original reports abstract

Incidence Trends of Melanoma and Nonmelanoma Skin Cancers in Jordan From 2000 to 2016

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PURPOSE Skin cancers are among the commonest cancers worldwide, and the incidence of melanoma and nonmelanoma skin cancer (NMSC) continues to rise worldwide. However, there are no comprehensive reports on skin cancer incidence in Jordan during the past two decades. This report investigates the incidence of skin cancers in Jordan, in particular their time trends for the period 2000-2016.

MATERIALS AND METHODS Data on malignant melanomas (MMs), squamous cells carcinomas (SCCs), and basal cell carcinomas (BCCs) were extracted from the Jordan Cancer Registry for the period between 2000 and 2016. Age-specific and overall age-standardized incidence rates (ASIRs) were computed.

RESULTS Two thousand seventy patients were diagnosed with at least one BCC, 1,364 with SCC, and 258 with MM. ASIRs were 28, 19, and 4 per 100,000 person-years for BCC, SCC, and MM, respectively. The BCC:SCC incidence ratio was 1.47:1. The risk of men developing SCCs was significantly higher than women (relative risks [RRs], 1.311; 95% CI, 1.197 to 1.436), but significantly lower for BCCs (RR, 0.929; 95% CI, 0.877 to 0.984) or melanomas (RR, 0.465; 95% CI, 0.366 to 0.591). Persons older than 60 years were at a significantly higher risk of developing SCCs (RR, 1.225; 95% CI, 1.119 to 1.340) or melanomas (RR, 2.445; 95% CI, 1.925 to 3.104), but at a significantly lower risk of developing BCCs (RR, 0.885; 95% CI, 0.832 to 0.941). The overall incidence rates of SCCs, BCCs, and melanomas increased over the 16-year study period, but this was not statistically significant.

CONCLUSION To our knowledge, this is the largest epidemiologic study regarding skin cancers in Jordan and in the Arab world. Despite low incidence rates in this study, rates are higher than reported regional figures. This is likely due to standardized, centralized, and mandatory reporting of skin cancers, including NMSC.

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INTRODUCTION

Skin cancers are among the commonest cancers worldwide.[1,2] The numbers of new cases of both malignant melanoma (MM) and nonmelanoma skin cancers (NMSCs) are rising rapidly, largely owing to aging and growing populations.[1] The prevalence rates of melanoma and NMSC increased between 1990 and 2017 by 310% for squamous cells carcinomas (SCCs), 161% for melanomas, and 77% for basal cell carcinomas (BCCs), and it is projected that this increase in cancer rates will continue into the coming decade.[3-5]

In 2012, skin cancers were the fifth most common cancers in Jordan.[6] However, there are no reports on the incidence of skin cancers in Jordan generally during the past two decades, particularly with respect to their time trends. Only one study reported on MMs in Jordan during the period from 1969 to 1983, before the establishment of the Jordan Cancer Registry (JCR) in 1996.[7] Since then, there have only been two reports on skin cancers in Jordan, both limited to Northern Jordan.[8,9] There is, therefore, a need to investigate the incidence and time trends of the major skin cancers in the entire country over a prolonged period to determine how this incidence compares with worldwide incidence generally and with countries with similar climate and socioeconomic development specifically.

MATERIALS AND METHODS

The JCR was established in 1996, and cancer notification to this registry is compulsory since 1996 through a ministerial decree from all notification sites in Jordan whether public, private, or military. Identification of cancer cases is established using the International Classification of Diseases for Oncology, third edition (ICD-O-3), as well as the morbidity and mortality coding system database from all referral sites. New cancer cases are identified through the hospital

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CONTEXT

Key Objective

Is skin cancer incidence changing in Jordan and reflective of worldwide and regional incidence trends?

Knowledge Generated

The overall incidence rates of basal cell carcinomas, squamous cells carcinomas, and melanomas have not increased significantly over the study period between 2000 and 2016. However, novel data relating to female:male ratios and incidence of various skin cancers per age are outlined.

Relevance

This study adds to the comparative picture of skin cancer incidence worldwide and comes at a time when reporting of skin cancer is affected significantly by turmoil and conflicts in the Middle East.

admissions and medical records departments, as well as hospital discharge reports and hospital-based registries. In addition, new cancer cases are identified through histopathology, cytology and hematology laboratories, both public and private, as well as forensic medicine records and death certificates. The primary site (topography) and histology (morphology) of the malignancies are identified and coded according to ICD-O-3, published by the WHO, 2000.[6]

For the period from January 1, 2000, to December 31, 2016, all new skin cancer cases were retrieved from the JCR using the skin topography codes (440-449) as well as the morphology codes for SCC (8051, 8070-8078, 8081, 8084, 8094), BCC (8090-8093, 9087, 8098), and MM (8720-8780). Further details regarding the sex and age of patients, as well as the date of diagnosis were also extracted from the JCR database.

Study covariates included the type of skin cancer (SCC, BCC, or MM), year of diagnosis, sex of patient, and age group (six categories). Crude incidence rate (CIR) and standardized incidence rate (SIR) were computed using epidemiologic equations per 100,000 persons. The age-specific rates were based on the WHO's age standardization rates.[10] All descriptive statistics, graphic distributions, and relative risks (RRs) were conducted using IBM's SPSS, version 22 (IBM, Armonk, NY). Statistical significance was considered when a 95% CI does not cross 1.00.

RESULTS

During the 16-year study period, 2,070 patients were diagnosed with at least one BCC, 1,364 with SCC, and 258 with MM. ASIRs were 28, 19, and 4 per 100,000 person-years for BCC, SCC, and melanoma, respectively (shown in Table 1; Fig 1). The BCC:SCC incidence ratio was 1.47:1. Men were shown to be at a significantly higher risk of developing SCCs than women (RR, 1.311; 95% CI, 1.197 to 1.436), but at a significantly lower risk of developing BCCs (RR, 0.929; 95% CI, 0.877 to 0.984) or melanomas (RR, 0.465; 95% CI, 0.366 to 0.591; shown in Table 2; Fig 2). Persons older than 60 years are at a significantly higher risk of developing SCCs (RR, 1.225; 95% CI, 1.119 to 1.340) or melanomas (RR, 2.445; 95% CI, 1.925 to 3.104) than those age 60 years or younger, but at a significantly lower risk of developing BCCs (RR, 0.885; 95% CI, 0.832 to 0.941; shown in Table 2; Fig 3). Moreover, although the overall incidence rates of SCCs, BCCs, and melanomas have increased over the 16-year study period, this was not statistically significant (shown in Fig 1). No significant difference was found between the various regions in Jordan (North, Middle, and South) in the prevalence of each cancer subtype (data available on request).

DISCUSSION

The incidence of melanoma and NMSC is rising rapidly worldwide and now constitutes the largest proportion of cancers globally.[1,2,11] It is estimated that the incidence of NMSC has increased by 33% worldwide from 2007 to 2017, with odds of developing NMSC of 1 in 10 for women and 1 in 7 for men.[1] In White populations in Europe, the United States, Canada, and Australia, the average increase of NMSC was 3%-8% per year since the 1960s.[12,13] This increase is largely due to aging and growing populations.[1] It has also been proposed that the degree of scrutiny can influence cancer detection rates leading perhaps to an over-representation of cancer incidence. This could potentially apply to cases with indolent disease, such as early and thin melanomas, particularly where there are purported risk factors with subsequent lower threshold to cancer screening and cancer diagnosis.[14,15] Detection bias as an example of scrutiny-dependent bias was reflected in one large study where the likelihood of skin cancer detection, in particular BCC and SCC, was increased in those undergoing routine health screening practice, regardless of risk factors.[16]

The lifetime risk of developing BCCs in the US White population was estimated to be 28%-33% (with an ASIR of 407-485 and 212-253 per 100,000 person-years in men and women, respectively) and 7%-11% for SCC (ASIRs of 81-136 and 26-59 per 100,000 person-years in men and women, respectively).[17] European data estimates an ASIR of SCC of 9-96 per 100,000 in males and 5-68 per 100,000 in females.[18] However, incidence rates of NMSC in Australia

TABLE 1. Standardized Incidence Rates of SCC, BCC, and Melanoma per 100,000 Persons by Sex, Age Group, and Year of Diagnosis in Jordan, 2000-2016 (N = 3,692)

Skin Cancer Categorization	SCC		BCC		Melanoma	
	Cases	Incidence[a]	Cases	Incidence[a]	Cases	Incidence[a]
Overall	1,364	19	2,070	28	258	4
By sex						
Male	909	25	1,213	33	107	3
Female	455	12	857	23	151	4
By age, years						
<40	145	3	139	3	76	2
40-49	155	17	245	26	36	4
50-59	235	32	420	58	49	7
60-69	341	70	640	130	56	11
70-79	328	120	469	171	26	10
≥80	160	144	157	142	15	14
By year						
2000	67	22	111	37	15	5
2001	56	19	93	31	16	5
2002	78	26	71	22	16	5
2003	78	24	97	31	12	3
2004	60	19	89	27	31	10
2005	53	15	77	22	14	3
2006	66	19	117	34	17	5
2007	64	17	125	34	17	5
2008	68	17	144	37	18	5
2009	90	22	148	36	9	2
2010	64	15	133	31	17	3
2011	72	15	128	29	5	2
2012	63	14	133	27	11	2
2013	118	24	147	29	7	2
2014	121	24	154	29	15	3
2015	113	20	137	26	15	3
2016	133	24	166	29	23	3

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cells carcinoma.
[a]Age-standardized incidence rates per 100,000 person-years.

were significantly higher with an estimated incidence of 1%-2% per year (1,000-2,000 per 100,000 person-years).[11,19,20] The incidence of SCC was estimated at 499 per 100,000 in men and 291 per 100,000 in women.[21] Despite these rising incidence rates, it is likely that these numbers are underestimated as some cases of NMSC are treated through destructive methods without histopathologic confirmation. Furthermore, information on NMSCs is not included in many cancer registries in the world, and information on incidence requires population-based epidemiologic surveys.

Reports in the past three decades have also suggested a shift in the BCC to SCC incidence ratio. In Australia, there has been a consecutive reduction in BCC to SCC ratio from 4 to 1 in 1985 to 2.5 to 1 in 1995.[21] A more recent study from the United States also reported a BCC to SCC ratio of 1, suggesting an alteration in BCC and SCC trends.[4] Furthermore, this is supported by epidemiologic studies that identified a higher incidence of BCCs over SCCs in younger populations, with a disproportionate increase in SCC in older populations.[22,23] Similarly, our data identified a BCC:SCC ratio of nearly 1.5:1; however, this could also reflect an underestimation of BCCs that could be treated in an office-based setting through noninvasive treatment methods or without histopathologic analysis. This could be of more relevance in the older age groups in our study, where the BCC:SCC ratio reaches 1:1 in the over 80s group.

Melanoma is the 20th most common cancer worldwide, with an estimated 287,723 new cases in 2018, and a 5-year prevalence of 965,623 cases.[24] The highest ASIRs are found in Oceania (28.3 per 100,000 person-years) and the lowest in Asia and Africa (0.48 and 0.51 per 100,000 respectively).[24] More recent studies have identified that the ASIR of melanoma in the North Africa and the Middle East region (including Arab countries such as Jordan, as well as Iran, Afghanistan, and Turkey) was among the lowest in the world at 1.66 (95% CI, 1.44 to 2.22) compared with the highest incidence rates in Australasia of 54.11 (95% CI, 4.07 to 7.78).[25]

Of interest is that the incidence of melanoma is also increasing globally at a higher pace than other cancers and it is estimated that 1 in 34 men and 1 in 53 women will develop cutaneous melanoma at some point in their lifetime.[26,27] The incidence of cutaneous melanomas has increased by more than 3% annually in the US White population, as well as the populations of the United Kingdom, Sweden, and Norway between 1982 and 2011.[3] This is despite possible underreporting largely because of decentralization of melanoma diagnosis, nonmandatory reporting of skin cancers in some countries, as well as outpatient treatment not requiring hospital admission.[28,29] The increase in melanoma incidence is a reflection of an increase in age-specific melanomas, particularly in those older than 80 years. Increased incidence could also be a reflection of increased incidence of thinner melanomas driven by skin cancer awareness and improved surveillance and subsequent earlier diagnosis.[30] By contrast, the incidence of melanoma is stabilizing in New Zealand and has been declining in Australia by approximately 0.7% annually since 2005. The reduction in incidence is mainly observed in younger age groups.[3,24,30]

Despite increases in the incidence of skin cancers generally, there are significant variations in incidence among countries. This is attributed to several factors including genetic, personal, and environmental factors such as skin phenotype, latitude, and sun exposure.[26,30,31] Studies have shown that skin type and geographical location clearly influence the estimated risk of developing cutaneous melanoma before the age 75 years.[30] This risk was shown to be lower in Mediterranean countries compared with Australia, New Zealand, United States, Europe, and Nordic countries.[30] This finding is similar to global

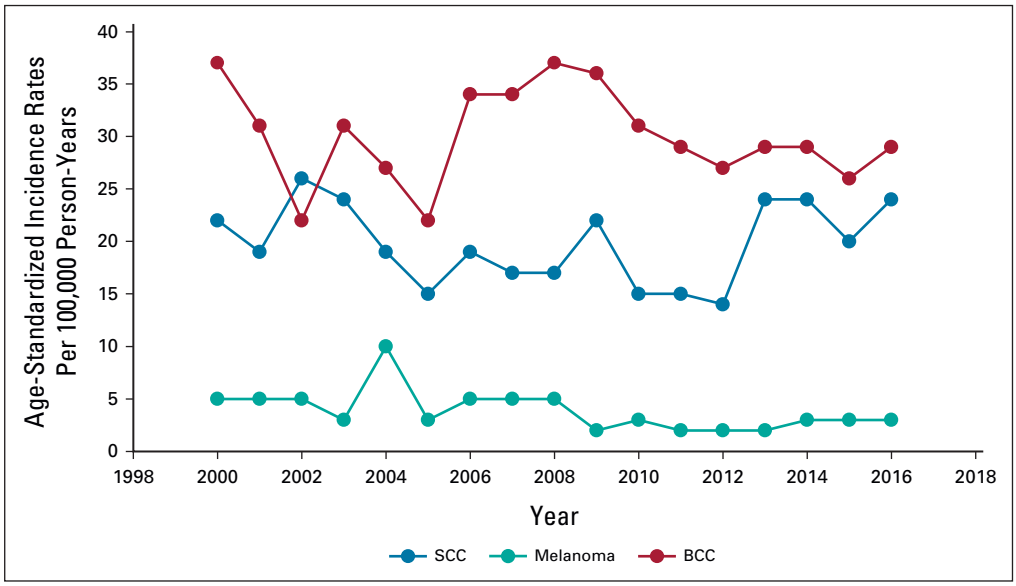

FIG 1. Skin cancer case trends by year of diagnosis of SCC, BCC, and melanoma in Jordan (2000-2016). BCC, basal cell carcinoma; SCC, squamous cells carcinoma.

comparative studies that showed ASIRs of melanoma in Middle Eastern countries to be 0-0.64 and 0-1.8 per 100,000 in women and men, respectively. However, the incidence of NMSC was 0-3.7 and 0-4.6 per 100,000 in women and men, respectively.[32]

A recent global skin cancer trend analysis study has estimated a stable trend in North Africa and the Middle East with an incidence of BCCs of 6.83 (5.50-8.26) in 2019 compared with 7.43 (6.23-8.67) in 1990. SCC incidence was 1.15 (1.01-1.30) in 2019 compared with 1.03 (0.91-1.16) in 1990, whereas melanoma incidence was 0.83 (0.55-1.00) in 2019 compared with 0.57 (0.34-0.80) in 1990. The same study showed higher skin cancer burden in men and in older adults from age 55 years onward.[2]

Interestingly, longitudinal analysis of the Global Burden of Disease Study database 1990-2017 has ranked Jordan in one of the top 10 countries with the largest decrease in the age-standardized prevalence rates of keratinocyte carcinoma per 100,000 population from 1990 to 2017.[5]

Migrant studies have also provided further insight into the effect of environmental factors on cancer risk and subsequent variation of cancer incidence among immigrants or hosting countries. For example, the incidence of melanoma in the Middle Eastern population of California was significantly higher than the rates for the Middle East. The incidence of MM in men of Middle Eastern origin was 3.52 per 100,000 compared with 1 per 100,000 in the Middle East (RR, 3.52) and 4.25 per 100,000 in women compared with 0.9 per 100,000 in the Middle East (RR, 4.73).[33] Furthermore, one study has suggested that reported reduction in the incidence of cutaneous melanoma in young Australians is possibly related to the increase in low-risk young individuals born or have parents born in countries of low risk of melanoma including the Middle East.[34] However, the risk of developing

TABLE 2. RR of SCC, BCC, and Melanoma by Sex and Age in Jordan, 2000-2016 (N = 3,692)

	SCC				BCC				Melanoma			
			95% CI				95% CI				95% CI	
Characteristic	Risk (%)	RR	Lower Limit	Upper Limit	Risk (%)	RR	Lower Limit	Upper Limit	Risk (%)	RR	Lower Limit	Upper Limit
Sex												
Male	40.8	1.311[a]	1.197	1.436	54.4	0.929[a]	0.877	0.984	4.8	0.465[a]	0.366	0.591
Female	31.1				58.6				10.3			
Age, years												
Below 60	36.1	1.225[a]	1.119	1.340	51.6	0.885[a]	0.832	0.941	11.1	2.445[a]	1.925	3.104
60 or older	29.5				58.4				4.6			

Abbreviations: BCC, basal cell carcinoma; RR, relative risk; SCC, squamous cells carcinoma.
[a]Statistically significant, 95% CI, does not cross 1.00.

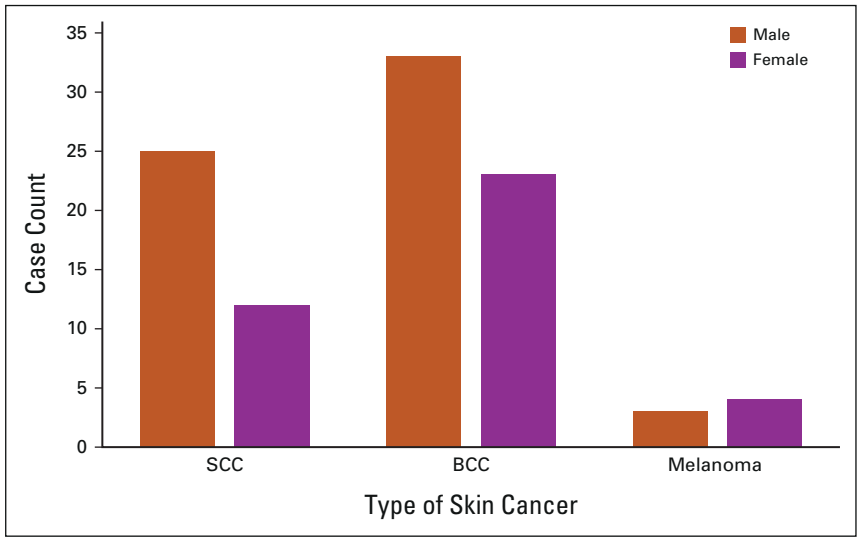

FIG 2. Skin cancer case count by sex in Jordan (2000-2016). BCC, basal cell carcinoma; SCC, squamous cells carcinoma.

MM in Australia was increased in subsequent Middle Eastern migrants compared with the first generation.[31]

Looking at skin cancer incidence rates in regional countries of similar latitude and/or socioeconomic status to Jordan, we find that skin cancers rank high among the total cancer incidence. In Turkey, skin cancers are the third most common cancers generally and second in women after breast cancer with an ASIR of 20.00/100,000 in men and 17.80/100,000 in women.[35] Melanoma incidence was 1.4 per 100,000 in men.[36]

In Iran, studies have shown that skin cancer is the most common type of cancer, estimated at 5.2% to 32.7% of the total cancers.[37,38] ASIRs of melanoma were 0.60 (95% CI, 0.56 to 0.64) and 0.46 (95% CI, 0.42 to 0.49) for males and females, respectively.[39] Another study from Iran showed incidence rates for BCC between 10.05 and 15.57 per 100,000.[40] In neighboring Iraq, skin cancer incidence rates were 2.03 per 100,000 men and 1.37 per 100,000 women.[41]

In Saudi Arabia, a recent study has indicated incidence rates of NMSC between 3.4 and 4.4 per 100,000.[42]

Jordan is located in the Eastern Mediterranean region with a latitude of 31°31′N and longitude of 37°38′E. Climate is characterized by 9-10 sunny months per year.[8,9,43] Jordan has high population growth rate with an expansive population pyramid where the proportion of adolescents and young adults between the ages 15-39 years, for example, account for 34.4% of the population.[44]

With regards to skin cancer incidence in Jordan, previous reports centered mainly on incidences in Northern Jordan and most collected data were via local pathology laboratory registries. In a report by Rawashdeh et al, the incidence of BCCs was 6.3:100,000 in 1992 and 8.8:100,000 in 2000 with a median age of 61.9 years. However, the incidence rates fluctuated between 1992 and 2000, and no specific trend was highlighted.[43] Another report by Omari et al looked at skin cancer trends in Northern Jordan between 1997 and

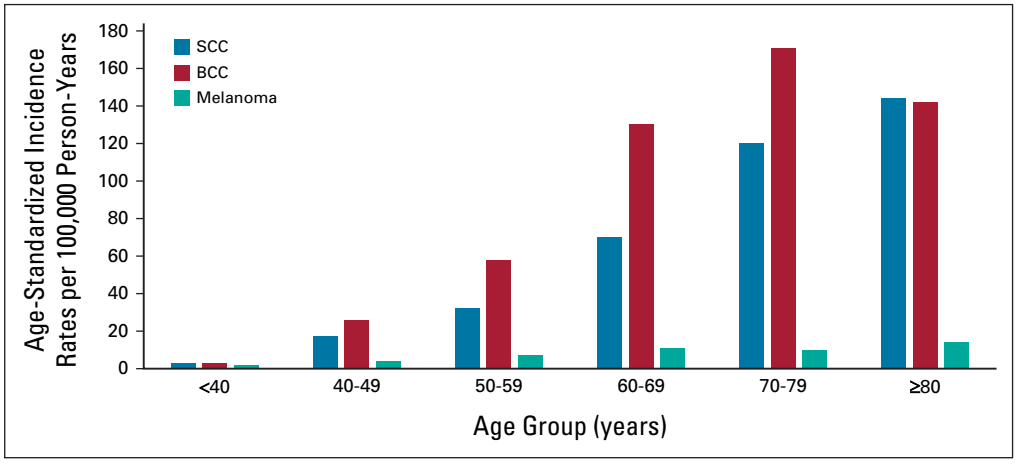

FIG 3. Skin cancer case trends by age at diagnosis of SCC, BCC, and melanoma in Jordan (2000-2016). BCC, basal cell carcinoma; SCC, squamous cells carcinoma.

2001 and found stable trends in cancer incidence with BCC yearly adjusted incidence rates of 19.7 and 23.34 per 100,000 for males and females, respectively. The ASIR of SCCs was 14.24 for males and 4.18 for females. Thirty-one cases of MM were identified during that study period (14 and 17 females), comprising 11.39% of all skin cancers (with female to male ratio of 1.2:1).[8] Furthermore, Al-Qarqaz et al explored the clinical and demographic features of BCC in Northern Jordan and identified stable incidence rates ranging from 1.5 to 3 per 100,000 population for the years 2004 to 2017. For the age group above 65 years, the incidence rates were higher (9-31 per 100,000 population).[9] The low incidence of skin cancers found in the aforementioned studies was attributed to a darker skin phenotype (generally that of Fitzpatrick skin type IV), chronic rather than intermitted sun exposure, as well as a socially and religiously driven modest attire.[8,9,43] Also, there is lack of public skin cancer awareness campaigns. Furthermore, the elderly might be less likely to seek medical attention for skin cancers and if evaluated, lesions might be treated with ablative measures without histopathologic assessment.[8,43]

The reported incidence rates in this paper, however, are higher than those found in previous limited Jordanian reports and some regional studies. This could be a reflection of improved and standardized data collection through the national JCR. In addition, the previous Jordanian reports were limited to Northern Jordan and mostly relied on pathology laboratory registries, before the foundation of JCR, which could explain the lower incidence rates in comparison. Furthermore, in comparison with many regional cancer registries, the JCR provides comprehensive data on skin cancer incidence on a national level in public, private, and military sectors, including reporting of NMSCs, which are often excluded from many cancer registries worldwide. Furthermore, the JCR collects data on non-nationals, including health tourists from neighboring countries and displaced populations, and it is of interest that the incidence rates outlined in this paper refers to Jordanian nationals only. Nevertheless, the increase in cancer incidence in this report is in keeping with projected increased cancer burden in low-middle–income countries of up to 60%, particularly in the Arab world because of aging, exposure to carcinogens, and improved cancer diagnosis.[45] Furthermore, regional conflicts have had repercussions as the increasing refugee influx since 2012 has caused a sharp increase in cancer registration in the JCR that includes non-Jordanian nationals. 2012 saw doubling of cancer registration of non-Jordanians.[46]

In conclusion, to our knowledge, this is the largest epidemiologic study regarding skin cancers in Jordan and in the Arab world. Despite low incidence rates of skin cancers in this study, these are substantially higher than reported regional figures. This is likely due to standardized, centralized, and mandatory reporting of skin cancers, including NMSC. In addition, a large refugee influx has led to demographic changes and increase in the reported cases of skin cancer cases. Further analysis is needed to investigate the staging and prognosis of diagnosed cases. This is needed to address possible issues such as delayed diagnosis and barriers related to lack of skin cancer and sun protection awareness, as well as misconceptions about development of skin cancer in Middle Eastern populations.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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