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Skin cancer healthcare impact: A nation-wide assessment of an administrative database

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ABSTRACT

Background: Skin cancer is an important health concern, with an increasing incidence worldwide.
Objective: To assess the clinical and economic burden of melanoma (MM) and non-melanoma skin cancer (NMSC) at public hospitals in mainland Portugal.
Methods: We used an administrative database containing a registration of all hospitalizations and ambulatory episodes occurred in Portuguese public hospitals between 2011 and 2015. We assessed all episodes with associated diagnoses of MM or NMSC regarding neoplasm location, metastases occurrence, length of stay, in-hospital mortality and hospital costs.
Results: We assessed 15,913 MM and 72,602 NMSC episodes. 14.3% of MM episodes presented with metastases, compared to 1.9% of NMSC episodes. Patients' median age was lower for MM (66 years) than NMSC (76 years). The trunk was the most common location for MM (32.5%), followed by the lower limbs (26.5%). NMSC presented with higher length of stay than MM (median 5 *versus* 4 days; $p < 0.001$), but with lower in-hospital mortality (7.3% *versus* 11.9%; $p < 0.001$). MM episodes had higher average hospital costs than NMSC episodes (1197.7 *versus* 1113.5 €; $p < 0.001$). Overall, NMSC episodes amounted a total of 80.8 million € in hospital costs *versus* 19.1 million € for MM episodes.
Conclusion: Skin neoplasms have substantial impact on healthcare services. NMSC is an important contributor to this burden. NMSC underreporting should be tackled and it should not be downplayed in skin cancer preventative strategies.

1. Introduction

The skin is the most common location of primary malignant neoplasms [1]. In fact, skin cancer has a higher incidence than all other cancers combined [2].

Despite encompassing less than 5% of all skin cancers, melanoma (MM) is responsible in Europe for more than 80% of skin cancer mortality [3], accounting for 1–2% of all cancer deaths [4,5]. According to the European Network of Cancer Registries (ENCR), more than 20 thousand deaths were estimated for MM in Europe in 2008, the largest share (35.5%) for Eastern and Central Europe [5]. Outside Europe, the highest rates of MM incidence are reported in other Caucasian and migrant populations, such as Europeans in Australia and New Zealand, where the annual incidence is more than double the highest rates in Europe [6,7]. Non-melanoma skin cancer (NMSC) incidence is also rising. This condition is often the cause of severe deformation and morbidity. Despite being rarely lethal, NMSC is so common that a relevant number of patients die annually from it, particularly those with advanced squamous cell carcinomas (SSC) [8]. Most NMSC (75–85%) are basal cell carcinomas (BCC), while 15–25% of them are SSC [9].

Overall, not only the incidence, but also the associated costs of skin cancer are increasing. The average annual total cost of skin cancer rose 126.2% in less than ten years in the United States, while the average annual total cost for all other types of cancer rose only by 25.1% [10]. Multiple factors may justify this substantial increment, namely the increase in the incidence of MM and NMSC, awareness of the population with higher diagnostic confirmations and the development of expensive medical treatments. Costs associated with skin cancer treatment are expected to continue to rise, increasing its economic impact for health services [11–15].

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Notwithstanding its frequency and importance, the epidemiology and health services impact of skin cancer remains insufficiently studied. Therefore, this study aims at assessing the clinical epidemiology and economic burden of MM and NMSC – particularly concerning their hospital costs, length of stay and in-hospital mortality – by analyzing an administrative database containing a registration of all public hospital episodes occurring in mainland Portugal from 2011 to 2015.

2. Methods

We assessed the administrative database containing a registration of all episodes (comprising hospitalizations and ambulatory episodes) occurred in public hospitals in Mainland Portugal between January 1, 2011 and December 31, 2015. This database was provided by the Portuguese Healthcare System Central Administration (*Administração Central do Sistema de Saúde*). For every episode, the database contains information regarding the respective main diagnosis (clinical condition responsible for patient's admission) and accessory diagnoses; diagnoses had been coded after discharge with International Classification of Diseases, 9th Clinical Modification (ICD-9-CM) codes. In order to assess episodes with associated diagnosis of malignant neoplasm of skin, we identified all hospitalizations flagged with the ICD-9-CM codes 172.x and 173.x as main or accessory diagnosis. These codes correspond, respectively, to the diagnoses of "MM of skin" and "other malignant neoplasm of skin".

We compared MM and NMSC hospitalizations and ambulatory episodes over their annual frequencies, inpatients' age and sex distributions, hospital costs (costs were indirectly calculated for each hospitalization and ambulatory episode, using a classification system based on Diagnosis Related Groups – All Patient (AP-) DRG Version 27 –, which mostly takes into account diagnoses, performed procedures, and inpatients' demographic characteristics), length of stay, and in-hospital mortality (these latter two variables only concern hospitalizations, but not ambulatory episodes). Hospitalizations were defined as episodes with hospital stays lasting for at least 24 h, while ambulatory episodes encompass medical diagnosis and/or therapeutic procedures lasting less than 24 h [16]. Subgroup analyses were performed for those episodes classified with "skin-cancer related DRG" (as those were episodes for which skin cancer was probably the main condition) - these DRG are listed in Supplementary Table 1. Additionally, for each type of skin cancer, we determined the frequency of episodes according to the anatomic location, occurrence and location of metastases, and performed procedures. For NMSC episodes, we performed separate analyses for BCC and SCC; nevertheless, information on the subtype of NMSC was only available for the period between 2013 and 2015.

We were able to estimate the number of individual patients by identifying episodes which shared the same patient's number, sex, birthdate and residence. We subsequently estimated the frequency of patients with MM and NMSC treated in public hospitals per 100,000 inhabitants (population data was provided by the National Institute of Statistics) [17], as well as average costs *per* patient (total costs – as calculated for hospitalization and ambulatory episodes – were divided by the number of patients). Additionally, we assessed the frequency of patients with skin cancer in each anatomical location according to their sex and age.

Categorical variables were described using absolute and relative frequencies; continuous variables were described using means and standard deviations or medians and interquartile ranges. Categorical variables were compared using the chi-square test, while continuous variables were compared using the Mann-Whitney U test. We performed linear regressions to identify variables associated with increased costs of melanoma and NMSC – independent variables (namely, sex, age, type of episode, presence of metastases, and neoplasm location and subtype) were firstly tested individually with simple linear regressions. Independent variables with marginal association ($p < 0.10$) with hospital costs were subsequently introduced in multiple linear regression models. Statistical analyses were performed using IBM SPSS Statistics®, version 24 (IBM, Armonk, NY).

Table 1
Characteristics of hospitalizations and ambulatory episodes with associated diagnosis of melanoma and non-melanoma skin cancer (NMSC) (Mainland Portugal; 2011–2015).

	Melanoma (n = 15,913)	NMSC (n = 72,602)	p value
Sex – females – n (%)	7986 (50.2)	35,267 (48.6)	< 0.001
Age (years) – median (Q1–Q3)	66 (55–75)	76 (67–83)	< 0.001
Hospital costs (€) – mean (SD) [median (IQR)]	1197.7 (2937.3) [723.7 (758.7)]	1113.5 (2390.9) [1255.0 (531.3)]	< 0.001
Hospitalization episodes[a]	2417.1 (5084.2) [1089.9 (1384.3)]	2563.1 (6715.3) [1535.5 (1384.3)]	0.017
Ambulatory episodes[b]	668.4 (476.7) [496.3 (758.7)]	929.0 (634.6) [1255.0 (531.3)]	< 0.001
Length of stay (days)[a] – mean (SD) [median (Q1–Q3)]	7.3 (12.3) [4 (2–8)]	9.0 (14.6) [5 (2–10)]	< 0.001
In-hospital mortality[a] – n (%)	575 (11.9)	603 (7.3)	< 0.001
Performed procedures[c] – n (%)			
Chemotherapy injection	5115 (32.1)	1232 (1.7)	< 0.001
Radiotherapy	1707 (10.7)	11,818 (16.3)	< 0.001
Antineoplastic biological response modifiers	283 (1.8)	113 (0.2)	< 0.001
Local excision	1720 (10.8)	18,434 (25.4)	< 0.001
Radical excision	4724 (29.7)	28,686 (39.5)	< 0.001

IQR = interquartile range; Q1 = 1st quartile; Q3 = 3rd quartile; SD = standard-deviation.
[a] These data concern hospitalization episodes only (n = 4817 for melanoma; n = 8198 for non-melanoma).
[b] These data concern ambulatory episodes only (n = 11,096 for melanoma; n = 64,404 for non-melanoma).
[c] ICD-9-CM codes for performed procedures were: Chemotherapy injection: 99.25; Radiotherapy: 92.2; Antineoplastic biological response modifiers: 99.28; Local excision: 86.3; Radical excision: 86.4.

3. Results

Between 2011 and 2015, there were 15,913 episodes with associated diagnosis of MM and 72,602 of NMSC (Table 1). During that period, there were, in total, 9,048,742 hospitalizations and ambulatory episodes recorded in the database. This corresponds to a frequency of 0.2% episodes with diagnosis of MM, and of 0.8% of NMSC. Among the latter, BCC comprised 72.0% of episodes occurring between 2013 and 2015 (n = 28,691), SCC stood for 25.4% (n = 10,103), and the remaining 2.6% episodes corresponded to NMSC of non-specified subtype (n = 1036) (Table 2). Hospitalizations represented 30.3% of all MM episodes and 11.3% of all NMSC episodes. These episodes occurred in 52,046 different patients with skin cancer, of whom 6567 had a diagnosis of MM, - corresponding to an average yearly incidence estimation of 13.2 cases/100,000 inhabitants (average of 2.4 episodes *per* patient). For NMSC, we identified 45,479 patients, with an average yearly incidence estimation of 91.6 cases/100,000 inhabitants (1.6 episodes *per* patient). We observed a higher average yearly incidence for BCC (95.9 cases/100,000 inhabitants; 1.2 episodes *per* patient) than for SCC (33.8 cases/100,000 inhabitants; 1.3 episodes *per* patient).

Median age was lower for MM (66 years) than for NMSC (76 years) episodes ($p < 0.001$). Among the latter, SCC episodes had a higher median age than those with BCC (80 years *versus* 75 years; $p < 0.001$). The trunk was the most common location for MM, comprising 32.5% of episodes in which the neoplasm location was reported (Table 3). Additionally, 14.3% of MM episodes presented with metastases, the most common involved sites being the lymph nodes (56.7% of all metastatic MM), the lungs and other respiratory organs (28.0%), and the central nervous system (22.7%) (Table 3). For NMSC, the face was the most common location (67.0%) both for SCC (61.3%) and BCC (70.7%)

Table 2
Characteristics of hospitalizations and ambulatory episodes with associated diagnosis of basal cell carcinoma and squamous cell carcinoma (Mainland Portugal; 2013–2015).

	Basal cell carcinoma (n = 28,691)	Squamous cell carcinoma (n = 10,103)	p value
Sex – females – n (%)	14,162 (49.4)	4712 (46.6)	< 0.001
Age (years) – median (Q1–Q3)	75 (66–82)	80 (73–86)	< 0.001
Hospital costs (€) – mean (SD) [median (IQR)]	1255.4 (1705.0) [1255.0 (531.3)]	1340.4 (4200.6) [1254.9 (531.3)]	< 0.001
Hospitalization episodes[a]	2424.4 (5433.1) [1297.0 (1329.2)]	2981.9 (9467.3) [1535.5 (1384.3)]	< 0.001
Ambulatory episodes[b]	1146.8 (544.9) [1255.0 (531.3)]	962.4 (560.4) [1255.0 (531.3)]	< 0.001
Length of stay (days)[a] – mean (SD) [median (Q1–Q3)]	7.5 (11.6) [4 (2–8)]	10.7 (16.3) [6 (2–12)]	< 0.001
In-hospital mortality[a] – n (%)	98 (4.0)	154 (8.1)	< 0.001
Performed procedures[c] – n (%)			
Chemotherapy injection	33 (0.1)	153 (1.5)	< 0.001
Radiotherapy	622 (2.2)	1032 (10.2)	< 0.001
Antineoplastic biological response modifiers	7 (0.02)	37 (0.4)	< 0.001
Local excision	8,655 (30.2)	2643 (26.2)	< 0.001
Radical excision	14,158 (49.3)	4239 (42.0)	< 0.001

IQR = interquartile range; Q1 = 1st quartile; Q3 = 3rd quartile; SD = standard-deviation.

[a] These data concern hospitalization episodes only (n = 2439 for basal cell carcinoma; n = 1891 for squamous cell carcinoma).

[b] These data concern ambulatory episodes only (n = 26,252 for basal cell carcinoma; n = 8212 for squamous cell carcinoma).

[c] ICD-9-CM codes for performed procedures were: Chemotherapy injection: 99.25; Radiotherapy: 92.2; Antineoplastic biological response modifiers: 99.28; Local excision: 86.3; Radical excision: 86.4.

(Table 4). Metastases were present in 0.4% of BCC and 4.0% of SCC, resulting in an overall frequency of 1.9% NMSC episodes with metastases (Table 4). The lymph nodes were the most frequent metastases site for both subsets of NMSC (29.8% for metastasized BCC and 47.8% for SCC), followed by the bones (23.4% for BCC and 20.0% for SCC). Similar results were found when assessing individual patients regarding the anatomical location of skin neoplasms and the frequency of metastases (Tables 3 and 4) – in fact, for individual patients, advanced age associated with an increased proportion of patients with MM in the head and neck, and with a decreased proportion of trunk MM (Fig. 1). However, in females, we found higher proportions of MM in the lower limbs throughout all ages. For NMSC, advanced age also associated with an increased proportion of patients (both male and female) with neoplasms in the head and neck, and with a decreased proportion of patients with trunk neoplasms (Fig. 1).

Overall, 57.1% of all episodes were of surgical type – this percentage was of 46.1% among MM episodes, and of 59.5% in NMSC episodes ($p < 0.001$). Chemotherapy and therapy with antineoplastic biological response modifiers were more common among MM than NMSC episodes. Overall, tumour excision was performed in 63.4% of NMSC episodes (77.5% for BCC and 66.2% for SCC), but in only 39.6% of MM episodes ($p < 0.001$) (Table 1).

Considering only hospitalizations, MM had a median length of stay of 4 days (average of 7.3 days), while the median length of stay for NMSC was of 5 days (average of 9.0 days) ($p < 0.001$). Within the studied period, episodes with diagnosis of MM amounted a total of 35,295 days in hospital stays, while the figures for NMSC were of 73,813 days (including 18,172 days for BCC and 20,149 days for SCC from 2013 to 2015). In-hospital mortality was also higher for MM hospitalizations than for NMSC (11.9% *versus* 7.3%; $p < 0.001$). Among the latter, SCC hospitalizations had higher mortality than those of BCC (8.1% *versus* 4.0%; $p < 0.001$) (Tables 1 and 2).

NMSC episodes had higher median hospital costs than MM episodes (1255.0 *versus* 723.7 €; $p < 0.001$), but lower average costs (1113.5 *versus* 1197.7 €). However, NMSC had higher average costs than MM when considering separately hospitalizations (2563.1 *versus* 2417.1 €;

Table 3
Neoplasm and metastases locations for episodes (hospitalizations and ambulatory episodes) and individual patients with associated diagnosis of melanoma and non-melanoma skin cancer (NMSC) (Mainland Portugal; 2011–2015).

	Melanoma		NMSC		P value[a]
	Episodes (n = 15,913)	Patients (n=6567)	Episodes (n = 72,602)	Patients (n=45,479)	
Neoplasms with specified location[b]	9,749	5,845	69,277	45,309	
Face – n (%)	1470 (15.1)	976 (16.7)	46,392 (67.0)	30,656 (67.7)	< 0.001
Lip	95 (1.0)	36 (0.6)	2434 (3.5)	1873 (4.1)	< 0.001
Eyelid (including canthus)	114 (1.2)	67 (1.1)	4495 (6.5)	3118 (6.9)	< 0.001
Other locations in the face	1,265 (13.0)	876 (15.0)	39,463 (57.0)	26,015 (57.4)	< 0.001
Ear and external auditory canal – n (%)	239 (2.5)	113 (1.9)	5104 (7.4)	2670 (5.9)	< 0.001
Scalp and neck – n (%)	591 (6.1)	299 (5.1)	6825 (9.9)	4148 (9.2)	< 0.001
Trunk – n (%)	3164 (32.5)	2006 (34.3)	6295 (9.1)	4233 (9.3)	< 0.001
Upper limb – n (%)	1222 (12.5)	768 (13.1)	3502 (5.1)	2202 (4.9)	< 0.001
Lower limb – n (%)	2585 (26.5)	1559 (26.7)	3619 (5.2)	2320 (5.1)	< 0.001
Other specified sites of skin – n (%)	534 (5.5)	152 (2.6)	594 (0.9)	237 (0.5)	< 0.001
Neoplasms presenting with metastases – n (%)[c]	2271 (14.3)	1128 (17.2)	1369 (1.9)	651 (1.4)	< 0.001
Lymph nodes – n (%)	1287 (56.7)	648 (57.4)	510 (37.3)	238 (36.6)	< 0.001
Skin – n (%)	294 (12.9)	146 (12.9)	174 (12.7)	59 (9.1)	0.834
Lungs and other respiratory organs – n (%)	637 (28.0)	368 (32.6)	234 (17.1)	140 (21.5)	< 0.001
Intestine and other GI organs – n (%)	208 (9.2)	132 (11.7)	44 (3.2)	35 (5.4)	< 0.001
Liver – n (%)	386 (17.0)	216 (19.1)	109 (8.0)	74 (11.4)	< 0.001
Central nervous system – n (%)	516 (22.7)	311 (27.6)	125 (9.1)	79 (12.1)	< 0.001
Bones – n (%)	327 (14.4)	204 (18.1)	269 (19.6)	138 (21.2)	< 0.001
Urinary tract organs – n (%)	17 (0.7)	12 (1.1)	5 (0.4)	4 (0.6)	0.148
Ovaries and adrenal glands – n (%)	63 (2.8)	47 (4.2)	11 (0.8)	11 (1.7)	< 0.001
No specified site – n (%)	220 (9.7)	108 (9.6)	405 (29.6)	170 (26.1)	< 0.001

[a] P values calculated for comparisons between melanoma *versus* NMSC episodes.

[b] Percentages for each location were calculated in relation to the total number of neoplasms with specified location.

[c] Percentages for each metastatic location were calculated in relation to the total number of neoplasms presenting with metastases.

Table 4
Neoplasm and metastases locations for episodes (hospitalizations and ambulatory episodes) and individual patients with associated diagnosis of basal cell carcinoma and squamous cell carcinoma (Mainland Portugal; 2013–2015).

	Basal cell carcinoma		Squamous cell carcinoma		*P* value[a]
	Episodes (*n* = 28,691)	Patients (*n* = 23,127)	Episodes (*n* = 10,103)	Patients (*n* = 7967)	
Neoplasms with specified location[b]	28,605	23,054	10,072	7,940	< 0.001
Face – *n* (%)	20,281 (70.7)	16,354 (70.7)	6176 (61.3)	4894 (61.4)	< 0.001
Lip	712 (2.5)	610 (2.6)	846 (8.4)	760 (9.6)	< 0.001
Eyelid (including canthus)	2241 (7.8)	1868 (8.1)	296 (2.9)	216 (2.9)	< 0.001
Other locations in the face	17,655 (61.7)	14,121 (61.1)	5114 (50.8)	3986 (50.2)	< 0.001
Ear and external auditory canal – *n* (%)	1680 (5.9)	1238 (5.4)	936 (9.3)	734 (9.2)	< 0.001
Scalp and neck – *n* (%)	2909 (10.2)	2285 (9.9)	1039 (10.3)	796 (10.0)	0.677
Trunk – *n* (%)	3063 (10.7)	2456 (10.6)	447 (4.4)	302 (3.8)	< 0.001
Upper limb – *n* (%)	962 (3.4)	776 (3.4)	1053 (10.5)	885 (11.1)	< 0.001
Lower limb – *n* (%)	1076 (3.8)	848 (3.7)	803 (8.0)	698 (8.8)	< 0.001
Other specified sites of skin – *n* (%)	132 (0.5)	116 (0.5)	88 (0.9)	37 (0.5)	< 0.001
Neoplasms presenting with metastases – *n* (%)[c]	124 (0.4)	97 (0.4)	400 (4.0)	278 (3.5)	< 0.001
Lymph nodes – *n* (%)	37 (29.8)	30 (30.9)	191 (47.8)	133 (46.0)	< 0.001
Skin – *n* (%)	10 (8.1)	6 (6.2)	32 (8.0)	22 (7.6)	0.975
Lungs and other respiratory organs – *n* (%)	20 (16.1)	16 (16.5)	34 (8.5)	27 (9.7)	0.015
Intestine and other GI organs – *n* (%)	3 (2.4)	2 (2.1)	12 (3.0)	10 (3.6)	0.975
Liver – *n* (%)	14 (11.3)	12 (12.4)	12 (3.0)	8 (2.8)	< 0.001
Central nervous system – *n* (%)	19 (15.3)	14 (14.4)	28 (7.0)	21 (7.3)	0.005
Bones – *n* (%)	29 (23.4)	22 (22.7)	80 (20.0)	57 (19.7)	0.417
Urinary tract organs – *n* (%)	1 (0.8)	1 (1.0)	1 (0.3)	1 (0.3)	0.964
Ovaries and adrenal glands – *n* (%)	1 (0.8)	1 (1.0)	1 (0.3)	1 (0.3)	0.964
No specified site – *n* (%)	42 (33.9)	33 (34.0)	140 (35.0)	102 (35.3)	0.818

[a] *P* values calculated for comparisons between basal cell carcinoma *versus* squamous cell carcinoma episodes.
[b] Percentages for each location were calculated in relation to the total number of neoplasms with specified location.
[c] Percentages for each metastatic location were calculated in relation to the total number of neoplasms presenting with metastasis.

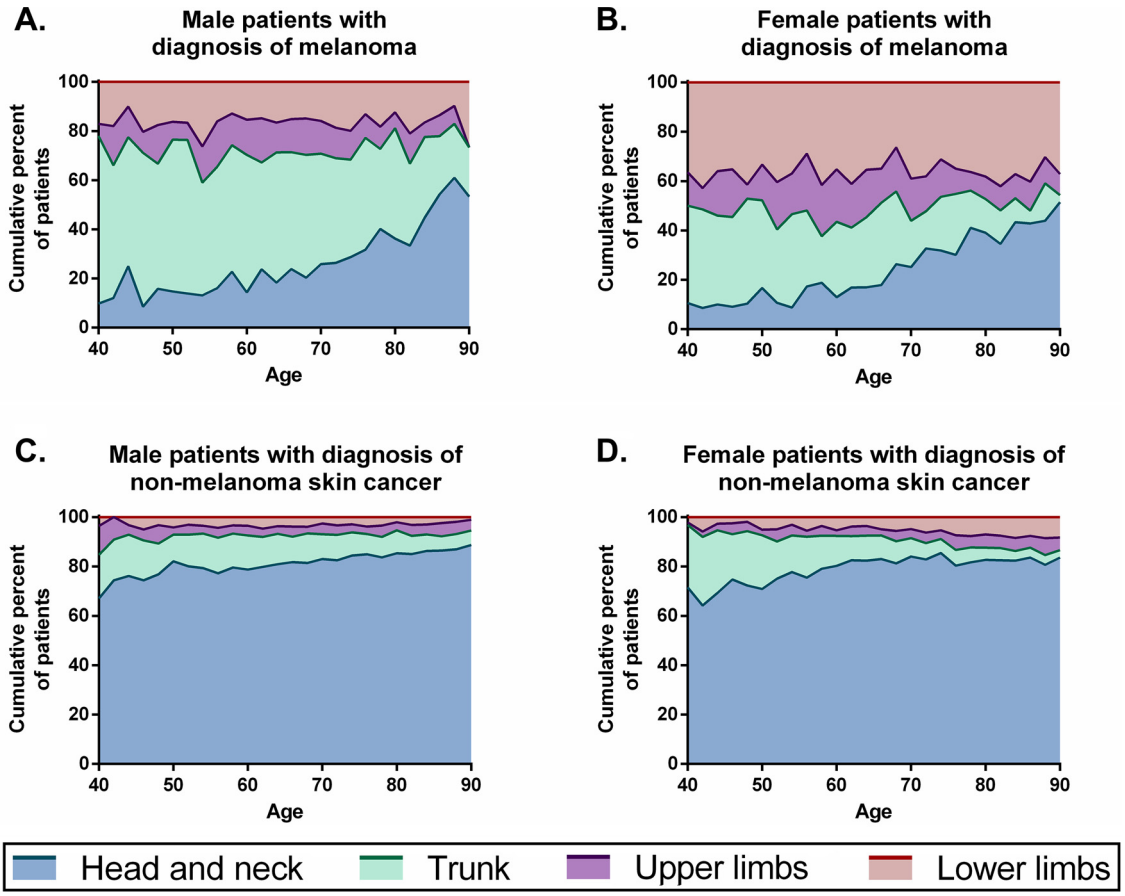

Fig. 1. Proportion of patients with skin neoplasms in each anatomical location according to their age and sex. Graphs concern male patients with diagnosis of melanoma (A), female patients with diagnosis of melanoma (B), male patients with diagnosis of non-melanoma skin cancer (C), and female patients with diagnosis of non-melanoma skin cancer (D) (Mainland Portugal; 2011–2015).

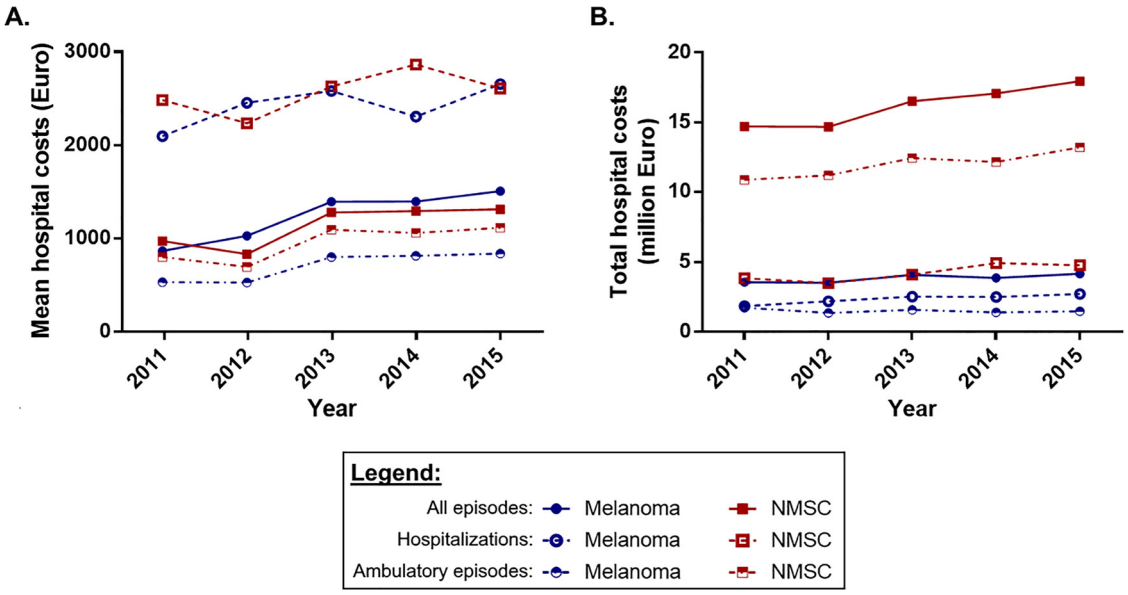

Fig. 2. Annual mean hospital costs (€) (A) and annual total hospital costs (B) among episodes with associated diagnosis of melanoma and non-melanoma skin cancer (NMSC), including all episodes, hospitalizations and ambulatory episodes (Mainland Portugal; 2011–2015).

$p = 0.017$) and ambulatory episodes (929.0 *versus* 668.4 €; $p < 0.001$) (Fig. 2A). Among NMSC, SCC episodes had higher average costs than BCC (1340.4 *versus* 1255.4 €; $p < 0.001$) (Tables 1 and 2) (regarding average costs *per* patient, MM had higher average costs than NMSC – 2902.3 € *versus* 1777.6 €; among NMSC, SCC was also associated to higher average costs *per* patient than BCC – 1699.8 € *versus* 1557.4 €). Overall, MM episodes amounted a total of 19.1 million € in hospital costs, while episodes with diagnosis of NMSC had charges of 80.8 million €; total hospital costs were of 36.0 for BCC and 13.5 million € for SCC (from 2013 to 2015). This corresponds to an average yearly total amount of 3.8 million € for MM episodes, and of 16.2 € for NMSC episodes (including 12.0 million € for BCC and 4.5 million € for SCC) (Fig. 2B).

In a multiple linear regression model, advanced age, performance of surgical procedures, and presence of metastases were found to be associated with increased MM episode costs. For NMSC, besides those same variables, head/neck and lower limb location were also associated with increased episode costs (Supplementary Table 2).

Most MM (89.4%) and NMSC (90.5%) episodes had been classified with a “skin cancer-related DRG”. An analysis restricted to those episodes provided similar results regarding the length of stay, in-hospital mortality and hospital costs (data not shown).

4. Discussion

In this study, we assessed over 15,000 MM and 72,000 NMSC episodes occurred within a period of 5-years. We found that MM episodes presented average hospital costs of 1197.7 € and a mean length of stay of 7.3 days. On the other hand, the average costs for NMSC episodes were of 1113.5 €, with a mean length of stay of 9.0 days.

The demographic and clinical characteristics of the assessed episodes are mostly consistent with the literature, particularly concerning patients’ age, neoplasm location and proportion of BCC and SCC [18,19]. However, for individual patients, the ratio NMSC:MM observed (7:1) was low, which might result from the fact that a high number of NMSC are treated in private institutions or left untreated.

As expected, in-hospital mortality was higher for MM than NMSC episodes. Although we have no information regarding the death cause, these results are consistent with the higher metastatic rate found for MM episodes. On the other hand, although BCC is considered the most common malignancy in Caucasians, metastases are extremely rare (from 0.0028% to 0.55%) [20]. It should be noted, however, that the proportion of metastatic episodes might have been overestimated (particularly concerning NMSC), as our study only comprises episodes occurred at public hospitals, where the most severe cases of skin cancer are treated; in addition, some locally infiltrative basal cell carcinomas might have been wrongly classified as metastatic episodes. Interestingly, we found that, both for MM and NMSC, ageing associated with increased frequency of neoplasms in chronically exposed areas such the head and neck, but decreased proportions of trunk neoplasms.

Although we provide an estimation of skin cancer hospital costs in Portugal, the reported values are probably underestimated, as this study has important limitations. In fact, this study does not take into account hospital costs of episodes occurring in private healthcare institutions; while most hospitalizations and ambulatory episodes occur in public hospitals, the role of private providers is expanding, particularly in the treatment of less severe conditions. The Public Portuguese Health System is overcrowded and the waiting list for diagnosis and treatment is usually long (6 months to 1 year or even more), as in other countries [21]. Although it has not been yet quantified, it is common that patients without financial difficulties and/or with health insurance recur to private institutions for diagnosis and treatment, and are referred to public hospitals only in particular cases, mainly if additional treatment is needed. The majority of NMSC are not high-risk tumors and may be treated effectively at outpatient surgery center settings. Furthermore, in general, treatment of a malignant skin lesion is less expensive when done in an office or ambulatory surgical center than at a hospital [22,23].

We were not able either to assess costs other than hospital charges – this is particularly important for MM, which associates with substantial productivity losses [24,25]. Additionally, as with most skin cancer economic studies [26], the costs of precursor lesions (particularly, actinic keratosis, the precursor of SCC) are not being considered– assessing these lesions would be important to understand the possible impact of early detection and treatment. Notwithstanding, the costs reported are consistent with those in an administrative database study performed in Germany – we estimated average yearly hospital costs of 0.4 million € per million inhabitants for MM and 1.6 million € for NMSC; this compares with 0.6 million € for MM and 1.6 million € for NMSC in Germany [27]. Therefore, despite its lower lethality, the economic impact of NMSC should not be underplayed - NMSC is one of the five most costly cancers to Medicare [28], accounting, according to our

analysis, for 81% of all skin cancer costs (this is consistent with previous studies, which found NMSC cost to be up to 80% of all skin cancer costs) [23,29].

As with hospital costs, the incidence of skin cancer is also probably underestimated, as patients seeking care in private hospitals were not assessed. Nevertheless, our annual estimates surpass the projections for 2015 and 2020 by the Portuguese National Cancer Registry [30]. In fact, cancer registries often underestimate the burden of skin cancer, as NMSC if often not reported, and registries do not consider multiple (synchronous or non-synchronous) primary tumors of the same histological group [27,31,32]. It should be noted, however, that, as data had been previously anonymized, individual patients in our studies were identified according to an algorithm based on patients' hospital number, sex, birthdate and residence. Additional limitations of our study include lack of information regarding the severity of episodes, as well as the histological classification of NMSC prior to 2013. Finally, the ICD-9-CM codes used to identify MM and NMSC codes have not been validated in Portugal – nevertheless, an Italian study assessed the validity of the ICD-9-CM code 172.x (used to identify melanoma), finding a sensitvity close to 100% and positive predictive values ranging from 77% to 88% [33]; on the other hand, an American study found the ICD-9-CM code 173.x (used to assess NMSC) in administrative databases to have a positive predictive value of 60% (*kappa* statistic = 0.61) [34].

Our study, however, has also several strong points. In particular, it has a nationwide scope, assessing all Portuguese public hospital episodes occurring within a 5-year period. The analysis of administrative databases allows such assessments to be performed in a time- and resource-efficient way; with the advantage that coding in Portugal is performed by specialized doctors and is frequently audited. In addition, we report not only information concerning the clinical and economic burden of these episodes, but also the frequency of neoplasm locations and metastases, as well as of the performed therapeutic procedures.

As in other regions, the economic burden of skin cancer in Portugal will probably continue to increase with the aging of the population [35–37]. Additionally, treatment of skin cancer is changing, especially for advanced stages, with the introduction of new – but expensive - antineoplastic biological response modifiers [38]. Early detection and treatment of MM and NMSC can reduce morbidity and, particularly in the case of MM, mortality [39,40]. Investment in skin cancer primary prevention strategies, along with early detection might bring a better health for the population [41], lower the costs burden for society, and redirect resources for non-preventable conditions. [15,42–48]. These preventative strategies should both focus on primary prevention – involving multidisciplinary efforts [49,50] – and secondary prevention [51,52]. In fact, skin cancer prevention campaigns are now considered highly cost-effective [15,53]; a Belgian study estimates that for every Euro invested in primary prevention, 3.6 € will be saved for the healthcare payer on the next 2 decades, while an Australian study estimates a saving of 2.2 Dollars per Dollar invested [53,54]. While most campaigns focus on melanoma [45], it is crucial not to underplay the importance of NMSC, as it is a common condition with a high economic burden.

In conclusion, our results demonstrate that substantial healthcare resources are consumed in public hospitals for skin cancer management, and that the cost of NMSC is about 4 times higher than MM. This study may raise the importance of skin cancer on public health and allow for more careful understanding and assertive political decisions on redirecting funds for skin cancer prevention.

Authorship contribution

Ana Filipa Duarte – conception and design, interpretation of data, drafting the article, final approval of the version to be published.

Bernardo Sousa-Pinto – acquisition of data, or analysis and interpretation of data, drafting the article, final approval of the version to be published.

Alberto Freitas – acquisition of data, or analysis and interpretation of data, final approval of the version to be published.

Luis Delgado – revising the article critically for important intellectual content, final approval of the version to be published.

Altamiro Costa-Pereira – conception and design, revising the article critically for important intellectual content, final approval of the version to be published.

Osvaldo Correia – conception, revising the article critically for important intellectual content and design, final approval of the version to be published.

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Conflict of interest statement

The authors of the manuscript "**Skin cancer healthcare impact: a nation-wide assessment of an administrative database"** have no conflict of interest to disclose.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2018.08.004.

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