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Direct Economic Burden of High-Risk and Metastatic Melanoma in the Elderly

Evidence from the SEER-Medicare Linked Database

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Abstract

Background: While the clinical implications of advanced melanoma have been extensively documented, little is known about the direct medical costs associated with the disease, particularly for elderly patients who carry the highest disease incidence and morbidity.

Objective: To document resource utilization and costs to the Medicare system for elderly patients with high-risk (stages IIB/C, IIIA/B, IIIC) or metastatic (stage IV) melanoma.

Methods: Data were taken from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database combining clinical information on incident cancer cases in the US between 1991 and 2002 with longitudinal (1991–2005) administrative Medicare claims. Subjects aged ≥65 years with at least one stage IIB or higher melanoma diagnosis were selected. An index date was identified corresponding to the first observed stage IIB or higher diagnosis. Subjects were then categorized into mutually exclusive index disease stages, based on the SEER-reported melanoma stage observed at the index date. All subsequent analyses were stratified according to the index disease stage. Subjects without a record of death were required to have at least 6 months of continuous Medicare Part A and Part B benefits coverage before and after their index date. Subjects who died <6 months after their index date were retained for analysis. Resource utilization and costs were evaluated for each patient from index date until death, benefits cessation or end of the database (31 December 2005). Cost data were inflated to 2007 $US and stratified by the care setting in which they were incurred: inpatient hospital, skilled nursing facility, emergency room, physician office, home healthcare, hospice and other ancillary.

Results: 6470 subjects met all inclusion criteria. Index stage distribution was: IIB/C (38%), IIIA/B (46%), IIIC (1%) and IV (15%). Median follow-up was 56, 39, 16 and 6 months, respectively. Patients with stage IV disease had 3.1 hospital days per month, compared with 0.5, 0.6 and 1.1 days for stage IIB/C, IIIA/B and IIIC patients, respectively. Adjusted inpatient costs for stage IV

subjects were $US5565 per patient per month versus $US1031, $US1440 and $US2275 for stage IIB/C, IIIA/B and IIIC patients, respectively ($p < 0.0001$). Adjusted total costs were $US11 471 per month for stage IV subjects, compared with $US2338, $US3395 and $US6885 for stages IIB/C, IIIA/B and IIIC, respectively ($p < 0.0001$).

Conclusion: The per-patient cost of advanced melanoma is high. Hospital services are the largest component of these costs. Monthly costs for subjects with stage IV melanoma were 67% higher than costs for subjects with stage IIIC disease and >3-fold higher than costs for patients with stages IIIA/B and IIB/C. However, when combining estimated monthly costs with median follow-up duration (a proxy for survival time), total costs incurred by Medicare appear to be highest for patients diagnosed at stage IIIA/B.

Background

Skin cancer has become the most common neoplasm in the US, with more than 1 million cases occurring annually.[1] Most of these cases are basal cell or squamous cell cancers, which have a high cure rate. However, the more serious form of skin cancer is melanoma, a proliferation of transformed melanocytes or pigment-producing cells. These tumours occur primarily on the skin, but also may arise in other tissues where pigmented cells are found. Overall, melanoma is the sixth most common cancer among both men and women in the US and causes 1–2% of all cancer deaths.[1,2] For localized melanoma, the 5-year survival rate is 99%, but this drops sharply to 65% and 15% for regional- and distant-stage diseases, respectively.[1]

While melanoma can be diagnosed in any age group, it is most common among persons of older age. Data collected from the Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute (NCI) indicate that 44% of all new cases of invasive cutaneous melanoma between 2000 and 2004 occurred in adults 60 years of age or older.[3] Furthermore, the incidence rate of melanoma from 2000 to 2004 was highest among persons aged 70–79 years (53 per 100 000 population), nearly six times the incidence rate found among those aged 20–29 years.[3]

With few effective therapeutic options available for advanced melanoma, the disease carries significant morbidity. The clinical implications of advanced melanoma have been extensively documented,[4,5] but little is known about the direct medical costs associated with the disease. One previous study audited medical charts from a regional referral centre to estimate per-patient expenditures for melanoma treatment,[6] while another study constructed an economic model using literature-based data to estimate the total annual costs of diagnosing and treating the disease.[7] However, no previous study has examined patient-level administrative data from real-world practice settings to estimate total all-cause direct medical costs incurred by third-party payers for patients with advanced melanoma, particularly elderly patients who carry the highest disease incidence and morbidity. To address this knowledge gap, we analysed a retrospective claims database with linked clinical information from a large cancer registry to document total per-patient monthly healthcare utilization and costs incurred by the Medicare system for elderly enrollees diagnosed with high-risk (stage IIB/C, IIIA/B or IIIC) or metastatic (stage IV) malignant melanoma.

Methods

Data Source

Data for this study were taken from the SEER-Medicare linked database. The SEER

cancer registry was initiated in 1972 by the NCI and currently comprises nine state and three metropolitan, population-based registries that periodically collect information on nearly all (98%) newly diagnosed cancer cases, including malignant melanoma, in persons residing in SEER areas.[8] The current SEER areas have been shown to be nationally representative[9] and to capture approximately 24% of the total US population.[8] The information collected on each incident cancer diagnosis in the SEER registry includes patient-level demographic characteristics, date of diagnosis, clinical data about the tumour (e.g. histology, morphology, topography, stage, grade), selected types of first-line treatments (surgery and radiation, but not chemotherapy) provided within 4 months of diagnosis, and date and cause of death.

The NCI and the Centers for Medicare and Medicaid Services began linking SEER registry data with Medicare claims in 1991. This linkage is updated approximately every 3 years. The result is a database of persons aged 65 years and older with detailed clinical information on incident cancer, linked with comprehensive longitudinal healthcare utilization and cost data from Medicare. At the time of this study, Medicare claims were linked for elderly SEER patients with an incident cancer diagnosis between 1991 and 2002. For these patients, Medicare claims through 2005 were available.

Medicare claims linked to SEER registry data provide information on all services and associated billings covered under Medicare Part A benefits, including inpatient, skilled nursing facility, home healthcare and hospice care. The database also provides data on approximately 95% of services and billings covered under Medicare Part B, including physician visits, outpatient care, durable medical equipment and home healthcare. Data on services not covered by Medicare prior to 2006, including routine physical examinations, long-term residential care and oral drugs dispensed through outpatient pharmacies, are not available from the database. In addition to the patient-level demographic information available from SEER, the linked Medicare database contains information on each patient's Medicare benefits eligibility, including start and stop dates of coverage, reason for Medicare entitlement and managed-care enrolment. Using the SEER-Medicare linked database, researchers can document patterns and associated costs of care among elderly patients with cancer, including initial and adjuvant chemotherapy regimens, radiation therapy, surgery and other downstream services, as well as co-morbidities and healthcare utilization prior to the initial cancer diagnosis.[10-13]

Study Population

Subjects aged 65 years or older with a new diagnosis of malignant melanoma (International Classification of Diseases for Oncology, 2nd Edition [ICD-O-2] code in the range of C44.x) between 1 January 1991 and 31 December 2002 were selected for initial study inclusion. The stage observed for each SEER-reported melanoma diagnosis was determined based on clinical criteria set forth by the Tumor, Node, Metastases staging system for melanoma used by the American Joint Committee on Cancer (AJCC).[14] The AJCC stage for each diagnosis was assigned using an algorithm comprising the raw SEER variables HSTST (historical stage: *in situ*, localized, regional or distant), E10PN (number of positive lymph nodes), E10SZ (tumour size in mm) and E10EX (extent of disease: with or without ulceration). Cases meeting the AJCC criteria for high-risk or metastatic melanoma were identified as follows:

- stage IV: HSTST = distant
- stage IIIC: HSTST = regional *and* E10PN ≥4
- stage IIIA/B: HSTST = regional *and* E10PN <4
- stage IIB/C: HSTST = localized *and* E10SZ >2 mm *and* E10EX = with ulceration.

Because our study focused on subjects diagnosed with high-risk or metastatic melanoma, we excluded subjects with a diagnosis of stage 0, I or IIA and no evidence of stage IIB/C, IIIA/B, IIIC or IV disease.

For each subject, an index date was defined as the date of the first observed melanoma diagnosis of stage IIB or higher. Subjects then were categorized into mutually exclusive index disease stages, based on the melanoma stage observed at

the index date. All subsequent analyses were stratified according to the index disease stage. Subjects without a record of death were required to have at least 6 months of continuous Medicare Part A and Part B benefits coverage before and after their index date. Furthermore, subjects who died <6 months after their index date were retained for analysis. All resource utilization and cost outcomes were analyzed for each subject from their index date until the earliest out of death, interruption of benefits coverage or end of the database (31 December 2005).

In addition to the inclusion criteria described above, subjects were also required to have no evidence of health maintenance organization (HMO) enrolment following their index date, because HMOs are not obligated to provide the Medicare system with information about treatments (i.e. administrative procedure codes) and their associated costs. This exclusion is a widely accepted practice in analyses of Medicare claims data.[15,16]

Baseline Subject Characteristics

Subject characteristics that were measured at the index date included age, sex, race, geographic location, urban status of subjects' residency and follow-up duration (measured as days between the index date and the earliest out of death, Medicare disenrolment or end of the database). The percentage of subjects who died at any point post-index was calculated, as were 1-year post-index survival rates. In addition to measuring these characteristics, the Charlson Comorbidity Index (CCI) was also computed to obtain a measure of subjects' overall co-morbidity burden. The CCI includes 17 categories of co-morbidities, as defined by the International Classification of Diseases (9th Edition), Clinical Modification diagnosis codes, with associated weights corresponding to the severity of the co-morbid condition of interest.[17,18] A higher CCI score represents a higher overall co-morbidity burden. A CCI score ranges from 0, for subjects with no evidence of any co-morbidity, to 33, for very rare cases in which all co-morbidities are present. CCI scores were calculated for each subject based on evidence of the relevant diagnoses during the 6 months prior to their index date. Because the objective of the CCI score was to evaluate underlying co-morbidity burden independent of malignant melanoma, diagnosis codes 172.xx and 173.xx for malignant melanoma were excluded from the CCI calculation.

Outcome Measures

All-cause resource utilization and costs were stratified by the major service sector in which they occurred, based on the place of service, revenue and other relevant codes associated with each Medicare claim. Specific categories that were evaluated included hospitalizations, skilled nursing facility admissions, emergency room (ER) visits, physician office visits, home healthcare and hospice care, all other outpatient ancillary care, and total resource utilization and costs. As noted, data on utilization and costs of prescription drugs dispensed through outpatient retail pharmacies were not available. All utilization and cost outcomes were aggregated across the entire follow-up period available for each subject and were reported at the level of per subject per month. As typically practiced in studies of healthcare costs, all cost data were inflated to 2007 $US at the claim level using year-specific inflators from the medical component of the US Consumer Price Index. For example, the observed reimbursed amount for any specific claim in 1995 was multiplied by the ratio of the average annual medical price index for 2007 to the corresponding index for 1995. Price indices for medical and other service sectors of the US economy are publicly available from the US Bureau of Labor Statistics.

Statistical Analyses

All analyses were carried out using SAS statistical software (version 9, Cary, NC, USA). Baseline subject characteristics and volume of healthcare utilization (e.g. hospital days, percentage of subjects with a hospital admission) were analysed with univariate descriptive statistics. Monthly per-subject healthcare costs reimbursed by the Medicare system were evaluated using multivariate generalized linear models (GLM) with a log link function to resolve the issue of skewed cost

distribution that is common in healthcare claims data.[19] In contrast to the traditional log ordinary least squares regression, GLM provides more robust coefficient estimates.[20] In addition, GLM allows for adjusted, predicted mean costs for subjects in each index disease stage to be directly calculated and statistically compared in the dollar scale, thereby avoiding the issue of potentially biased estimates that may result from the Duan smearing method for back-transformation of logged coefficients.[21] Co-variates included in the GLM models were age, sex, race, geographic location, urban status of subjects' residency, follow-up duration and the year of subjects' index date.

Results

We identified a total of 6470 subjects who met all study inclusion criteria (table I). The distribution of stage at index date was 2431 subjects (38%) with stage IIB/C disease, 2971 (46%) with stage IIIA/B, 88 (1%) with stage IIIC and 980 (15%) with stage IV. Subjects were mostly male, almost exclusively White, and evenly distributed across age categories. Sex, race and age distributions did not vary substantially by the index disease stage, with the exception of stage IIIC subjects who were more disproportionately male (69%). As expected, stage IV subjects had the highest post-index mortality rate (95%) and the lowest 1-year post-index survival rate (35%). Median follow-up duration for the overall study population was 40 months, with follow-up decreasing substantially with increasing stage: 56, 39, 16 and 6 months for stages IIB/C, IIIA/B, IIIC and IV, respectively.

Tables II and III, along with figure 1, present the results of our analysis of all-cause healthcare utilization and costs among Medicare enrollees with high-risk or metastatic melanoma. On average, subjects with stage IV disease had 3.1 hospital days per month, compared with 0.5, 0.6 and 1.1 days per month for subjects with stage IIB/C, IIIA/B and IIIC melanoma, respectively. However, the percentage of subjects with at least one hospital admission was highest among subjects with stage IIIC disease at index (figure 1). Adjusted mean inpatient costs among subjects with stage IV disease derived from the GLM regression models were $US5565 per subject per month versus $US1031, $US1440 and $US2275 for subjects with stages IIB/C, IIIA/B and IIIC disease, respectively (all $p < 0.0001$). Subsequent analyses, in which we examined only hospitalizations with a primary or secondary discharge diagnosis of malignant melanoma, indicated that >50% of all hospitalization costs among stage IIIC or stage IV subjects were directly attributable to the disease. The proportion of all hospitalization costs attributable to melanoma in subjects with stage IIB/C and stage IIIA/B disease was only 11% and 25%, respectively.

Physician office visits and other ancillary services also constituted a significant proportion of total healthcare utilization and costs. Unlike hospital services, office visits were utilized most intensely by subjects with stage IIIC melanoma. On average, subjects with stage IIIC disease at index incurred 2.4 office visits per month, compared with 1.3, 1.5 and 2.0 visits per month for subjects with stage IIB/C, IIIA/B and IV melanoma, respectively. Adjusted mean office visit costs incurred by the Medicare system for subjects with stage IIIC disease were $US2415 per subject per month versus $US634, $US921 and $US2132 for stages IIB/C, IIIA/B and IV, respectively (all $p < 0.05$). Adjusted per-subject monthly costs for other ancillary services, a residual category of care that excludes all inpatient, office, ER, home and hospice services, were estimated at $US3697 for subjects with stage IV disease at index, compared with $US661, $US934 and $US1531 for stages IIB/C, IIIA/B and IIIC, respectively (all $p < 0.0001$). Adjusted total costs, inclusive of all noted service categories, were $US11 471 per month for stage IV subjects, compared with $US2338, $US3395 and $US6885 for stages IIB/C, IIIA/B and IIIC, respectively (all $p < 0.0001$).

Discussion

The magnitude of cost differences we found between subjects with stage IV melanoma and subjects with less advanced disease is consistent

Table I. Characteristics of the study sample

Patient characteristic	Melanoma stage at index date							
	IIB/C		IIIA/B		IIIC		IV	
	n	%	n	%	n	%	n	%
All patients	2431	37.57	2971	45.92	88	1.36	980	15.15
Sex								
Male	1495	61.50	1765	59.41	61	69.32	619	63.16
Female	936	38.50	1206	40.59	27	30.68	361	36.84
Age at index date (y)								
65–69	534	21.97	537	18.07	25	28.41	189	19.29
70–74	594	24.43	621	20.90	25	28.41	240	24.49
75–79	528	21.72	679	22.85	20	22.73	210	21.43
80–84	429	17.65	570	19.19	12	13.64	189	19.29
≥85	346	14.23	564	18.98	6	6.82	152	15.51
Race/ethnicity								
White	2388	98.23	2874	96.74	81	92.05	935	95.41
Non-White	43	1.76	97	3.26	7	7.95	45	4.59
SEER registry location[a]								
Northeast	565	23.24	588	19.79	19	21.59	210	21.43
South	211	8.68	328	11.04	12	13.63	85	8.68
Midwest	658	27.07	566	19.05	16	18.18	210	21.43
West	997	41.03	1489	50.11	41	46.59	475	48.46
Location description								
Big metro	1551	63.80	1681	56.58	52	59.09	517	52.76
Metro/urban	721	29.66	1023	34.44	30	34.10	378	38.57
Less urban/rural	159	6.54	267	8.98	6	6.82	85	8.68
Survival								
Died post-index date	1310	53.89	2086	70.21	79	89.77	927	94.59
Survived ≥1 y post-index	2274	93.54	2536	85.36	59	67.05	341	34.80
Follow-up duration (mo)								
Mean ± SD	64.50 ± 41.76		45.42 ± 35.42		28.83 ± 31.92		15.37 ± 22.80	
Median	56		39		16		6	
Range	1–175		1–177		3–163		1–171	
CCI score								
Mean ± SD	1.67 ± 2.22		1.64 ± 2.21		1.58 ± 2.07		2.09 ± 2.89	
Median	1		1		1		1	
Range	0–16		0–15		0–11		0–16	

a SEER areas included in the data analysed for this study were San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose, Los Angeles, rural Georgia, greater California, Kentucky, Louisiana and New Jersey.

CCI = Charlson Comorbidity Index; **SEER** = Surveillance, Epidemiology, and End Results.

with cost data in previous literature that were derived under alternative methods. Tsao et al.[7] for example, estimated that stage IV disease represented approximately 55% of annual expenditures for treatments in the broader melanoma population. Stage I and II disease, by comparison, collectively represented only 5% of total melanoma expenditures. With stage III representing 34% of total expenditures, Tsao et al.[7] concluded that nearly 90% of annual melanoma costs in 1997 were attributable to the relatively small proportion (approximately

Table II. All-cause healthcare utilization per patient per month following index date

Healthcare utilization	Melanoma stage at index date			
	IIB/C (n = 2431)	IIIA/B (n = 2971)	IIIC (n = 88)	IV (n = 980)
Hospital services				
Number of admissions				
mean ± SD	0.069 ± 0.155	0.099 ± 0.155	0.164 ± 0.161	0.386 ± 0.474
median	0.029	0.051	0.100	0.222
range	0–3	0–2	0–1	0–3
Days in hospital				
mean ± SD	0.496 ± 1.375	0.644 ± 1.424	1.101 ± 2.00	3.069 ± 4.659
median	0.116	0.205	0.441	1.142
range	0–19	0–22	0–16	0–31
SNF service				
Number of admissions				
mean ± SD	0.014 ± 0.049	0.021 ± 0.066	0.028 ± 0.071	0.067 ± 0.198
median	0	0	0	0
range	0–1	0–1	0–1	0–2
Days in SNF				
mean ± SD	0.292 ± 1.028	0.458 ± 1.518	0.533 ± 1.852	1.049 ± 3.066
median	0	0	0	0
range	0–13	0–23	0–16	0–24
Emergency room				
Number of visits				
mean ± SD	0.071 ± 0.136	0.084 ± 0.147	0.107 ± 0.142	0.271 ± 0.443
median	0.033	0.042	0.073	0.091
range	0–2	0–2	0–1	0–4
Office visits				
Number of visits				
mean ± SD	1.338 ± 0.987	1.457 ± 1.235	2.356 ± 1.675	1.974 ± 1.825
median	1.111	1.182	2.000	1.500
range	0–8	0–11	0–8	0–17
Home healthcare				
Number of visits				
mean ± SD	0.408 ± 1.519	0.620 ± 1.831	1.197 ± 2.565	1.046 ± 2.986
median	0	0	0.185	0
range	0–32	0–42	0–15	0–55
Hospice				
Days in hospice care				
mean ± SD	0.339 ± 2.453	0.629 ± 2.586	1.434 ± 2.932	2.643 ± 7.019
median	0	0	0.128	0
range	0–31	0–31	0–31	0–31
Other outpatient or ancillary services				
Number of encounters				
mean ± SD	1.000 ± 1.231	1.300 ± 1.384	1.954 ± 1.513	3.718 ± 3.552
median	0.625	0.901	1.636	2.571
range	0–15	0–18	0–9	0–29

Continued next page

Table II. Contd

Healthcare utilization	Melanoma stage at index date			
	IIB/C (n = 2431)	IIIA/B (n = 2971)	IIIC (n = 88)	IV (n = 980)
Total healthcare utilization				
Total number of encounters				
mean ± SD	2.910 ± 2.701	3.602 ± 3.150	5.853 ± 3.669	7.588 ± 5.958
median	2.227	2.724	5.160	6.183
range	0–41	0–46	0–20	0–62

SNF = skilled nursing facility.

20%) of subjects diagnosed with advanced-stage disease.

Despite the findings of our study and those of Tsao et al.[7] regarding stage-specific cost differences, it remains unclear whether subjects with stage IV melanoma present higher long-term costs when considering the substantially shorter survival times typical of patients with metastatic disease. Extrapolation of our monthly per patient cost estimates to the median follow-up months shown in table I, which crudely proxies survival time, suggests that Medicare incurs the highest total cost for subjects diagnosed at stage IIIA/B ($US3395 per month × 39 months = $US132 405), and the lowest total cost for individuals diagnosed at stage IV disease ($US11 417 per month × 6 months = $US68 826). While such calculations are informative, further study is needed to more formally compare the stage-specific costs of equivalent episodes of care. Furthermore, our study identifies and follows patients from the point of their first observed diagnosis of high-risk melanoma (i.e. stage IIB or higher) and does not examine subsequent disease progression or the costs associated with each disease stage *within* a given patient. Future study to explore the costs associated with disease progression is needed.

Our study is subject to several limitations inherent in analyses of Medicare claims data. First, because of the lack of a Medicare prescription drug (i.e. Part D) benefit prior to 2006, data on the use and costs of orally administered prescription drugs dispensed via outpatient retail pharmacies were not captured in our study data. Without such a pharmacy component, our analysis may understate all-cause medical costs incurred by patients with high-risk or metastatic melanoma. Second, our study relies primarily on administrative claims submitted solely for purposes of Medicare reimbursement and not for purposes of research, with no access to information collected from either the attending physician or the subject. Coding errors, for example, may have caused some utilization and cost measures to be incorrectly identified, and may also have caused some hospitalizations in the noted subanalysis to be incorrectly attributed to melanoma. The impact of potential misclassification bias stemming from analyses of claims data has been described in previous research.[22,23] Third, our cost analyses represent direct medical costs incurred by the Medicare system. Our study therefore ignores the costs paid by non-Medicare payers (e.g. managed-care organizations, Medicaid) and the broader societal costs of melanoma, including caregiver burden and lost workplace productivity. Fourth, the extent of clinical trial enrolment in our study population is unknown. Data on services received by trial enrollees that were reimbursed by study sponsors, and not by Medicare, were not captured in our data, thereby causing further potential for underestimation of all-cause costs.

Finally, this study includes only those subjects aged 65 years or older. Findings presented here therefore may not be representative of the general population of patients with high-risk or metastatic melanoma. Younger patients diagnosed with high-risk or metastatic melanoma, for example, are likely to engage in more active, aggressive and potentially more costly treatment regimens than those undertaken by elderly patients due to better underlying health and greater tolerance of adverse treatment effects. Other

Table III. Adjusted all-cause healthcare costs (2007 $US values) per patient per month following index date

Healthcare costs	Melanoma stage at index date			
	IIB/C (n = 2431)	IIIA/B (n = 2971)	IIIC (n = 88)	IV (n = 980)
Hospital costs				
Mean ± SD	1031 ± 890†	1440 ± 974†	2275 ± 1567†	5565 ± 2360
Median	754	1216	2044	5879
Range	113–7025	85–8153	84–8422	39–11 625
SNF costs				
Mean ± SD	341 ± 213†	522 ± 295†	1187 ± 5997*	1706 ± 853
Median	310	469	238	1692
Range	42–1255	32–2406	5–56 395	11–4796
Emergency room costs				
Mean ± SD	22 ± 18†	29 ± 23†	43 ± 51†	99 ± 52
Median	16	22	31	96
Range	2–123	1–206	1–386	1–294
Office visit costs				
Mean ± SD	634 ± 315†	921 ± 553†	2415 ± 2068*	2132 ± 1044
Median	570	826	1929	1952
Range	122–2851	43–4076	99–9823	172–5544
Home healthcare costs				
Mean ± SD	178 ± 179†	244 ± 203†	452 ± 1316**	590 ± 300
Median	118	181	211	554
Range	13–629	13–2513	61–12 307	11–2109
Hospice costs				
Mean ± SD	196 ± 142†	279 ± 209†	796 ± 1617**	994 ± 515
Median	164	229	424	1003
Range	18–1014	10–1579	20–11 230	2–3849
Other outpatient or ancillary costs				
Mean ± SD	661 ± 594†	934 ± 646†	1531 ± 1142†	3697 ± 1683
Median	452	784	1381	3817
Range	92–5908	62–7517	87–8070	30–9996
Total costs				
Mean ± SD	2338 ± 1780†	3395 ± 2063†	6885 ± 4409†	11 471 ± 4467
Median	1769	2985	6308	12 045
Range	370–16 246	242–19 208	443–31 613	177–20 794

SNF = skilled nursing facility; * $p < 0.05$; ** $p < 0.01$; † $p < 0.0001$ vs stage IV.

utilization data examined in our study suggest that elderly patients with melanoma do, in fact, follow a generally conservative treatment approach: less than half (42%) of all subjects with stage IV melanoma received radiation therapy following their index date, while slightly more than one-quarter (27%) received chemotherapy. Chemotherapy usage was even lower among patients diagnosed at stages IIB/C (14%) and IIIA/B (21%), although it was substantially higher in the small sample of patients diagnosed at stage IIIC (45%). However, without data on subjects aged <65 years, we cannot empirically compare treatment patterns and associated costs between younger and elderly patients with advanced melanoma.

Despite these limitations, our large study cohort, with linked clinical and healthcare utilization

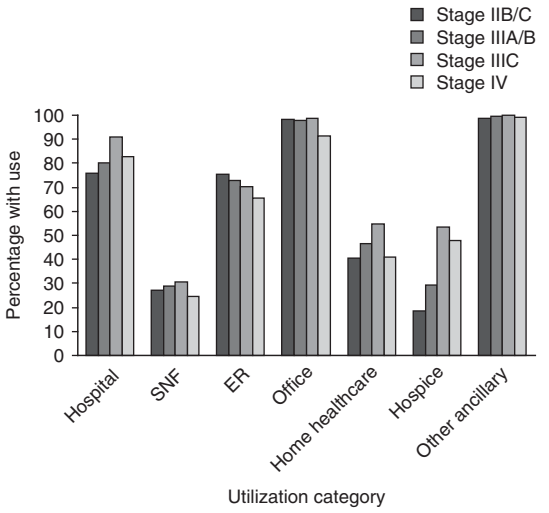

Fig. 1. Percentage of subjects with use of healthcare services. **ER** = emergency room; **SNF** = skilled nursing facility.

data, provided a unique opportunity to examine the direct economic burden associated with high-risk and metastatic melanoma. Future studies including data on prescription drug utilization, subjects aged <65 years of age and information on indirect societal costs are needed to fully evaluate the economic implications of advanced melanoma.

Conclusions

This study is the first to provide a comprehensive, stage-specific evaluation of the real-world direct cost burden of high-risk and metastatic malignant melanoma using administrative claims data. Our findings suggest that the per-subject cost burden of advanced melanoma to the Medicare system is high and that hospital services are the largest component of these costs. Not surprisingly, subjects with stage IV melanoma imposed the highest burden, with costs nearly 5-fold higher than those for stage IIB/C subjects, more than 3-fold higher than those for stage IIIA/B subjects and approximately 67% higher than those for stage IIIC subjects. Further study is needed to assess whether patients with stage IV disease carry higher long-term or overall costs than individuals with lower-staged high-risk melanoma, in light of the substantially shorter survival time typical in metastatic melanoma.

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