

Resource utilization and costs of managing patients with advanced melanoma: a Canadian population-based study

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ABSTRACT

Background The use and detailed costs of services provided for people with advanced melanoma (AMEL) are not well known. We conducted an analysis to determine the use of health care services and the associated costs delineated by relevant attributable costs, which we defined for subjects in the province of Ontario.

Methods Through the Ontario Cancer Data Linkage Project, a cohort of AMEL patients with diagnoses between 31 August 2005 and 2012 (follow-up to 2013) and with valid *International Classification of Diseases* (9th revision, Clinical Modification) 172 codes and histology codes was identified. A cohort of individuals with AMEL having a combination of at least 1 palliative, 1 medical oncology, and 1 hospitalization code was generated. The health system services used by this population were clustered into hospitalization, palliation, physician medical visits, medication, homecare, laboratory, diagnostics, and other resources. Overall rates of use and disaggregated costs were determined by phase of care for the entire cohort.

Results The mean age for the 2748 individuals in the cohort was 67 years. The greater proportion of the patients were men (65.6%) and were more than 65 years of age (>50%). In this advanced cohort, fewer than 45% of patients were alive 3 years after the malignant melanoma diagnosis. The average annual cost per patient over the time horizon was \$6,551. At \$15,830, year 1 after diagnosis was the most expensive, followed by year 2, at \$8,166.

Conclusions Our data provide a baseline for the costs associated with AMEL treatment. Future studies will include newer agents and comparative effectiveness research for personalized therapies.

Key Words Advanced melanoma, resource utilization cost, outcomes of treatment, Ontario cd-link

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INTRODUCTION

Melanoma is a malignant tumour arising from melanocytes in the skin; it accounts for more than 95% of all melanomas¹. Estimates suggest that, worldwide, approximately 132,000 people will be diagnosed with melanoma each year and that about 37,000 people will die of the disease annually². Mean age at diagnosis is 50 years, and in 10% of melanoma patients, metastasis has already occurred at the time of diagnosis². In Canada, it is estimated that 6500 new cases of melanoma and 1050 melanoma-related deaths will occur in 2014 (3500 men and 3000 women will be diagnosed with melanoma, and 660 men and 400 women will die from it)³.

Prognosis is related primarily to stage at diagnosis, which is determined by the thickness, ulceration, and mitotic rate of the primary lesion and also by the presence and number of micro- or macrometastases in the regional lymph nodes or metastases at distant sites. For those diagnosed with stage IIIc melanoma, 5-year survival is 40%⁴. Historically, the median survival duration for subjects with stage IV melanoma remains short, at approximately 6 months, with 26% of patients being alive at 1 year⁵. The 5-year survival rate is less than 10%⁶, and median progression-free survival is 1.7 months^{5,7}.

In Canada, despite the personal and social burden of melanoma, the economic burden of unresectable (stage IIIc) and metastatic (stage IV) disease is not well

understood. In the present study, we used the Ontario Cancer Data Linkage Project ["cd-link" (<http://www.ices.on.ca/Research/Research-programs/Cancer/cd-link>)] administrative database to estimate the resource utilization and costs of managing patients with advanced melanoma (aMEL) from a health system perspective.

METHODS

The purpose of the analysis was to determine, for patients with aMEL, the use of health care services and the associated costs within various clusters of costs defined for the province of Ontario. These specific objectives were included:

- To determine the annual total direct medical costs of managing patients with aMEL
- To disaggregate the total cost into costs attributed to hospitalization; hospice care; outpatient visits; and treatment management, palliative care, and other costs based on the available cd-link data
- To identify whether annual direct costs for aMEL differ by year from the time of diagnosis and by cost cluster
- To estimate the direct health system costs of treating brain metastases

A cohort of patients with aMEL was identified using a cd-link dataset obtained through a formal request to the Institute for Clinical Evaluative Sciences. Through the cd-link program, we identified a cohort of individuals with a diagnosis of melanoma [*International Classification of Diseases*, 9th revision, Clinical Modification (ICD-9-CM) 172 codes]. That administrative dataset was used to select patients with diagnoses between 31 August 2005 and 31 August 2012 and with valid ICD-9-CM 172 codes and histology codes. The dataset included data compiled from the Ontario Cancer Registry, the Discharge Abstract Database and the Standardized Discharge Summary, the Ontario Health Insurance Plan claims database, Ontario Drug Benefit claims, the National Ambulatory Care Reporting System, the Home Care Database (services, assessments, and admissions), the Continuing Care Reporting System (chronic care), and the National Rehabilitation Reporting System.

By filtering the retrieved individuals according to a defined algorithm, an aMEL cohort was created. Specifically, if a given patient had specific Ontario Health Insurance Plan fee codes relating to palliation, hospitalization, and medical oncology, they were considered part of the aMEL cohort (Table 1). We also identified patients with aMEL who had brain metastases (ICD-9-CM N103, N151, N152, and E901 codes), and we examined the costs for that cohort.

Once created, the aMEL cohort was linked by encrypted unique patient identifier to several provincial health system administrative databases to determine resource utilization and costs, including physician billing codes and hospitalization codes for treatment and palliation. The types of health care services used were stratified by cost of disease and by phase of care. Health system resources were organized into cost clusters (Table 11): medical visits, hospitalization, procedures, physician, diagnostics, homecare, palliative care, telemedicine, medications, counselling, laboratory, and monitoring. Medical oncologists who treat

patients with aMEL provided insight into the management of the disease. Their guidance on the specific management of such patients included providing appropriate physician billing codes with respect to medication, diagnostics, clinic visits, and palliation, and reasons for hospitalizations. Management information was then translated into the corresponding billing and hospitalization codes for the province of Ontario.

An average cost per metastatic melanoma patient was then determined from a public health system perspective. Ontario unit costs (2012 Canadian dollars) were derived from a number of sources, including the Ontario Case Costing Initiative, the Ontario Drug Benefit formulary, the Ontario Health Insurance Plan, and hospital sources for diagnostics. An overall cost per patient, which included all resources used, was calculated. Costs for individuals who used particular resources and for those who did not use those resources were included in the overall analysis.

Because of varying follow-up times for the individuals in the cohort, a phase-based costing approach was used. The per-person cost data were used to calculate annual aggregate costs associated with metastatic melanoma. The calculation was performed by generating the total expenditure for all individuals who survived to a given year (or who were censored at that year), yielding the total cost for all individuals who survived within their time bracket. For instance, a patient who lived for 3 years would be included only in the 3-year bracket.

We followed patients throughout their trajectory of care and used death dates where available; otherwise, patient records were censored at the date of the last known visit. Some individuals were lost to follow-up (no mortality data were available); others had died. The dataset included no individuals with records at the end of follow-up period (because of either mortality or censoring).

RESULTS

We generated a cohort of 2748 aMEL patients diagnosed from 2005 to 2012 based on our algorithm-defined criteria. Of those 2748 patients, 127 (5%) were identified as having brain metastases. The greater proportion of the patients were men (64.6%) and were more than 65 years of age. Mean age in the cohort was 67 years. Most patients lived in an urban environment (Table III).

Table IV provides details about the total costs for the entire cohort by phase of care—namely, pre-diagnosis and follow-up years 1 to 8 and beyond. Total cost for each of the resources used in the entire cohort are presented. The sample sizes for the patients using the resource are also provided. For example, at the end of year 1, 1220 patients had used a total of \$175,925 in counselling resources. The overall total cost for the cohort was \$103,019,266 over the entire analysis period. The overall cost for the entire cohort at the end of year 1 was \$43,278,269 for 2734 patients. The average annual cost per patient for the time horizon was \$6,551. At \$15,830, year 1 after diagnosis was the most costly, followed year 2, at \$8,166.

Table V details the direct costs of brain metastasis. For the entire cohort, the mean cost was \$60,759 (range: \$12,801–\$206,640). Only 127 patients had codes for brain

TABLE 1 Cohort identification codes

Service	Code		
<i>Palliative coding</i>			
Special palliative care consultation (office, home, OPD)	A945	C43.30 Malignant melanoma of unspecified part of face	C4330
Special palliative care consultation (in hospital)	C945	C43.31 Malignant melanoma of nose	C4331
Palliative care support (approximately 20 minutes)	K023	C43.39 Malignant melanoma of other parts of face	C4339
Palliative care case management	G512	C43.4 Malignant melanoma of scalp and neck	C434
Palliative care support (>20 minutes)	K023	C43.5 Malignant melanoma of trunk	C435
Special visit for purpose of providing palliative care (07h00–24h00)	B998	C43.51 Malignant melanoma of anal skin	C4351
In-hospital palliative subsequent day 2 and 3	C122	C43.52 Malignant melanoma of skin of breast	C4352
In-hospital palliative subsequent day 2 and 3	C123	C43.59 Malignant melanoma of other part of trunk	C4359
In-hospital-palliative care assessment (<20 minutes)—GP, acute	C882	C43.6 Malignant melanoma of upper limb, including shoulder	C436
In-hospital-palliative care assessment (<20 minutes)—specialist, acute care	C982	C43.60 Malignant melanoma of unspecified upper limb, including shoulder	C4360
In-hospital-palliative care assessment (<20 minutes)—GP, chronic care or rehab	W882	C43.61 Malignant melanoma of right upper limb, including shoulder	C4361
In-hospital-palliative care assessment (<20 minutes)—specialist, chronic care or rehab	W982	C43.62 Malignant melanoma of left upper limb, including shoulder	C4362
In-hospital-palliative care assessment (<20 minutes)—GP, long-term care	W872	C43.7 Malignant melanoma of lower limb, including hip	C437
In-hospital-palliative care assessment (<20 minutes)—GP, acute	W972	C43.70 Malignant melanoma of unspecified lower limb, including hip	C4370
In-hospital case conference (acute, chronic, rehab) palliative care	K121	C43.71 Malignant melanoma of right lower limb, including hip	C4371
Outpatient palliative case conference	K700	C43.72 Malignant melanoma of left lower limb, including hip	C4372
Physician-to-physician telephone counselling—palliative care	K734	C43.8 Malignant melanoma of overlapping sites of skin	C438
Physician-to-physician telephone counselling—palliative care	K735	C43.9 Malignant melanoma of skin, unspecified	C439
<i>Hospitalizations (all)</i>			
Melanoma	C430–C445	C44.0 Malignant neoplasm of skin of lip	C440
C43 Malignant melanoma of skin	C43	C44.1 Malignant neoplasm skin eyelid, including canthus	C441
C43.0 Malignant melanoma of lip	C430	C44.2 Malignant neoplasm skin ear and external auric canal	C442
C43.1 Malignant melanoma of eyelid, including canthus	C431	C44.3 Malignant neoplasm skin other or unspecified parts face	C443
C43.10 Malignant melanoma of unspecified eyelid, including canthus	C4310	C44.4 Malignant neoplasm skin of scalp and neck	C444
C43.11 Malignant melanoma of right eyelid, including canthus	C4311	C44.5 Malignant neoplasm of skin of trunk	C445
C43.12 Malignant melanoma of left eyelid, including canthus	C4312	C44.6 Malignant neoplasm skin upper limb, including shoulder	C446
C43.2 Malignant melanoma of ear and external auricular canal	C432	C44.7 Malignant neoplasm skin lower limb, including hip	C447
C43.20 Malignant melanoma of unspecified ear and external auricular canal	C4320	C44.8 Overlapping malignant lesion of skin	C448
C43.21 Malignant melanoma of right ear and external auricular canal	C4321	C44.9 Malignant neoplasm of skin unspecified	C449
C43.22 Malignant melanoma of left ear and external auricular canal	C4322	<i>Medical Oncology</i>	
C43.3 Malignant melanoma of other and unspecified parts of face	C433	Full consultation	A135
		Limited consultation	A435
		Repeat consultation	A136
		Specific assessment	A133
		Specific re-assessment	A134
		Complex re-assessment	A131
		Partial assessment	A138

OPD = outpatient department; GP = general practitioner.

TABLE II Other direct health care costs

Resource	Description
Counselling	All physician-billed counselling services were identified using billing codes and costed by billing code.
Diagnostics	Physician billing codes and costs of magnetic resonance imaging, positron-emission tomography, radiography, and ultrasonography were used to determine the cost of diagnostics.
Homecare	All homecare resources administered to the cohort by Community Care Access centres were identified. Homecare activities included nursing care, personal support workers, case management, and allied health professionals. The number of visits per homecare used was multiplied by the unit cost of a homecare visit.
Hospitalization	Costs for hospitalizations (disease- and complication-related) were derived from the Ontario Case Costing Initiative. The “most responsible” diagnoses for admissions were coded using the <i>International Classification of Diseases</i> , revision 9, Clinical Modification (ICD-9-CM), and costs were derived from the current Ontario Case Costing Acute Inpatient Database. The cost per day was calculated by dividing the total admission cost by the mean length of stay for each corresponding ICD-9-CM code (Appendix A).
Laboratory	Melanoma-related laboratory tests—complete blood count, bone marrow, AST, ALT, renal, bilirubin, triglycerides, cholesterol, T3-free, TSH, and creatinine—were identified, valued, and then costed. The Ontario Schedule of Benefits was used for the unit costs (Appendix A).
Physician	<p><i>Medical visits</i></p> <p>Costs of physician billing for clinic visits, medication administration or management, diagnostics, procedures, and hospitalization. Physician services identified by medical oncologists as being used by patients with advanced melanoma included medical oncology, radiation oncology, dermatology, neurology, ophthalmology, neurosurgery, family practice, and emergency medicine. The Ontario Schedule of Benefits was used to identify physician billing codes and values. All physician-billed medication services were identified using billing codes and were priced out as such (Appendix A).</p> <p><i>Administration of chemotherapies</i></p> <p>Billing codes for the administration of chemotherapies were identified from the billing sheets of two different academic centres in the province. All physician-billed medication services were identified via billing codes and priced out as such. All activities were costed using the Ontario Schedule of Benefits (Appendix A).</p>
Monitoring	Monitoring was defined as physician telephone monitoring and was costed using the associated billing code (Table I).
Medications	Drugs prescribed within the Ontario Drug Benefit formulary were identified and quantified. The Ontario Drug Benefit formulary provides access to individuals more than 65 years of age and to those on social assistance. Unit costs for the medications were based on the Ontario Drug Benefit formulary costs per medication. To lower the noise and cost from non-cancer medications, we generated a list of medications that would be appropriate for a metastatic melanoma population. Medications included antineoplastics, interferons, anti-infectives, anticonvulsants, analgesics, antidepressants, antiemetics, and hematopoietic agents (Appendix A).
Palliative care	All physician-billed palliative services were identified using billing codes and priced out as such. All activities were costed using the Ontario Schedule of Benefits (Appendix A).
Procedures	Procedures identified as important to the management of the cohort included biopsies, lymph node resections, craniotomy, excision; and the physician billing codes associated with those procedures were used. All activities were costed using the Ontario Schedule of Benefits (Appendix A).
Telehealth	All physician-billed palliative services were identified using billing codes and priced out as such. All activities were costed using the Ontario Schedule of Benefits (Appendix A).
Transfusions	Transfusion-related activities included exchange transfusion, donor cell pheresis, transfusion support, and plasma exchange. All activities were costed using the Ontario Schedule of Benefits (Appendix A).

AST = aspartate aminotransferase; ALT = alanine aminotransferase; T3-free = free triiodothyronine; TSH = thyroid-stimulating hormone.

metastasis, and their mean cost exceeded the mean cost for the entire cohort by \$23,270 (Table iv).

DISCUSSION AND INTERPRETATION

Our study is one of the first to examine the costs associated with the management of aMEL in Canada. Our results show that, at \$15,830, year 1 after diagnosis is the most costly, followed by year 2, at \$8,166. Comparable costing data from a Canadian perspective are limited. The cost for year 1 in our algorithm-derived aMEL population was higher (\$15,830) than the cost reported by de Oliveira *et*

*al.*⁸, which, in year 1, was less than \$10,000. Their lower cost is most likely due to a lower proportion of patients with aMEL. In other words, they included patients that were not exclusively late stage III and stage IV. The lower costs might also be a result of more expensive treatments being more readily available after 2010.

A recent literature review identified a resource utilization study conducted in Europe in patients with unresectable malignant melanoma⁹. The results of that study, which included 3 countries (United Kingdom, Italy, and France), showed that the hospitalization costs were highest in France. In contrast, outpatient costs were highest in the

TABLE III Demographic characteristics of the study patients with advanced malignant melanoma

Variable	Value
Patients (n)	2748
Sex [n (%)]	
Women	974 (35.4)
Men	1774 (64.6)
Age (years)	
Mean	66.8
95% CI	52.4 to 81.3
Median	69
Age group [n (%)]	
≤29 Years	41 (1.5)
30–39 Years	109 (4.0)
40–49 Years	248 (9.0)
50–59 Years	393 (14.3)
60–69 Years	563 (20.5)
70–79 Years	759 (27.6)
80–89 Years	572 (20.8)
≥90 Years	63 (2.3)
Rural residence [n (%)] ^a	
No	2308 (84.0)
Yes	436 (15.9)
Unknown	4 (0.2)
Income group [n (%)] ^b	
Urban	
Lowest	387 (14.1)
Second lowest	416 (15.1)
Middle	418 (15.2)
Second highest	499 (18.2)
Highest	585 (21.3)
Rural	
Lowest	84 (3.1)
Second lowest	82 (3.0)
Middle	74 (2.7)
Second highest	93 (3.4)
Highest	99 (3.6)
Unknown	11 (0.4)

^a Based on postal code information from Statistics Canada.^b Based on postal code information and incomes for the relevant postal code from Statistics Canada.

CI = confidence interval.

United Kingdom. Hospitalization rates were consistently higher for supportive care compared with systemic therapy. In the study, cumulative costs were generally higher for long-term survivors, but monthly per-patient costs were generally lower.

Our study spans a greater number of years and has a larger cohort for analysis. Moreover, treatment regimens and response to treatment have improved since 2005. In the study published by Alexandrescu¹⁰, the costs associated with treatment for malignant melanoma patients 5

years after diagnosis at each melanoma stage—including treatment, surveillance, loss of income, and terminal care—were considered. Approximately half of all medical costs for treating patients with malignant melanoma were attributable to 15% of the patients with advanced disease¹⁰.

The economic burden of melanoma in France was assessed by Chevalier *et al.*¹¹, who determined that hospital costs for melanoma care were less than 1% of total cancer-related hospital costs because melanoma treatment in France relies on outpatient care. Compared with our study, the Chevalier *et al.* study included hospital costs during only 1 year (2004), and ICD version 10 codes were used to create the cohort.

Chang *et al.*¹² proposed a therapy-based economic analysis of the care for patients registered in the U.S. IMS PharMetrics Plus database who had 2 or more primary malignancies (ICD-9-CM 172.xx codes) between 1 January 2009 and 30 September 2012, 1 or more metastasis diagnoses (ICD-9-CM 196.xx–198.xx codes) between 1 July 2009 and 30 September 2012, or pre-existing metastasis during 1 January–30 June 2009, treated with contemporary therapies in the United States. Vemurafenib was not significantly different from older chemotherapies¹². The database did not include laboratory results, treatment response, or disease progression information.

In a study published by Toy *et al.*¹³, the costs, resource utilization, and treatment patterns for patients with malignant melanoma were examined for a 6-month period, which included the advent of ipilimumab and vemurafenib therapies. Their population consisted of 834 patients who had at least 1 diagnosis of melanoma (ICD-9-CM 172.xx codes), 1 diagnosis of a secondary malignant neoplasm (ICD-9-CM 196.xx, 197.xx, 198.xx, 199.xx codes), and who had initiated metastatic melanoma treatment with certain therapies (ipilimumab, vemurafenib, interleukin 2, dacarbazine, temozolomide, paclitaxel) between 25 May 2011 and 30 September 2012. The cost was high, and it varied between the treatment cohorts¹³. The most frequently used therapies were ipilimumab and vemurafenib (60%).

Compared with our study, the two foregoing reports^{12,13} included novel therapeutic agents, but smaller numbers of patients. The authors also included the ICD-9-CM 196.xx, 197.xx, 198.xx and 199.xx codes, which were unavailable at the time of our proposed study.

In their study, Arondekar and colleagues¹⁴ conducted a retrospective administrative claims-based analysis of the MarketScan commercial and Medicare supplemental databases. The population included 2621 patients who had at least 1 diagnosis of melanoma (ICD-9-CM 172.xx code) and who initiated treatment with paclitaxel, vemurafenib, ipilimumab, dacarbazine, temozolomide, high-dose interleukin 2, or interferon alfa monotherapy between 1 January 2005 and 30 April 2012. The results showed that the cost of specific treatment-related adverse events of the most commonly used therapies in malignant melanoma can be substantial. Compared with our study, that therapy-based study included newer agents and reported monthly costs¹⁴. However, in our model, because of varying follow-up times, the overall cost of health care services used was determined by phase of care (namely, pre-diagnosis and follow-up years), which better represents usual care and the subsequent cost of care.

TABLE IV Phase-based overall average cost of advanced melanoma per year, 2012 Canadian dollars

Year	Cohort size (N)	Mean cost and individuals receiving service [\$ (n)]							
		Counselling	Diagnostics	Homecare	Hospitalization	Laboratory	Medical visits	Chemotherapy administration	
Pre ^a	2748	58,236 (453)	709,286 (1369)	9,651 (189)	11,242,009 (668)	84,987 (1908)	1,345,057 (2370)	45,142 (291)	
1	2275	175,925 (1220)	3,063,086 (2085)	51,091 (904)	30,467,311 (2121)	89,018 (1868)	3,947,113 (2629)	682,210 (787)	
2	1802	85,148 (640)	1,770,268 (1434)	14,866 (323)	11,154,316 (501)	72,025 (1497)	2,540,544 (2048)	147,997 (454)	
3	1487	59,089 (459)	1,248,602 (1037)	10,785 (230)	6,190,430 (311)	54,573 (1,158)	1,801,697 (1,537)	98,827 (317)	
4	1254	41,501 (322)	890,471 (728)	8,201 (180)	3,851,177 (187)	38,999 (820)	1,428,229 (1,120)	67,191 (220)	
5	1117	22,415 (207)	552,436 (492)	4,901 (103)	2,284,381 (108)	26,373 (570)	850,047 (779)	39,316 (166)	
6	1032	18,807 (141)	295,138 (299)	3,182 (64)	1,534,765 (68)	19,207 (406)	561,139 (522)	19,205 (98)	
7	986	7,884 (78)	163,075 (167)	2,665 (46)	510,056 (31)	11,082 (234)	299,857 (315)	10,202 (59)	
8+	951	3,657 (35)	83,517 (79)	1,136 (20)	365,952 (14)	4,328 (101)	140,212 (147)	3,424 (33)	
		Monitoring	Medications	Palliative care	Procedures	Telemedicine	Transfusions	TOTAL	Mean cost per patient
Pre ^a	2748	2,886 (50)	467,087 (1350)	55,200 (346)	287,392 (1210)	0 (0)	533 (3)	14,307,470 (2664)	5,371
1	2275	9,482 (246)	2,450,804 (1824)	580,905 (1086)	1,761,058 (1514)	0 (0)	261 (3)	43,278,269 (2734)	15,830
2	1802	6,197 (156)	1,389,914 (1348)	586,121 (915)	384,592 (466)	0 (0)	352 (3)	18,152,346 (2223)	8,166
3	1487	3,537 (89)	831,684 (1010)	427,095 (641)	237,839 (288)	0 (0)	253 (3)	10,964,418 (1667)	6,577
4	1254	3,311 (75)	405,121 (731)	316,138 (494)	132,937 (200)	0 (0)	554 (4)	7,183,836 (1233)	5,826
5	1117	2,620 (53)	307,082 (524)	202,564 (321)	125,747 (157)	0 (0)	0 (0)	4,417,886 (863)	5,119
6	1032	1,236 (28)	215,654 (333)	106,308 (201)	47,651 (95)	0 (0)	32 (1)	2,822,329 (576)	4,900
7	986	372 (11)	108,453 (198)	49,986 (114)	24,498 (47)	0 (0)	0 (0)	1,188,135 (352)	3,375
8+	951	252 (8)	57,829 (112)	32,823 (59)	11,439 (21)	0 (0)	0 (0)	704,577 (186)	3,788

^a Pre-diagnosis costs.

TABLE V Direct patient-level costs of brain metastasis for 127 patients, 2012 Canadian dollars

Service	Cost variable (\$)				
	Mean	SD	Minimum	Maximum	Median
Counselling	201	178	0	816	188
Diagnostics	6,873	4,340	1,160	27,639	5,416
Homecare	33	60	0	500	21
Hospitalization	34,043	34,485	2,154	169,225	21,664
Laboratory	115	156	0	1,081	70
Medical visits	6,999	3,237	1,637	15,754	6,387
Chemotherapy administration	551	893	0	4,046	12
Monitoring	15	33	0	146	0
Medications	3,716	8,643	0	53,648	115
Palliative care	1,457	1,680	31	9,769	886
Procedures	6,756	3,386	1,969	25,120	6,165
Telemedicine	0	0	0	0	0
Transfusions	0	0	0	0	0
OVERALL	60,759	37,481	12,801	206,640	49,631

SD = standard deviation.

We validated our cohort's features against a prospective dataset from a longitudinal registry collected through the Canadian Melanoma Research Network (CMRN)^{a-c}. Age distributions indicated that patients in the cohort at the Institute for Clinical Evaluative Sciences were slightly older than those in the CMRN cohort, and yet the distribution of the dataset based on other clinical and demographic features coincided nicely. Our cohort had a mean age of 66.8 ± 14.42 years; the CMRN cohort had a mean age of 57.7 ± 14.8 years. Sex distributions were similar in the two cohorts (cd-link: 35.4% women, 64.6% men; CMRN: 37.1% women, 62.9% men).

Our analysis provides costing from a health system perspective. However, the analysis has limitations:

- The cohort was not defined according to recorded stage characteristics. We used surrogate indicators based on expert clinical opinion and algorithms to define this cohort with metastatic melanoma, but a comparison showed that it was representative of the CMRN dataset.
- In terms of therapeutic drug use, we captured a number of antineoplastics used in aMEl management (for example, temozolomide, interferon, and so on). However, the dataset contained no data about systemic chemotherapy agents. Newer, more costly drugs such as vemurafenib and ipilimumab were not yet being used in this population and were therefore not available for costing. The drug database had information only on patients who were more than 65 years of age or on social assistance; however, the greater proportion of our population was 65 years of age and older.
- It is possible that resources outside the ones identified in the analysis were used in our cohort; however, the resources included were validated by clinicians treating patients with metastatic melanoma. We did

not capture the cost of homecare or of allied health professionals involved in the management of the patients. Only the resources deemed attributable by the medical oncologists for the management of aMEl were identified and included.

- In terms of unit costs, we determined the costs in 2012 Canadian dollars, regardless of year of management. Consequently, our costs for medications could now represent an underestimate because of the evolving nature of treatment options for patients with metastatic melanoma, including immuno-oncology agents, targeted therapies, and anti-PD-1 therapies. Those new drug data will be available in the future for an updated analysis.

CONCLUSIONS

In an era in which new therapeutic agents are available to treat patients with aMEl, it is important to have real-world data that illustrate both the costs and the outcomes for

- a Ernst S, Petrella P, Joshua A, Gwadry-Sridhar F, Hamou A, TenHaaf A. Use of clinical information for prediction of disease progression in melanoma patients: a retrospective and prospective study using the Canadian Melanoma Research Network (CMRN) National Clinical Melanoma Database. Presented at: Canadian Melanoma Conference; Whistler, BC; 19–22 February 2015.
- b Ernst S, Petrella P, Joshua A, Gwadry-Sridhar F, Hamou A, TenHaaf A. Survival outcomes in treating malignant melanoma: a retrospective and prospective observational survey using the Canadian Melanoma Research Network (CMRN)—a national clinical melanoma registry. Presented at: Canadian Melanoma Conference; Whistler, BC; 19–22 February 2015.
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patients undergoing various treatments. As the system moves toward value-based care and reimbursement, the ability to utilize both administrative data and real-world evidence through registries provides the needed granularity of information to understand cost drivers and attributable outcomes alike.

Our data provide a baseline for the costs associated with AMEL treatment. The marked increase in drug costs for the new targeted agents and immunotherapies is expected to be the major determinant in the cost of managing patients with metastatic and locally advanced disease in the future. Not only will those agents become the standard of care for most patients, but they might also be used for increasing lengths of time. Patients will remain on active treatment longer as they realize the survival benefit attributable to the introduction of the new agents. Adverse drug reactions and complications, especially those associated with the immunotherapies, will remain an issue and will certainly factor into both the cost and the duration of therapy. Future studies will include newer agents and comparative effectiveness analyses that consider the personalized therapies that account for the gene status of patients.

Targeted therapies that potentially produce better outcomes with reduced toxicity are the way of the future. However, the role of real-world data from registries such as the CMRN will be more relevant as clinicians aim to supplement data from clinical trials (efficacy data) with real-world effectiveness data. The value of those observational data comes from an ability to continually re-examine the effect of therapy and to make use of the data to improve the quality of care.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare the following interests: SE has participated in a speakers' bureau, designing speaker materials for Bristol-Myers Squibb and Novartis; has acted in a consulting or advisory role for Bristol-Myers Squibb, Roche, Merck, and Novartis; has received research funding from Bristol-Myers Squibb, Novartis, Merck, and Roche; and has acted as supervisor for an Astellas Pharma clinical trial. TP has received honoraria from Merck, Novartis, Bristol-Myers Squibb, GlaxoSmithKline, and Roche; has acted in a consulting or advisory role for Merck, Novartis, Bristol-Myers Squibb, GlaxoSmithKline, and Roche; and has received research funding from Roche. FGS, SN, AH, SJS, AMJ, and NM have no disclosures to make.

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