Trends in incidence of cutaneous malignant melanoma in Canada: 1992-2010 versus 2011-2015

To the Editor: The incidence of cutaneous malignant melanoma (CMM) worldwide continues to rise.[1] We recently reported a comprehensive, population-based study of CMM in Canada during 1992-2010 and demonstrated a steady increase in its incidence across the Canadian provinces and territories, with a slight male predominance. Geographically, the highest CMM incidence rates were documented in the provinces of Nova Scotia and Prince Edward Island.[2] We extended this study and examined data on CMM incidence by using the Canadian Cancer Registry (2015 version) for the years 2011 to 2015 for all Canadian provinces except Quebec by using the *International Classification of Diseases for Oncology, Third Edition*, codes for all CMM subtypes, in a manner similar to that previously reported[2]; we identified 27,095 patients (Table I).

Consistent with the previously reported trends,[2] this malignancy had a higher age-standardized incidence in males (23.2 cases per 100,000 in males per year vs 17.7 in females). The mean age of diagnosis was 64.9 ± 14.7 years for males and 60.4 ± 18.8 years for females (62.8 ± 16.8 years for both sexes during 2011-2015 versus 58.5 ± 21.6 during 1992-2010) (Table II). Age range analysis confirmed these findings and showed that 60.3% of patients with CMM in Canada during the period from 2011 to 2015 were age 60 years or older (vs 48.7% in 1992-2010) (Table I), with an overall increased percentage of the Canadian population older than 60 years in 2011-2015 (20.8% vs 17.4% in 1992-2010). This finding suggests that increasing age of the population contributes significantly to the increasing incidence of CMM.

Analysis of the anatomic location of CMM in 2011-2015 revealed trends similar to those in 1992-2010, where the majority (63%) of CMMs in males developed on the head and trunk, however, in females, the lower extremities were preferentially affected and accounted for 31.7% of cases (Table I), further highlighting differences in sun exposure behaviors as possible contributing factors for these findings.

The age-standardized CMM incidence rate in Canada in 2011-2015 was 20.06 cases per 100,000 individuals per year (95% confidence interval, 19.82-20.30), as compared with the 1992-2010 rate of 12.27 (95% confidence interval, 12.18-12.36), demonstrating an ongoing steady increase. Age-standardized CMM incidence was highest in the province of Prince Edward Island, followed by Nova Scotia. The incidence rates for all provinces and territories are summarized in Table II. These findings highlight a consistent trend of increasing CMM incidence in Canada with the expected north-to-south gradient. Several factors may contribute to the high incidence of CMM in Prince Edward Island, including the province's aging population, proportion of individuals with Fitzpatrick type skin I to III, and relative abundance of water and sand (which are known to have

Table I. Clinical characteristics of CMM patients in Canada that were diagnosed in 2011-2015

		Males		Females		Both sexes	
	Characteristic	n*	%	n*	%	n*	%
Age, y	0-19	25	0.17	50	0.40	75	0.28
	20-39	830	5.68	1440	11.54	2275	8.39
	40-59	4000	27.36	4415	35.38	8415	31.05
	60-79	7255	49.62	4795	38.42	12,050	44.46
	>80	2495	17.07	1780	14.26	4285	15.81
Location	Skin of the lip	15	0.10	25	0.20	35	0.13
	Eyelid	45	0.31	40	0.32	85	0.31
	External part of the ear	560	3.83	135	1.08	695	2.57
	Skin of other parts of the face	1560	10.67	1065	8.53	2625	9.69
	Skin of the scalp and neck	1320	9.03	440	3.53	1760	6.50
	Skin of the trunk	5705	39.02	2770	22.20	8470	31.26
	Skin of the upper limb and shoulder	3235	22.13	3590	28.77	6825	25.19
	Skin of the lower limb and hip	1460	9.99	3955	31.69	5415	19.99
	Overlapping lesion of skin	70	0.48	30	0.24	105	0.39
	Skin, not otherwise specified	650	4.45	430	3.45	1080	3.99
	Total	14,615	100	12,480	100	27,095	100

Age and anatomic distribution analysis is presented for males and females.
CMM, Cutaneous malignant melanoma.
*Rounded to a multiple of 5.

Table II. CMM incidence rates and mean age at diagnosis across the Canadian provinces (except Quebec) and the territories during the periods 1992-2010 and 2011-2015

Province	1992-2010		2011-2015	
	Age-adjusted incidence rate per 100,000 person-years (95% CI)	Mean age at diagnosis, y (SD)	Age-adjusted incidence rate per 100,000 person-years (95% CI)	Mean age at diagnosis, y (SD)
Prince Edward Island	18.89 (17.22-20.56)	60.00 (16.33)	28.59 (24.84-32.34)	62.27 (14.84)
Nova Scotia	18.03 (17.42-18.64)	59.28 (16.23)	26.37 (24.97-27.77)	61.95 (15.17)
Ontario	14.28 (14.12-14.43)	59.33 (26.45)	21.42 (21.07-21.76)	63.40 (17.76)
British Columbia	14.96 (14.69-15.23)	58.24 (16.84)	19.82 (19.26-20.38)	63.11 (15.65)
New Brunswick	14.45 (13.83-15.06)	58.35 (16.55)	19.27 (17.94-20.60)	62.88 (15.21)
Alberta	13.13 (12.82-13.44)	55.84 (17.1)	17.31 (16.69-17.94)	60.4 (15.88)
Newfoundland and Labrador	10.37 (9.75-11.00)	57.76 (16.86)	16.32 (14.84-17.79)	60.09 (15.22)
Manitoba	10.95 (10.51-11.39)	59.38 (17.44)	15.96 (14.96-16.97)	63.40 (15.73)
Saskatchewan	11.60 (11.11-12.08)	59.65 (17.23)	14.43 (13.40-15.45)	62.02 (15.98)
Northern territories (Northwest Territories, Nunavut, and Yukon)	5.92 (4.60-7.24)	48.53 (13.33)	6.54 (4.14-8.95)	56.13 (9.26)
Canada	12.27 (12.18-12.36)	58.50 (21.6)	20.06 (19.82-20.30)	62.81 (16.83)

Age-standardized incidence rates are per 100,000 person-years.
CI, Confidence interval; SD, standard deviation.

increased surface reflection of ultraviolet radiation in comparison with that of grass).[3] Finally, analysis of CMM incidence by age group confirmed that the incidence increases with age, with important sex differences for each age category (Table I).

The observed trends of increasing CMM incidence in the aforementioned preferential anatomic sites in men versus in women and differences in incidence rates across Canada further highlight the continuity of the aforementioned trends[2] and emphasize important sex- and age-specific differences in the incidence of melanoma. To decrease CMM incidence, stronger targeted public health efforts must be made. Specifically, we must strive to improve patient education in Canada and address sex-specific sun-seeking habits and exposures.

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Abnormal erythrocyte morphology in drug reaction with eosinophilia and systemic symptoms

To the Editor: Drug rash with eosinophilia and systemic symptoms (DRESS) is a potentially fatal adverse drug reaction that is difficult to diagnose because of its wide range of clinical findings. Diagnosis is commonly made by using the Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) scoring criteria, which include rash, fever, lymphadenopathy, eosinophilia, leukocyte abnormalities, thrombocytopenia, transaminitis, and other organ involvement.[1] Incidental abnormal erythrocyte morphology (AEM) is not in the existing diagnostic criteria, and to our knowledge, it has not been associated with DRESS in the literature. This study aimed to assess whether AEM is associated with DRESS.

A retrospective review of the charts of adult patients whose disease was diagnosed by the inpatient dermatology service at Wake Forest Baptist Medical Center and who experienced a drug eruption between January 2012 and July 2018 was performed. Demographics, RegiSCAR criteria, and presence or absence of AEM were noted. Patients with RegiSCAR scores of 2 or higher, indicating possible, probable, or definite cases of DRESS, were included in the DRESS cohort.[2] Patients in the control cohort were inpatients with a diagnosis of morbilliform drug eruption, Stevens Johnson syndrome, or toxic epidermal necrolysis. Only patients who had a complete blood count with differential performed at Wake Forest Baptist Medical Center were included. A Fisher exact test was performed to compare the prevalence of AEM between patients with DRESS and those with other drug eruptions.

Table I. Frequencies of erythrocyte abnormalities in the DRESS cohort

Erythrocyte abnormality	Patients with DRESS and AEM, n (%) (n = 21)
Poikilocytosis	10 (48)
Polychromasia	10 (48)
Burr cells	7 (33)
Ovalocytes	7 (33)
Schistocytes	5 (24)
Target cells	4 (19)
Acanthocytes	2 (10)
Tear drop cells	2 (10)
Nucleated erythrocytes	1 (5)

AEM, Abnormal erythrocyte morphology; *DRESS*, drug rash with eosinophilia and systemic symptoms.

Table II. Frequency of other clinical findings in the DRESS cohort

Clinical finding	Patients with a RegiSCAR score of ≥2, n (%) (n = 38)
Fever (temperature of ≥100.4°F)	27 (71)
LAD	6 (16)
Eosinophilia	29 (76)
Thrombocytopenia	10 (26)
Thrombocytosis	3 (8)
Hepatic abnormalities	23 (60)
Kidney abnormalities	14 (37)
Other systemic abnormalities noted	5 (13)
Biopsy performed	9 (24)
Abnormal erythrocyte morphology	21 (55)

DRESS, Drug rash with eosinophilia and systemic symptoms; *LAD*, lymphadenopathy; *RegiSCAR*, Registry of Severe Cutaneous Adverse Reactions.

The DRESS cohort included 38 patients. Their average age at diagnosis was 55 years. Fourteen patients were male. More than half (55%) of these patients had AEM (Table I). The rates of other clinical findings associated with DRESS are displayed in Table II. Of the patients with DRESS who had AEM, 86% had eosinophilia and 67% had hepatic abnormalities. Of the patients with DRESS without AEM, 65% had eosinophilia and 41% had hepatic abnormalities. The cohort of patients with other drug eruptions included 246 patients; however, 31 were excluded because a complete blood count with differential was not performed during their hospitalization. Of the 215 patients included, 52 (24%) had AEM. AEM was more prevalent with DRESS than the other drug eruptions ($P = .0003$).