melanoma diagnosis date. Based on information relayed by hospice staff, Kris and colleagues concluded that 3 or fewer days was an insufficient amount of time for patients and hospice staff to fully communicate on the planning and implementation of hospice care, so we adopted this common classification approach whereby the number of hospice service days was categorized into 3 groups: no hospice care, 1 to 3 days of hospice care, and 4 or more days of hospice care.[6,12]

Statistical Analysis

We conducted a univariate analysis using χ^2 test. Multivariate analysis was performed with a standard of $P < .05$ to determine the significance of association of outcomes and variables. A Cox proportional hazards model controlling for potential explanatory variables was used to assess the relationship between hospice use and overall survival. All hazard ratios (HRs) were calculated with 2-sided P value and 95% confidence intervals (CIs). Survival rates were calculated from Kaplan-Meier estimation. Since all patients died within the observation window, no censored cases occurred. The generalized linear model with a gamma distribution was used for validating the outcome of the Cox model.

To minimize potential selection bias, we used propensity score–based 1:N match (1 case matched with N controls) in the survival and cost models. Since a 3-group propensity score–matching algorithm is not available, and survival for patients with no hospice care was similar to that of patients who used 1 to 3 days hospice, we combined these 2 groups into 0 to 3 days of hospice use and further matched with patients who used 4 or more days of hospice care by applying a propensity score–based 1:N match algorithm developed by Parsons.[13] In this algorithm, all the demographic variables were included in the propensity score logistic model to generate the predicted probability that is used for matching. To maximize the sample size from a 5-matching scenario (1:N, N is 1 to 5), we used a 1:5 match-optimized cohort by using an 8-to-1-digit matching algorithm.[13] In the matched cohort,

a Cox proportional hazards model stratified by matched pair evaluated the associations between 4 or more days of hospice care or 0 to 3 days of hospice care and overall survival time in months.

To conduct the economic analysis, we divided the total cost of care after diagnosis into 3 phases based on the phase-of-care approach developed by Riley and colleagues.[14] The majority of resources are typically consumed in the initial phase, when a patient's disease is diagnosed and treated, and during the final (end-of-life) phase, when extensive efforts are employed to extend the patient's life or to improve quality of life. Thus, the costs calculated from this method would follow a U-shaped pattern, with the highest costs on the 2 end points. In our study, the initial phase, which lasts an average of 3 months, was defined as the period during which medical intervention was implemented for advanced melanoma and might include the times of diagnosis, surgery, chemotherapy, and radiation therapy. The end-of-life phase is defined as the last 3 months immediately preceding death. The interim months of continuing care after the initial phase include surveillance and routine therapy costs.

We calculated the cost difference by comparing the total Medicare payments incurred by patients receiving 4 or more days of hospice care with those incurred by patients not receiving hospice care prior to death and those patients receiving 1 to 3 days of hospice care. The total cost of care for patients was calculated as the sum of reimbursements authorized by Medicare. Medicare claims reimbursements were adjusted for inflation to 2009 dollars using the Prospective Pricing Index for Part A claims and the Medicare Economic Index for Part B claims.[15] Costs were adjusted for geographic variation using the geographic adjustment factor for Part A claims and the geographic practice cost index for Part B claims.[15] These adjusting factors are acquired from direct communication with the National Cancer Institute's Health Services and Economics Branch of the Applied Research Program. These indices were matched via the state and county codes for each patient and then multiplied with the costs from each file in the database. Since the median survival time for metastatic melanoma patients is less than 1 year, discounting was not applied to cost or survival time. Costs were further analyzed in a generalized linear model with a gamma distribution controlling for patient demographic and clinical covariates.[16]

The cost-effectiveness analysis utilized the mean of costs from all 3 phases of cancer care and survival. The incremental cost-effectiveness ratio (ICER) = $(C_1 - C_2) / (E_1 - E_2) = \Delta C / \Delta E$, where C_x equals cost of group x and E_x is effectiveness at group x, with the quotient representing cost per life-year gained. In the cost-effectiveness model, a bootstrap simulation analysis was implemented to assess the statistical uncertainty. We performed an analysis with 1000 bootstrap estimates of the ICER in both the original cohort and the 1:5 matched cohort. Statistical analysis was conducted using SAS version 9.3 (SAS Institute, Inc, Cary, North Carolina).

RESULTS

Patient and Tumor Characteristics

Characteristics of the entire cohort and matched cohort as well as univariate analysis of hospice use and patient characteristics are shown in **Table 1**. Of 862 patients, 225 (26%) had no hospice care after diagnosis, 523 (61%) had 1 to 3 days of hospice care, and 114 (13%) had 4 or more days of hospice care. All covariates were evenly balanced in the matched cohort.

Overall Survival

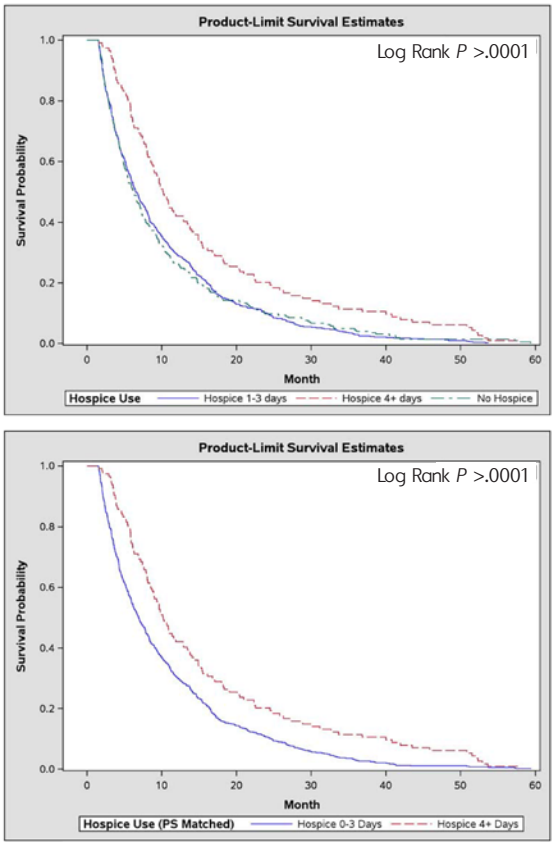
At the end of the 60-month study period, the unadjusted survival curves for the entire cohort categorized by hospice use are shown in **Figure 1A**. The median survival time was 6.1 months for patients who did not enroll in hospice, 6.5 months for patients who enrolled in hospice for 1 to 3 days, and 10.2 months for patients who enrolled in hospice for 4 or more days. The survival curves for the propensity score–matched cohort after combining the groups of patients with no hospice use or only 1 to 3 days of hospice use are shown in **Figure 1B**. The overall survival rates at all-time points for the patients enrolling in 4 or more days of hospice care were significantly better than those for the comparison group (log-rank test, P <.001).

In Cox proportional hazards models, 4 or more days of hospice care was associated with an improvement in survival when adjusting for other characteristics (**Table 2**). The estimated improvements in survival for 4 or more days of hospice use were similar in the original-cohort Cox proportional hazards model (HR, 0.63; 95% CI, 0.52-0.77, P <.0001) and propensity score–matched model (HR, 0.66; 95% CI, 0.54-0.81, P <.0001). Patients enrolled in 4 or more days of hospice care had 3.9 months longer median survival time in the unmatched cohort model (P <.0001), and 3.3 months longer median survival time in the propensity score–matched cohort model (P <.0001). The findings were similar across various models and cohorts, suggesting that the overall association between 4 or more days of hospice use and reduced mortality was not affected by statistical modeling methods.

Table 1. Univariate Analysis for the Entire Cohort

	Original Cohort				Propensity Score 1:5 Matched Cohort		
	No Hospice N (%) 225 (26.1)	Hospice Care 1-3 Days N (%) 523 (60.7)	Hospice Care 4+ Days N (%) 114 (13.2)	*P*	Hospice Care 0-3 Days N (%) 570 (83.3)	Hospice Care 4+ Days N (%) 114 (16.7)	*P*
Year of death				.10			.23
2000-2001	34 (15.1)	49 (9.4)	12 (10.5)		63 (11.1)	12 (10.5)	
2002-2003	37 (16.4)	94 (18.0)	15 (13.2)		98 (17.2)	15 (13.2)	
2004-2005	53 (23.6)	115 (22.0)	22 (19.3)		125 (21.9)	22 (19.3)	
2006-2007	47 (20.9)	124 (23.7)	39 (34.2)		136 (23.9)	39 (34.2)	
2008-2009	54 (24.0)	141 (27.0)	26 (22.8)		148 (26.0)	26 (22.8)	
Age at diagnosis				.13			.26
65-69 y	42 (18.7)	72 (13.8)	12 (10.5)		85 (14.9)	12 (10.5)	
70-74 y	52 (23.1)	122 (23.3)	26 (22.8)		138 (24.2)	26 (22.8)	
75-79 y	63 (28.0)	134 (25.6)	25 (21.9)		145 (25.4)	25 (21.9)	
≥80 y	68 (30.2)	195 (37.3)	51 (44.7)		202 (35.4)	51 (44.7)	
Gender				.69			.66
Male	158 (70.2)	356 (68.1)	75 (65.8)		387 (67.9)	75 (65.8)	
Female	67 (29.8)	167 (31.9)	39 (34.2)		183 (32.1)	39 (34.2)	
Marital status				.92			.94
Married	133 (59.1)	317 (60.6)	68 (59.7)		342 (60.0)	68 (59.7)	
Other	92 (40.9)	206 (39.4)	46 (40.4)		228 (40.0)	46 (40.4)	
Median household income				.36			.10
Lowest quartile	59 (26.2)	121 (23.1)	28 (24.6)		144 (25.3)	28 (24.6)	
2nd quartile	50 (22.2)	124 (23.7)	33 (29.0)		128 (22.5)	33 (29.0)	
3rd quartile	56 (24.9)	119 (22.8)	32 (28.1)		128 (22.5)	32 (28.1)	
Highest quartile	53 (23.6)	137 (26.2)	17 (14.9)		148 (26.0)	17 (14.9)	
Education <12 years				.32			.54
Lowest quartile	53 (23.6)	130 (24.9)	22 (19.3)		140 (24.6)	22 (19.3)	
2nd quartile	52 (23.1)	127 (24.3)	26 (22.8)		130 (22.8)	26 (22.8)	
3rd quartile	48 (21.3)	132 (25.2)	27 (23.7)		136 (23.9)	27 (23.7)	
Highest quartile	63 (28.0)	106 (20.3)	34 (29.8)		132 (23.2)	34 (29.8)	
Comorbidity scores				.96			.92
0	132 (58.7)	317 (60.6)	69 (60.5)		334 (58.6)	69 (60.5)	
1	54 (24.0)	112 (21.4)	25 (21.9)		128 (22.5)	25 (21.9)	
≥2	39 (17.3)	94 (18.0)	20 (17.5)		108 (19.0)	20 (17.5)	
Geographic region				.10			.24
West	115 (51.1)	217 (41.5)	48 (42.1)		261 (45.8)	48 (42.1)	
Northeast	51 (22.7)	142 (27.2)	22 (19.3)		142 (24.9)	22 (19.3)	
Midwest	18 (8.0)	58 (11.1)	15 (13.2)		57 (10.0)	15 (13.2)	
South	41 (18.2)	106 (20.3)	29 (25.4)		110 (19.3)	29 (25.4)	
Hospice density				.96			.93
0	31 (13.8)	58 (11.1)	14 (12.3)		68 (11.9)	14 (12.3)	
1-4	109 (48.4)	263 (50.3)	53 (46.5)		284 (49.8)	53 (46.5)	
5-9	43 (19.1)	104 (19.9)	24 (21.1)		113 (19.8)	24 (21.1)	
≥10	42 (18.7)	98 (18.7)	23 (20.2)		105 (18.4)	23 (20.2)	

Figure 1. Comparison of Survival Time Among the Patients Who Did Not Use Hospice, Who Used Hospice for 1 to 3 Days, and Who Used Hospice for 4 or More Days—Entire Cohort



A
Propensity Score 1:3 Matched Cohort
No Hospice:
Median: 6.1 months
CI: 5.27-7.3 months
Hospice Care 1-3 Days:
Median: 6.5 months
CI: 5.9-7.5 months
Hospice Care 4+ Days:
Median: 10.2 months
CI: 8.7-12.9 months

B
Log-Rank Test in Entire Cohort, *P* <.0001; Log-Rank Test in Matched Cohort, *P* <.0001
Hospice Care 0-3 Days:
Median: 6.9 months
CI: 6.1-7.7 months
Hospice Care 4+ Days:
Median: 10.2 months
CI: 8.7-12.9 months

CI indicates confidence interval; PS, propensity score.

Cost Analysis

The mean overall costs of care from diagnosis until death for patients with metastatic melanoma was $56,266 for patients who received no hospice care, $49,411 for patients enrolled in 1 to 3 days of hospice care, and $66,022 for patients enrolled in 4 or more days of hospice care. As shown in Figure 2 (A, B, and C), patients with 4 or more days of hospice care had lower costs in the last 3 months of life than did patients from the other 2 groups (*P* <.0001, $14,594 vs $22,647 for the patients with 1-3 days of hospice care, vs $28,923 for patients with no hospice care). The end-of-life costs of care for patients with 1 to 3 days of hospice care were also lower than those of patients who received no hospice care.

Predictors of End-of-Life Cost

We found age and use of hospice care to be the only factors significantly associated with end-of-life costs. Among patients who were enrolled in 4 or more days of hospice care, the end-of-life costs decreased by $14,680 (*P* <.0001) in the model with the original cohort, and by $9576 (*P* <.0001) in the model with propensity score–matched cohort.

Cost-Effectiveness Analysis

As shown in Figure 3A, mean incremental cost was $29,426 (95% CI, $723-$63,634) per life-year gained for patients who received 4 or more days of hospice care. The incremental cost increased to $33,209 (95% CI, $12,852-$66,280) per life-year gained in the propensity score–matched cohort in Figure 3B.

DISCUSSION

We observed that patients who enrolled in hospice for 4 or more days experienced longer median survival than patients who did not use hospice care or who enrolled in hospice care for only 1 to 3 days after being diagnosed with metastatic melanoma. We performed sensitivity analyses to examine the survival time for a relatively homogeneous cohort in which we excluded patients who died within 3 months of diagnosis to eliminate those with particularly rapid pace of disease. The positive association between 4 or more days of hospice use and longer survival was similar to that for the initial study cohort.

Our results are consistent with those of previous studies showing that election of hospice care does not shorten survival after metastatic cancer diagnosis.[5,6] In a study by Connor and colleagues, patients with congestive heart failure, lung cancer, or pancreatic cancer who enrolled in hospice experienced significantly longer median overall survival than those who did not. Our findings that median survival time did not differ between patients who received no hospice care and those who only received 1 to 3 days of hospice care is consistent with results from Earle and colleagues,[17] suggesting that a short stay in hospice may not impact survival.[7,18-20]

We also found that the costs of care in the final 3 months of life were lower among patients who received 4 or more days of hospice care after metastatic melanoma

diagnosis. Other researchers have shown that patients close to the end of life who received hospice care incurred less cost than other patients.[21,22] Pyenson and colleagues analyzed Medicare claims from 1999 to 2000 and found that hospice enrollment was a significant predictor of lower costs among patients with congestive heart failure, liver cancer, and pancreatic cancer, even when controlling for age and gender.[21] The cost difference we observed between the patients receiving 4 or more days of hospice care and those who received 0 to 3 days of hospice care is consistent with that observed by Pyenson and colleagues. Furthermore, our observed incremental cost-effectiveness ratio for patients who received 4 or more days of hospice care ($29,000 per life-year gained) lies well below the current willingness-to-pay thresholds.[23]

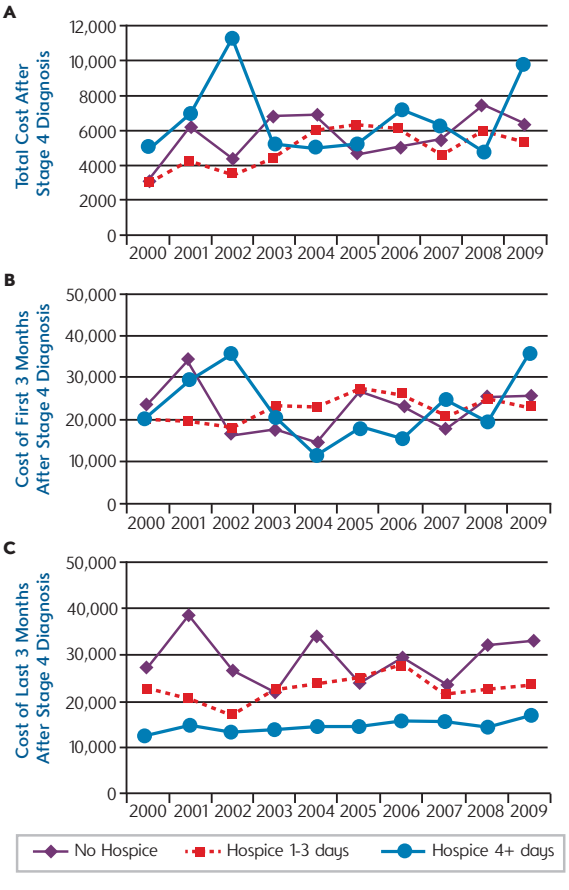
Our study has current policy relevance given that the proportion of Medicare expenditures during the last year of life has been stable for 20 years, with 26.9% to 30.6% of all Medicare expenditures occurring during that interval.[24] Furthermore, Lubitz and colleagues found that 70% of total costs of care is attributable to the consumption of healthcare resources in the last 6 months of life, with the largest percentage of this cost burden falling to Medicare (61% of costs), followed by Medicaid (10%), other payers (12%), and patients or families (paying the remaining 18% out of pocket).[24,25] Taylor and colleagues quantified the cost savings for the Medicare patients who received hospice care[26] and found the average cost savings for hospice users to be $2309 for the last year of life

Table 2. Hazard Ratios (95% CI) for Melanoma Patients and the Predictors After Propensity Score Adjustment (Cox Proportional Hazards Regression)

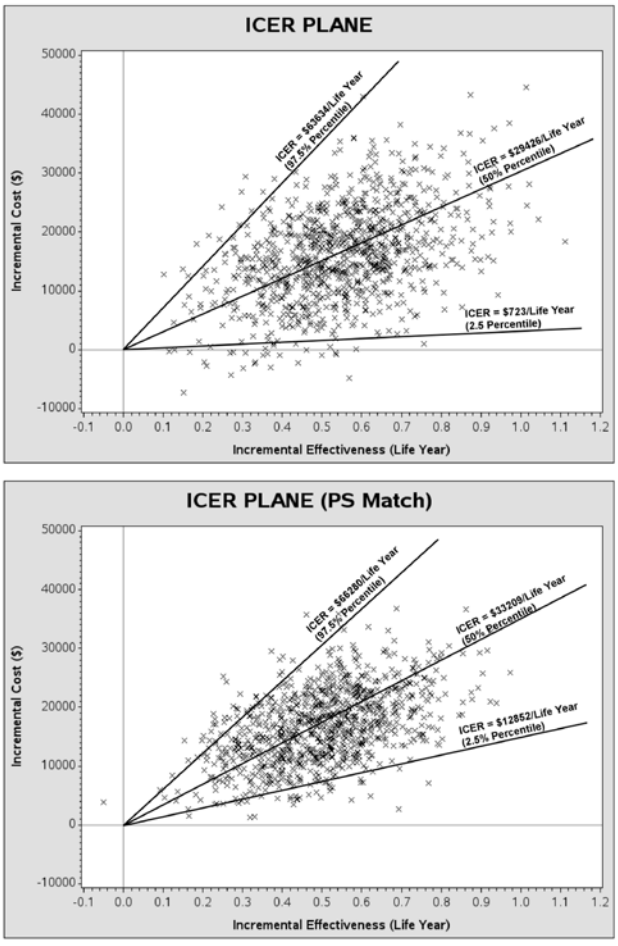
	Original Cohort (N = 862)			Propensity Score-Matched Model (N = 558)		
	HR	95% CI	*P*	HR	95% CI	*P*
End-of-Life Care						
Hospice care 0-3 days	1.00	Reference	—	1.00	Reference	—
Hospice care 4+ days	0.63	0.52-0.77	<.0001	0.66	0.54-0.81	<.0001
Year of death						
2000-2001	1.00	Reference	—			
2002-2003	0.65	0.50-0.85	<.01			
2004-2005	0.55	0.43-0.70	<.0001			
2006-2007	0.57	0.44-0.73	<.0001			
2008-2009	0.50	0.39-0.64	<.0001			
Marital status						
Other	1.00	Reference	—			
Married	0.86	0.75-0.98	0.03			

CI indicates confidence interval; HR, hazard ratio.

Figure 2. Comparison of Costs at the End of Life After Diagnosis, 3 Months After Diagnosis, and Last 3 Months Before Death, Stratified by Year and by Group (in $)



■ **Figure 3.** The Estimates of Incremental Cost-Effectiveness Ratio in the Cost-Effectiveness Plane (95% confidence interval lines are noted)



A
The incremental cost-effectiveness ratio and 95% confidence interval with original cohort.

B
The incremental cost-effectiveness ratio and 95% confidence interval with adjusted cohort.

ICER indicates incremental cost-effectiveness ratio; PS, propensity score.

compared with the costs of care for patients not receiving hospice care.[26]

Emanuel[27] challenged studies showing cost savings with hospice care, noting that several methodological issues could invalidate the findings of cost savings for hospice care, such as selection bias, different time frames for assessing costs, fewer cost components evaluated, and generalizability of the studies. Since that 1996 report, the methodology for analyzing cost implications of hospice care has improved—for instance, more medical cost data are available for evaluation compared with the 1990s, when only Medicare Part A was available. Moreover, the author concluded that the use of hospice does not increase costs and does yield better quality of life and increased autonomy at the end of life.[27]

Of the inherent limitations to the use of retrospective claims data, our study's main limitation was inability to obtain data on patient and provider preferences regarding hospice election. Another limitation is that the outcome variable examined was limited to survival time, which does not capture effects on quality of life; therefore, quality-adjusted life-years, the preferred measure in cost-effectiveness studies, cannot be estimated. This measure is of particular value for patients at the end of life. Hospice care aims to provide a better quality of life, and indeed, previous studies have shown better quality of life for patients who enroll in hospice care.[28-30] However, that the survival time of patients enrolled in hospice was longer than that of patients not electing hospice remains notable. Another consideration is that patients who survived longer might have had more opportunity to use hospice care and for longer durations than those who survived for a shorter period of time. Finally, the years encompassed by our study predate the diffusion of targeted molecular agents such as vemurafenib and ipilimumab, which have recently been shown to improve outcomes for patients with metastatic melanoma.[31] Therefore, it remains to be seen whether continued treatment with newer life-prolonging treatments such as those mentioned might mitigate the survival improvement associated with 4 or more days of hospice use observed in our study.

CONCLUSIONS

Our study showed a significantly longer median survival time for the patients diagnosed with metastatic melanoma who enrolled in 4 or more days of hospice care compared with those who had 0 to 3 days of hospice care, and this improved overall survival was accompanied by lower end-of-life costs. Our evaluation of the survival times and costs of care contributes to the understanding of the potential clinical and economic effects of hospice care on outcomes for patients with metastatic melanoma. Implications of our findings are that communication and

education regarding the benefits of hospice care should be a particular priority for patients diagnosed with metastatic melanoma.

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