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ORIGINAL ARTICLE

Skin Cancer Incidence and Mortality in Spain: A Systematic Review and Meta-Analysis☆

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KEYWORDS
Basal cell carcinoma;
Squamous cell carcinoma;
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Epidemiology;
Mortality;
Incidence;
Review;
Meta-analysis

Abstract
Introduction and objectives: The aim of this systematic review was to describe the incidence and mortality of basal cell carcinoma, squamous cell carcinoma, melanoma, and Merkel cell carcinoma in Spain.
Material and methods: We performed a search of the MEDLINE and Embase databases and reviewed articles from the Spanish Network of Cancer Registries (REDECAN) and the International Agency for Research on Cancer (IARC). The methodological quality of the studies was evaluated and statistical heterogeneity was measured using the I^2 index. A random-effects model was used to perform the meta-analysis because of the heterogeneity of the data.
Results: Thirty-two papers were included in the systematic review. The crude incidence rate for basal cell carcinoma was 113.05 (95% CI, 89.03-137.08) cases per 100 000 person-years for the studies based on the registration methodology normally used by registries (in which only 1 tumor with histological confirmation is counted per person). However, the same incidence rate calculated on the basis of clinical and histologic criteria and counting tumors rather than individual patients was 253.23 (95% CI, 273.01-269.45) cases per 100 000 person-years. The incidence was 38.16 (95% CI, 31.72-39.97) cases per 100 000 person-years for squamous cell carcinoma, 8.76 (95% CI, 7.50-10.02) cases per 100 000 person-years for melanoma, and 0.28 (95% CI, 0.15-0.40) cases per 100 000 person-years for Merkel cell carcinoma.

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Conclusions: The registration methodology normally used by cancer registries probably underestimates the incidence rates of basal cell and squamous cell carcinoma in Spain. The incidence rates of cutaneous melanoma and Merkel cell carcinoma are lower in Spain than in other European countries.

PALABRAS CLAVE
Carcinoma de células basales;
Carcinoma de células escamosas;
Carcinoma de células de Merkel;
Epidemiología;
Mortalidad;
Incidencia;
Revisión;
Metaanálisis

Incidencia y mortalidad del cáncer cutáneo en España: revisión sistemática y metaanálisis

Resumen

Introducción y objetivos: El objetivo de la revisión sistemática es describir la incidencia y mortalidad en España del carcinoma basocelular, carcinoma espinocelular, melanoma y carcinoma de células de Merkel.

Material y métodos: Se realizó una búsqueda en Medline, Embase y revisión de artículos de la Red Española de Registros de Cáncer (REDECAN) y la Agencia Internacional de Investigación sobre el Cáncer (IARC). Se evaluó la calidad metodológica de los estudios. La heterogeneidad estadística se midió usando el estadístico I^2. Para el metaanálisis de los datos se empleó un modelo de efectos aleatorios debido a la heterogeneidad de los resultados.

Resultados: Se incluyeron un total de 32 trabajos en la revisión sistemática. La tasa de incidencia del carcinoma basocelular global cruda fue 113,05 (IC 95%: 89,03-137,08)/100.000 personas-año para los estudios que emplean la metodología de los registros de cáncer (contando un solo tumor por persona y diagnóstico histológico). La tasa de incidencia mediante criterios clínicos e histológicos, y contando tumores en lugar de personas, fue de 253,23 (IC 95%: 273,01-269,45)/100.000 personas-año. La incidencia de carcinoma espinocelular fue de 38,16 (IC 95%: 31,72-39,97)/100.000 personas-año, de 8,76 (IC 95%: 7,50-10,02)/100.000 personas-año para el melanoma y 0,28 (IC 95%: 0,15-0,40)/100.000 personas-año para el carcinoma de células de Merkel.

Conclusiones: La tasa de incidencia del carcinoma basocelular y espinocelular en España está probablemente infraestimada al utilizar el método habitual de los registros. La tasa de incidencia del melanoma cutáneo es baja en comparación con otros países europeos, al igual que la tasa de incidencia del carcinoma de células de Merkel.

Introduction

Skin cancers are divided into 2 categories according to epidemiological and prognostic differences: cutaneous melanoma, and nonmelanoma skin cancer (NMSC). The 2 main types of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

The incidence of cutaneous melanoma continues to rise in Europe, with considerable geographical differences in mortality.[1,2] Owing to the higher incidence of NMSC compared to other skin tumors and the difficulty of quantifying the condition,[3] NMSC tumors are not consistently reported in cancer registries.

Both cutaneous melanoma and NMSC represent a significant economic burden to the Spanish National Health Service. Thus, it is essential to know the true burden of disease attributable to skin cancer in Spain.

The main objective of this systematic review is to describe the incidence and mortality of skin cancer in Spain, including cutaneous melanoma, BCC, SCC, and Merkel cell carcinoma.

Material and Methods

Criteria for Article Inclusion

Types of Studies

We reviewed all the epidemiological studies in the literature that assessed the incidence rate of skin cancer in Spain. To investigate the incidence of melanoma, we reviewed articles that included other forms of cancer, and particularly articles derived from data from population-based cancer registries in Spain.[4] For the other types of skin tumors, given the methodological difficulties involved in any assessment of the epidemiology of NMSC, we only reviewed articles that had as their main objective to describe the incidence of any form of NMSC.

Only articles referring to a Spanish population and reporting incidence rates and the corresponding CI (or providing sufficient data to calculate the CI) were finally included. We excluded studies of skin tumors in at risk populations (syndromes, immunocompromized patients, and other special populations, etc.), data on in situ tumors, and data from

modeling studies. In the case of different studies dealing with the same population and cancer type, we included only the most recent data.

Search Strategy

Details of the search strategy used are included in the supplementary material (Appendix 1).

The search was not restricted by language or date range.

Electronic Search

On 28 April 2015, we searched the Medline database (via PubMed) and the EMBASE database (via Ovid, 1980-2015).

Other Data Sources

We searched for data published by the Spanish population-based cancer registries and the International Agency for Research on Cancer-World Health Organization in addition to unpublished studies. We also reviewed the primary sources of articles involving secondary analysis of data and sought expert opinion.

Data Collection and Analysis

The articles were divided into 4 groups and screened on the basis of the abstract by 8 reviewers (2 reviewers for each group of articles). If there was a discrepancy between the 2 initial reviewers, the article was reviewed by a third person. Duplicate articles were also excluded. The complete text of the selected articles was then reviewed using the Covidence tool (https://www/covidence.org/).

The PRISMA flow diagram (Fig. 1) shows the results of the search, screening, selection, and inclusion processes.

Data Extraction

Data were extracted by 2 reviewers (IGD and MAD), both of whom had training in epidemiology. When an article included various types of cancer, a separate data form was created for each type. When data were reported jointly they were included under the category NMSC.

Assessment of Methodological Quality

The methodological quality of the studies was assessed using criteria adapted from Lomas et al.[3] One point was allocated for each of the 10 criteria (Table 1).

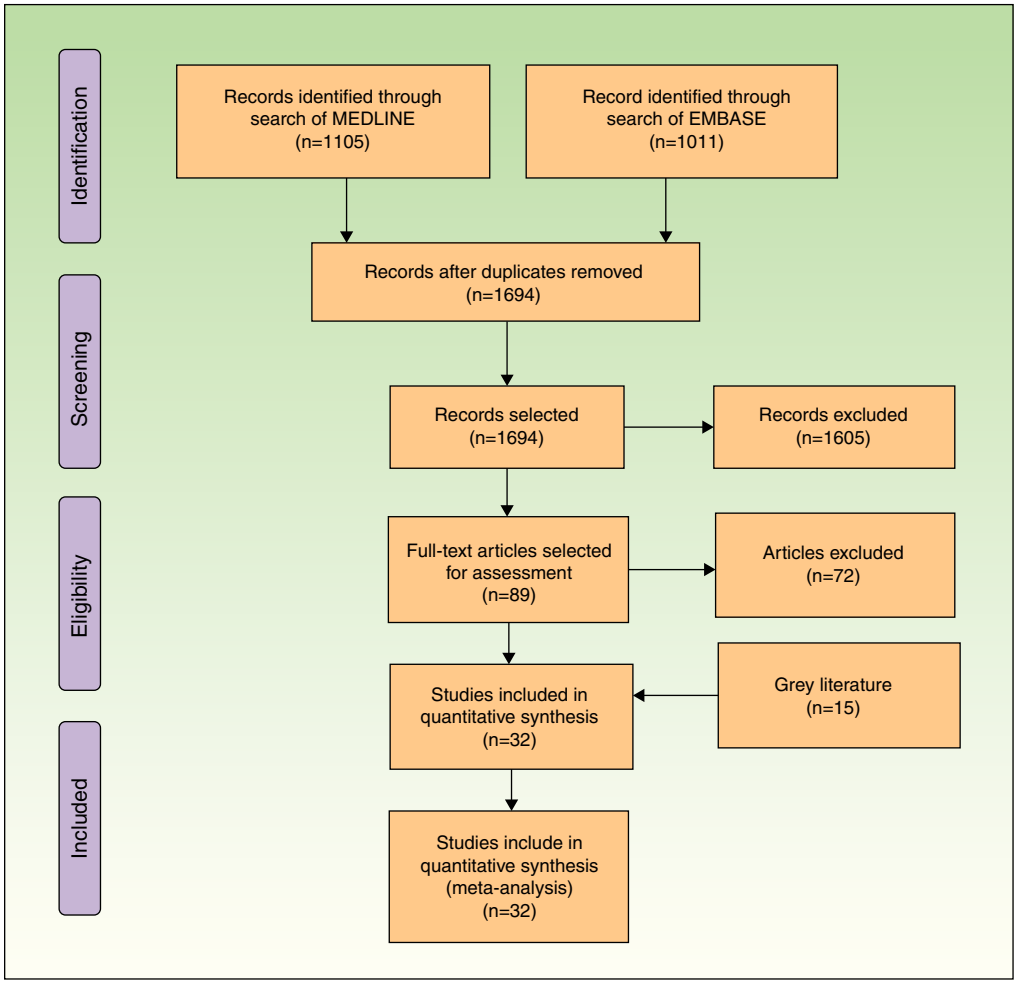

Figure 1 PRISMA flow diagram.

Table 1 Criteria Used to Assess the Methodological Quality of the Studies[a]

Internal validity

Data collection

1. Did the study directly sample the population, as opposed to using data from registries?

Description of methods

2. Is the method of counting tumors stated (number of tumors or number of patients)?
3. Does this study specify whether the data relate to primary tumors?
4. Is there histological confirmation?

Reporting of incidence rates

5. Were separate rates reported for different types of tumors?
6. Are gender-specific incidence rates reported?
7. Were the rates stratified by age?
8. Were the rates age standardized?
9. Were confidence intervals reported or can they be calculated (based on standard error or number of tumors and population)?

External validity

10. Were the data standardized to a major population (European, world, USA)?

[a] One point is assigned for each positive response. The maximum score is 10.

Data Synthesis, Heterogeneity, and Subgroup Analysis

Meta-analysis of the data was performed using a random effects model. The following values were calculated for each tumor type: incidence, standardized incidence (direct and using the same standard), and mortality rate (only for melanoma and NMSC). The analyses were performed by separating these rates using clinical and/or histological criteria. A separate analysis was performed on the more recent data collected in the last 11 years. The data were analyzed using the Stata 14 software package (StataCorp. 2015. Stata Statistical Software: Release 14).

Results

The search strategy identified 1694 articles. Of these, 89 were selected on the basis of a reading of the abstract. After a review of the full texts, 17 were selected for analysis. To these we added a further 15 articles identified by the search of the ''gray literature'' outside of PubMed and EMBASE. In total, 32 studies were included in the review (Fig. 1).

The selected studies, which are listed in Table 2, analyze data from different provinces, regions, or the whole country relating to the period from 1989 to 2015.

The score for methodological quality ranged from 2 to 9 points. Twenty-four studies (75%) achieved a high quality score, but none achieved the maximum score of 10. Most of the studies (84.8%) included histological confirmation. (Table 3)

Basal Cell Carcinoma

The overall incidence for BCC in the meta-analysis was 113.05 (95% CI, 89.03-137.08) cases per 100 000 person-years for the studies based on the registration methodology normally used by registries (in which only 1 tumor with histological confirmation is counted per person) (Fig. 2). Only 1 study calculated the incidence using both clinical and histological criteria and counting tumors rather than patients, reporting an incidence of 253.23 (95% CI, 273.01-269.45) cases per 100 000 person-years.[6] The incidence rates for these studies standardized to the world population are shown in Fig. 1, Appendix 1.

Squamous Cell Carcinoma

The overall incidence rate for SCC was 38.16 (95% CI, 29.82-46.49) cases per 100 000 person-years in the meta-analysis (Figs. 2 and 3). The incidence rate standardized to the world population is shown in Figure 2, Appendix 1.

The mortality rate for NMSC was reported in 2 studies: 1 based on data from Navarre,[5] with a mortality rate of 0.90 (95% CI, 0.54-1.25) cases per 100 000 person-years; and the other on data for Spain as a whole, with a mortality rate of 1.10 (95% CI, 1.00-1.20) cases per 100 000 person-years (Fig. 3, Appendix 1). Only the Navarre study reported the mortality rate standardized to the world population (Fig. 4, Appendix 1).

Melanoma

Melanoma has been the subject of more studies than any other skin cancer (n = 24). The meta-analysis yielded a crude incidence rate of 8.82 (95% CI, 7.59-10.04) cases per 100 000 person-years (Fig. 4). Of the studies in which the diagnosis of melanoma was confirmed histologically, the study reporting the highest incidence rate was in Marbella (Malaga) between 2002 and 2011, with a rate of 17.53 (95% CI, 15.64-19.41) cases per 100 000 person-years.[9] The lowest incidence was reported in Zaragoza[19] in 1986, with 3.63 (95% CI, 2.33-4.92) cases per 100 000 person-years. The only study based on both clinical and histological confirmation reported an incidence rate in Guipúzcoa of 10.15 (95% CI, 9.08-11.23) cases per 100 000 person-years for the period from 1998 to 2002.[10] Based on both histological and clinical data, Cabanes et al.[23] calculated a crude incidence rate for Spain in 2006 of 1.90 (95% CI, 1.77-2.03), but in a study with an high risk of bias. The data standardized to the world population are shown in Figure 5, Appendix 1.

The overall crude mortality rate for melanoma was 2.17 (95% CI: 1.78-2.55) cases per 100 000 person-years for studies based on histological diagnoses in the provinces of Navarre,[5] Girona,[8] and Tarragona[12] (Fig. 6, Appendix 1). Cayuela et al.,[7] who analyzed data from death certificates, identified a crude mortality rate for Spain in 2001 of 1.82 (95% CI, 1.69-1.95) cases per 100 000 person-years. The mortality rates for melanoma standardized to the world population are shown in Figure 7, Appendix 1.

Table 2 List of Articles Selected in the Systematic Review.

Authors	Journal	Title	Year	Geographic Area
Ardanaz et al.[5]	An Sist Sanit Navar	[Incidence and mortality due to cancer in Navarre, 1998-2002. Trends in the last 30 years]	2007	Navarre[a]
Bielsa et al.[6]	Br J Dermatol	Population-based incidence of basal cell carcinoma in a Spanish Mediterranean area	2009	Barcelona
Cayuela et al.[7]	Br J Dermatol	Has mortality from malignant melanoma stopped rising in Spain? Analysis of trends between 1975 and 2001	2005	Spain
Clèries et al.[8]	Clin Trans Oncol	Time trends of cancer incidence and mortality in Catalonia during 1993-2007	2014	Girona, Tarragona[a]
Fernández-Canedo et al.[9]	Piel	Epidemiología del melanoma en una población multicultural mediterránea	2014	Malaga
Larrañaga et al.[10]	Gacet Sanit	Incidencia del cáncer en Guipúzcoa (1998-2002 y tendencias desde 1986	2008	Guipúzcoa
Marcos-Gragera et al.[11]	MedClin	Incidencia del cáncer en Cataluña, 1998-2002	2008	Tarragona, Girona[a]
Marcos-Gragera et al.[12]	J Eur Acad Dermatol Venereol	Rising trends in incidence of cutaneous malignant melanoma and their future projections in Catalonia, Spain: Increasing impact or future epidemic?	2010	Tarragona, Girona[a]
Montero Pérez et al.[13]	Aten Primaria	[Importance of skin cancer (non-melanoma): A study of 89 cases]	1989	Cordoba
Ocaña-Riolaet al.[14]	Eur J Epidemiol	Population-based study of cutaneous malignant melanoma in the Granada province (Spain), 1985-1992	2001	Granada[a]
Puig et al.[15]	Acta Dermato-Venereologica	Melanoma incidence increases in the elderly of Catalonia but not in the younger population: Effect of prevention or consequence of immigration?	2015	Catalonia
Revenga Arranz, et al.[16]	J Eur Acad Dermatol Venereol	Descriptive epidemiology of basal cell carcinoma and cutaneous squamous cell carcinoma in Soria (north-eastern Spain) 1998-2000: A hospital-based survey	2004	Soria
Rubio Ruiz et al.[17]	Med Clin (Barc)	Estudio epidemiológico y clínico del melanoma maligno cutáneo en el área sanitaria de León	1991	León
Verdecchia et al.[18]	Ann Oncol	A comparative analysis of cancer prevalence in cancer registry areas of France, Italy and Spain	2002	Basque Country, Mallorca, Navarre, Tarragona[a]
Vergara Ugarriza[19]	Neoplasia	Incidencia de cáncer en la población de Zaragoza	1995	Zaragoza
Vilar-Coromina et al.[20]	Med Clin (Barc)	Cáncer cutáneo distinto de melanoma: tendencia de la incidencia poblacional en Girona, 1994-2007	2011	Girona[a]
Vilar-Coromina et al.[21]	Med Clin (Barc)	Carcinoma de células de Merkel cutáneo: incidencia y supervivencia poblacional, 1995-2005	2009	Girona[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Albacete[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Asturias[a]
Forman et al.,[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Basque Country [a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Canary Islands[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Ciudad Real[a]

Table 2 (*Continued*)

Authors	Journal	Title	Year	Geographic Area
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Cuenca[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Girona[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Granada[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	La Rioja[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Mallorca[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Murcia[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Navarre[a]
Forman et al.[22]	http://ci5.iarc.fr	Cancer incidence in five continents, Vol. X (electronic version)	2013	Tarragona[a]
Cabanes et al.[23]	Instituto de Salud Carlos III	La situación del cáncer en España, 1975-2006	2009	Spain [a]
Pujol et al.[24]	Informe	Proyecto Incaces	2007	Malaga, La Coruña, Barcelona, Madrid

[a] Data taken from a population-based cancer registry.

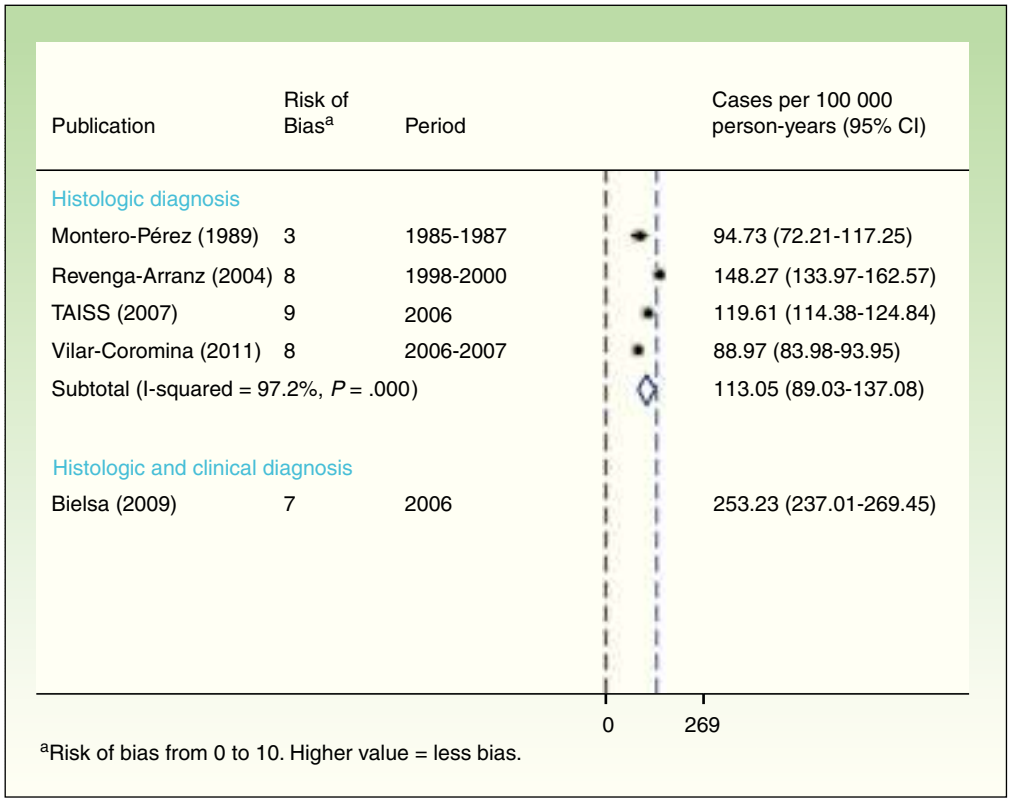

Figure 2 Incidence rate for basal cell carcinoma. All ages.

Table 3 Risk of Bias.

Author	Sample	Specifies Unit of Analysis	Separates Primary Tumors	Histological Confirmation	Rates by Tumor Type	Rates by Sex	Rates by Age	pcAge Standardized	95% CI Included	Direct Standardization	Total
Fernandez-Canedo, 2014[9]	No	No	No	Yes	Yes	No	No	No	No	No	2
Montero Pérez, 1989[13]	No	Yes	No	Yes	Yes	No	No	No	No	No	3
Rubio Ruiz, 1991[17]	No	No	No	Yes	Yes	Yes	No	No	No	No	3
Verdecchia, 2002[18]	No	No			Yes	No	Yes	No	Yes	No	3
Cayuela, 2005[7]	No	No		No	Yes	No	No	Yes	Yes	Yes	4
Cabanes, 2009[23]	No	No	No	No	Yes	Yes	No	Yes	No	Yes	4
Clèries, 2014[8]	No	No		Yes	Yes	Yes	No	Yes	No	Yes	5
Larrañaga, 2008[10]	No	No	No	Yes	Yes	Yes	No	Yes	No	Yes	5
Ardanaz, 2007[5]	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Ocaña-Riola, 2001[14]	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Puig, 2015[15]	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Marcos-Gragera, 2008[11]	No	Yes		Yes	Yes	Yes	No	Yes	Yes	Yes	7
Marcos-Gragera, 2010[12]	No	Yes		Yes	Yes	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Albacete[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Asturias[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Basque Country[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Canary Islands[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Ciudad Real[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Cuenca[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. La Rioja[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Mallorca[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Forman, 2013. Murcia[22]	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Bielsa, 2009[6]	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7
Revenga Arranz, 2004[16]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	8
Vergara Ugarriza, 1995[19]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Vilar-Coromina, 2011[20]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Forman, 2013. Girona[22]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Forman, 2013. Granada[22]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Forman, 2013. Navarre[22]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Forman, 2013. Tarragona[22]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Vilar-Coromina, 2009[21]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Pujol, 2007[24]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9

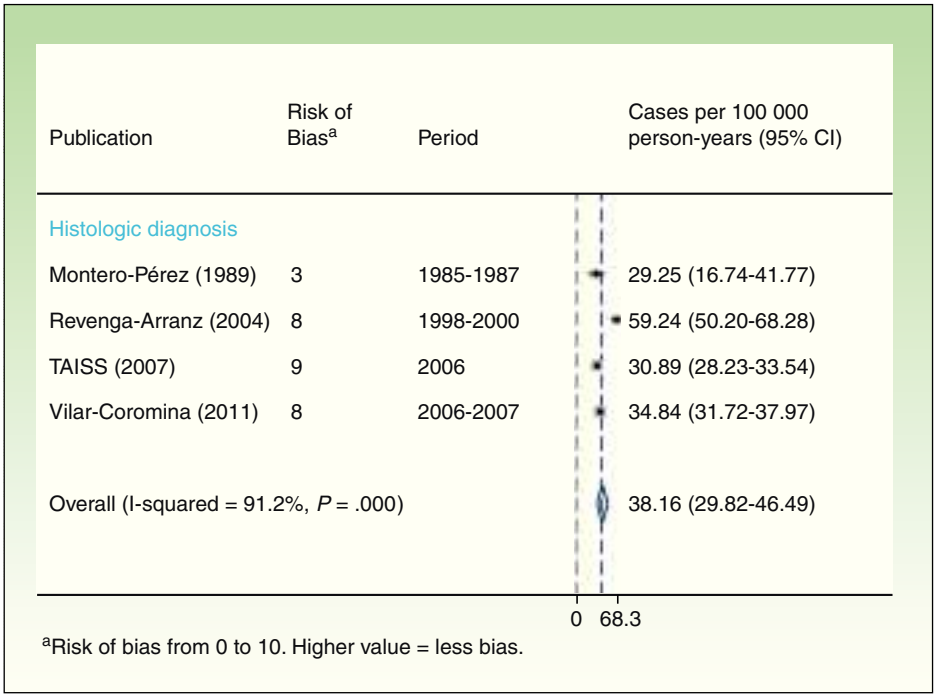

Figure 3 Incidence of squamous cell carcinoma. All ages.

Merkel Cell Carcinoma

In the only study that has reported the incidence rate for Merkel cell carcinoma in Spain the data are from the province of Girona and the crude incidence rate was 0.28 (95% CI, 0.15-0.4) cases per 100 000 person-years, with a rate standardized to the world population of 0.12 (95% CI, 0.04-0.2) cases per 100 000 person-years.[21] None of the studies in the literature analyzed the mortality rate for this tumor.

Analysis of the Most Recent Studies

In the meta-analysis for the studies published in the last 11 years, which represent the most recent data (1998-2000 and later), overall incidence rates were 118.22 (95% CI, 90.25-146.2) for BCC, 42.33 (95% CI, 30.67-49.78) for SCC, and 9.72 (95% CI, 8.91-10.52) for melanoma.

Discussion

The present systematic review included 32 studies on the incidence and mortality of skin cancer in Spain. This is the largest review on this subject to date.

The main objective of this review was to determine the burden of disease attributable to skin cancer in order to ensure adequate planning of available resources. The work was carried out as part of the *White Book on Skin Cancer* being prepared by the Foundation of the Spanish Academy of Dermatology and Venereology (FAEDV). In this discussion we will focus on the crude incidence rate, since the primary objective of age-standardized incidence rates is to allow comparison between groups with differing age structures, but such rates are less useful for planning purposes.

The results for BCC differ depending on the method used to calculate incidence. The overall crude incidence rate in Spain was 113.05 cases per 100 000 person-years when only histologically confirmed tumors were included and only the first tumor for each patient was counted (the usual methodology used by cancer registries). However, when the primary objective is to evaluate the demand for the care of BCC it is preferable to also include tumors not confirmed histologically and all the tumors occurring in any patient. The only study that used this methodology was carried out in the Barcelonès Nord area and reported a crude incidence rate of 253.23 cases per 100 000 person-years,[6] more than twice the rate estimated by earlier studies. It is likely that this figure more reliably represents the real need for care.

The incidence rate of the meta-analysis standardized to the world population was 55.87 cases per 100 000 person-years, similar to rates reported for Scotland, United Kingdom, and Germany, and much lower than the rate reported for Finland.[3]

The crude incidence rate for SCC was 38.16 (95% CI, 29.82-46.49) cases per 100 000 person-years. As this result was also obtained using the methodology typical of registries, it is very likely that it underestimates the need for care.

The incidence rate standardized to the world population based on the results of the meta-analysis of available studies was 13.38 per 100 000 person-years. These incidence rates are relatively low when compared to those of countries such as Germany and Slovakia, and are lower than countries such as Sweden, Switzerland and Wales.[3]

The mortality rate for NMSC is low, and predominantly associated with SCC, particularly because of the existence of a high-risk subgroup.[25]

In the case of melanoma, the crude incidence rate upon meta-analysis was 8.82 cases per 100 000 person-years.

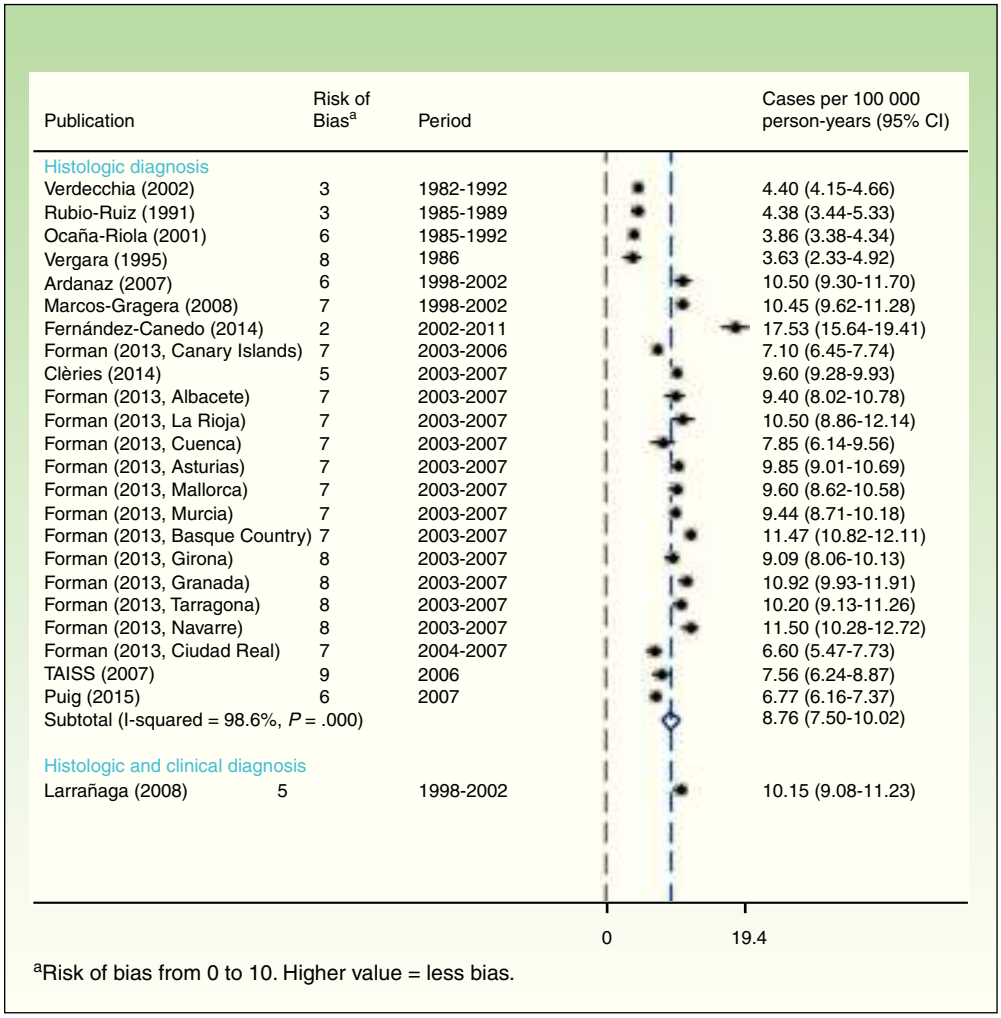

Figure 4 Incidence of melanoma. All ages.

Differences can be observed between the results obtained several decades ago, 3 to 4 cases per 100 000 person-years,[14,17–19] and those reported by studies carried out in the 1990s and later, with rates of 7 cases per 100 000 person-years and higher.[8,12,15,22,24,26] These differences may reflect an increase in the incidence of melanoma[27] and the greater risk of bias in older studies. Of particular interest is the study by Fernández-Canedo et al.,[9] who reported a high incidence rate of 17.56 cases per 100 000 person-years in a study of Marbella in the province of Malaga. This result is attributed to the high proportion of people from central and northern Europe in the population of the study area.

The standardized incidence rate in Spain is low compared to other European countries, reflecting the recognized difference in Europe between north and south and between east and west, with a rate that varies from 6 cases per 100 000 person-years in eastern Europe to 10 in southern Europe and up to 19 in northern Europe.[28] The incidence rate in Spain is much lower than the more than 20 cases per 100 000 person-years reported in the USA,[29] and more than 60 reported for New Zealand and Australia.[30]

On the basis of the only 3 studies available, the crude mortality rate upon meta-analysis was 2.17 cases per 100 000 person-years.[5,8,12] While relatively low at present, this rate may continue to increase in coming years, particularly in the older population.[7,12] Such an increase would be in contrast to the trend in more northern European countries, where the mortality rates have tended to plateau and even decrease. Among the reasons for this difference are the fact that the Spanish population is older and that melanomas occurring at a later age tend to be thicker and have a more aggressive phenotype.[31]

Finally, in the only study on Merkel cell carcinoma, Vilar-Coromina et al.[21] reported an incidence rate for this tumor of 0.28 cases per 100 000 person-years calculated on the basis of data from the Cancer Registry in the province of Girona. This rate is similar to that obtained in similar studies in Denmark[32] and Finland,[33] but lower than that reported in Australia, where the incidence rate adjusted to the US population is 0.8 cases in western Australia and 1.6 cases per 100 000 person-years in north-eastern Australia (Queensland), rates 10 times those reported in European studies.[34] This epidemiological difference is probably explained by the difference in population phenotype and levels of exposure to ultraviolet radiation.[35]

The present systematic review provides a good account of the incidence and mortality of skin cancer in Spain in recent years. The study has, however, a number of limitations. The

main limitation of the study is that most of the data on which it is based were obtained using the methodology generally used by cancer registries, which is appropriate for the study of etiological factors but tends to underestimate the need for care, especially in the case of BCC, in which patients often present multiple tumors and are treated without histological confirmation. In light of our results, the approximate underestimation could be 50%. Other limitations of the review are that the studies analyzed do not cover the whole population of Spain or all reported tumors (no data are included on neural, hematolymphoid, adnexal, or soft tissue tumors), and that the data refer to different time periods. Finally, not all the studies based on data from cancer registries explicitly stated that in situ tumors were excluded, but such an exclusion was assumed for the purposes of this analysis.

In conclusion, the data indicate that BCC and SCC are very common tumors in Spain. At least in the case of BCC, the need for care is higher than the level that could be determined from registry data. The incidence rate for cutaneous melanoma in Spain is low compared to other European countries. Finally, the incidence rate for Merkel cell carcinoma is low and similar to that reported for other countries in Europe.

Ethical Disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that no private patient data are disclosed in this article.

Right to privacy and informed consent. The authors declare that no private patient data are disclosed in this article.

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Conflict of Interests

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.adengl.2016.02.015.

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