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Original Research

Systematic review of the evidence on the epidemiology of herpes zoster: incidence in the general population and specific subpopulations in Spain

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ABSTRACT

Objectives: Herpes zoster (HZ) is an important cause of morbidity around the world, especially among the adult population aged >50 years.

Study design: A systematic review of the literature (up to October 31, 2016) was performed to identify available evidence on incidence of HZ in the general population and in a specific subpopulation in Spain.

Methods: PubMed and Embase databases were searched, combining the following search terms: 'herpes zoster', 'diabetes mellitus (DM)', 'chronic obstructive pulmonary disease (COPD)', 'chronic heart failure', 'mental disorders' and 'immunocompromised'. Supplements for local scientific congresses, non-indexed Spanish journals and official epidemiological reports, potentially HZ related, were also manually searched. The inclusion criteria were the following: English or Spanish publications reporting incidence of HZ in the Spanish general population and/or specific subpopulations. No restrictions were applied on the study design or population age.

Results: Among 269 references retrieved (48 PubMed, 148 Embase and 73 manual searching), 34 were finally included. Incidence of HZ in the general population ranged from 2.1 to 5.5/1000 person-years. HZ incidence ranged from 9.4 to 15.3/1000 patients with DM and from 11.0 to 11.4/1000 population with COPD or cardiovascular disease. In asthmatic patients, 6.9 HZ cases/1000 subjects were reported. The highest HZ incidence (1.3–400.0/1000 person-years) was in immunocompromised persons (10.0/1000 patients with cancer, 12.5/1000 patients with AIDS, from 5.0 to 240.0/1000 transplanted patients and from 6.6 to 27.0/1000 population with rheumatic diseases). Three studies estimated an increased risk of HZ in comparison with general population, for patients with DM (24%), COPD (39%) and COPD receiving inhaled corticosteroids (61%).

Conclusions: The results suggest a high risk of HZ in certain age groups and specific subpopulations. This study could contribute to identify target age populations and at-risk groups if implementation of HZ vaccination programmes in Spain would be considered.

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Introduction

Varicella-zoster virus (VZV) is an alpha herpes virus that causes two different clinical diseases: varicella (chickenpox) and herpes zoster (HZ).[1] HZ is characterised by a painful vesicular eruption, usually unilateral, distributed over a dermatome. It is the local manifestation of reactivation of VZV, which remains latent in the dorsal or cranial sensory root ganglia after the primary varicella infection.[2–4] The HZ appearance occurs as a result of decreased cellular immunity, which may occur naturally as a result of age, or be the consequence of treatments and/or diseases that cause immunosuppression.[5,6]

HZ is considered an important cause of morbidity, especially among the adult population aged >50 years.[7] It is estimated that 20–30% of patients infected with VZV will develop HZ throughout their life, and this rate increases to up to 50% in people aged >85 years.[8,9]

It is estimated that in Spain, the rate of HZ hospitalizations in patients older than the age of 30 years is around 0.13/1000 population. There is an increasing trend up with increasing age, with rates rising to 0.54/1000 population in patients older than the age of 80 years.[10]

A characteristic of this disease is that in some of the affected patients, usually within the elderly population, the HZ-related pain persists for 1–3 months after the onset of HZ in the dermatome affected by the eruption. These patients may develop the so-called postherpetic neuralgia (PHN), which is one of the most common complications,[11] that affects 10–15% of patients with HZ and up to 28% of patients older than 70 years.[12]

Typically, in most cases, HZ resolves within 1 month, whereas PHN can persists for at least 3 months, and in some cases, patients may have pain for years.[13,14]

Both the acute pain associated with HZ and PHN have a negative impact on patients' health-related quality of life, significantly influencing sleep and daily activities, and may lead to physical disability and emotional distress.[15–17] The annual incidence of HZ in the general population ranges from 2.0 to 4.6 cases/1000 person-years in Europe.[18] This incidence increases in patients older than 60–65 years, reaching 10 cases/1000 person-years in patients older than the age of 80 years.[19] Although there are few studies on the epidemiology of HZ in Spain, an average annual HZ incidence of approximately 4.6/1000 person-years has been reported in the general population.[20]

A relationship between specific subpopulations and an increased occurrence of HZ is suspected by several studies. It is widely accepted that advanced age, psychological stress, human immunodeficiency virus infection, organ transplantation, bone marrow, solid tumours, haematological malignancies, depression, use of immunosuppressive drugs and other conditions that reduce cellular immunity are risk factors for the development of HZ.[9,21,22] In addition, certain chronic diseases such as respiratory diseases (chronic obstructive pulmonary disease [COPD] and asthma) and diabetes mellitus (DM) are also associated with an increased occurrence of HZ.[23–26]

The therapeutic approach for HZ consists of the systemic administration of antiviral drugs (acyclovir, valacyclovir, famciclovir and brivudine) which may reduce inflammation, symptoms and the healing time and relieve pain, especially when administered within 72 h after the onset of symptoms,[27] although the use of antivirals may have limited impact on PHN rates. In addition, HZ can be prevented by vaccination. Since 2014, a live attenuated vaccine for the prevention of HZ and PHN has been available in Spain.[28] This vaccine has been associated with a reduction in the incidence of the disease (51% in people older than 60 years)[29] and the frequency of onset of PHN.[30,31] A new adjuvanted subunit vaccine that has shown 97.2% of vaccine efficacy (95% confidence interval [CI]: 93.7–99.0) for populations older than the age of 50 years[32] and 91.3% (95% CI: 86.8–94.5) for adults aged 70 years or older[33] in phase III clinical trials is also authorized in the US and Canada and is being submitted for approval in Europe.

Despite the availability of effective vaccines to prevent HZ and its complications in elderly adults, there is relatively scarce use of the current live attenuated vaccine in Spain.

In addition to the elderly, there may be other specific risk groups that may benefit from vaccination. However, figures for the number of people at risk of HZ in Spain are not known. There is, therefore, a need to collate the available evidence of HZ incidence in Spain to get a more accurate estimate of the potential number of persons who may benefit from vaccination.

The main objective of this study was to perform a systematic review to identify the available scientific evidence on the incidence of HZ in the general population and specific, increased risk of subpopulations in Spain.

Materials and methods

Identification of studies

A systematic review of the literature following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[34] was carried out using MEDLINE (PubMed) and Embase electronic databases to identify articles that included epidemiological data on HZ in Spain up to October 31st, 2016.

The search strategy has been developed through the combination of the following search terms: 'herpes zoster', 'diabetes mellitus', 'chronic obstructive pulmonary disease', 'chronic heart failure', 'mental disorders' and 'immunocompromised' (see Appendix 1 and Appendix 2).

In addition, three manual searches were conducted on the following: (1) Spanish journals not indexed in the electronic databases well known in the infectious disease field; (2) supplements of local journals, to identify communications to national scientific congresses related to HZ; and (3) websites of the Autonomous Communities—primarily those of the Health Councils—to check for the existence of official regional epidemiological reports and/or data from the Sentinel Network of General Practitioners at the autonomous community level.

Manual searches were limited to the articles published from 2010 to 2016. The official publication was determined for the following scientific societies that were relevant to the areas of interest (dermatology, public health and/or preventive medicine, infectious diseases, pain and vaccinology) and a review of the content indexes of Spanish journals that were

not indexed in PubMed and/or Embase (Appendix 3). Also, the website of scientific journals, which were identified as publishing supplements of communications to national scientific congresses, were additionally reviewed (Appendix 3).

Selection of studies

The following inclusion criteria were used for the selection of articles: related to the incidence of HZ in the general population and/or specific subpopulations, developed in Spain, published until October 31st, 2016, and written in English or Spanish. There were no restrictions regarding the study design and age of the study population. The articles excluded from the study were those that did not contain the keywords used in the search strategy, duplicate publications, studies performed in the non-Spanish population and other types of studies such as reviews, case reports and vaccination recommendations (Fig. 1).

Data extraction

An initial selection of localised references was performed by reading the title and abstract. Subsequently, the selected studies were reviewed in full text.

The selection was performed by one author (M.M.) and later reviewed by another author (I.O.). Possible discrepancies were solved after joint review and discussion of each individual article. The final articles included in the study were analysed in depth, using an extraction matrix of the data of interest related to the authors, study type, objective, year(s) of study, population included, subpopulation data, number of cases with HZ, epidemiological incidence data (proportion per 1000 persons or incidence rate per 1000 person-years) and CI (95% CI) of HZ incidence.

The PRISMA statement was used as a guide to enhance the quality of reporting in this review. Therefore, the systematic review was performed in accordance with the checklist suggested by the PRISMA (Appendix 1).[34]

Results

A total of 269 potentially relevant articles were identified (48 in PubMed, 148 in Embase and 73 in manual searches). Of the 269 references, a total of 119 articles were excluded; 17 because they were duplicates and 102 because they did not meet the inclusion criteria. After reading the full text of the 150 selected articles, 116 articles (77%) were excluded because they were

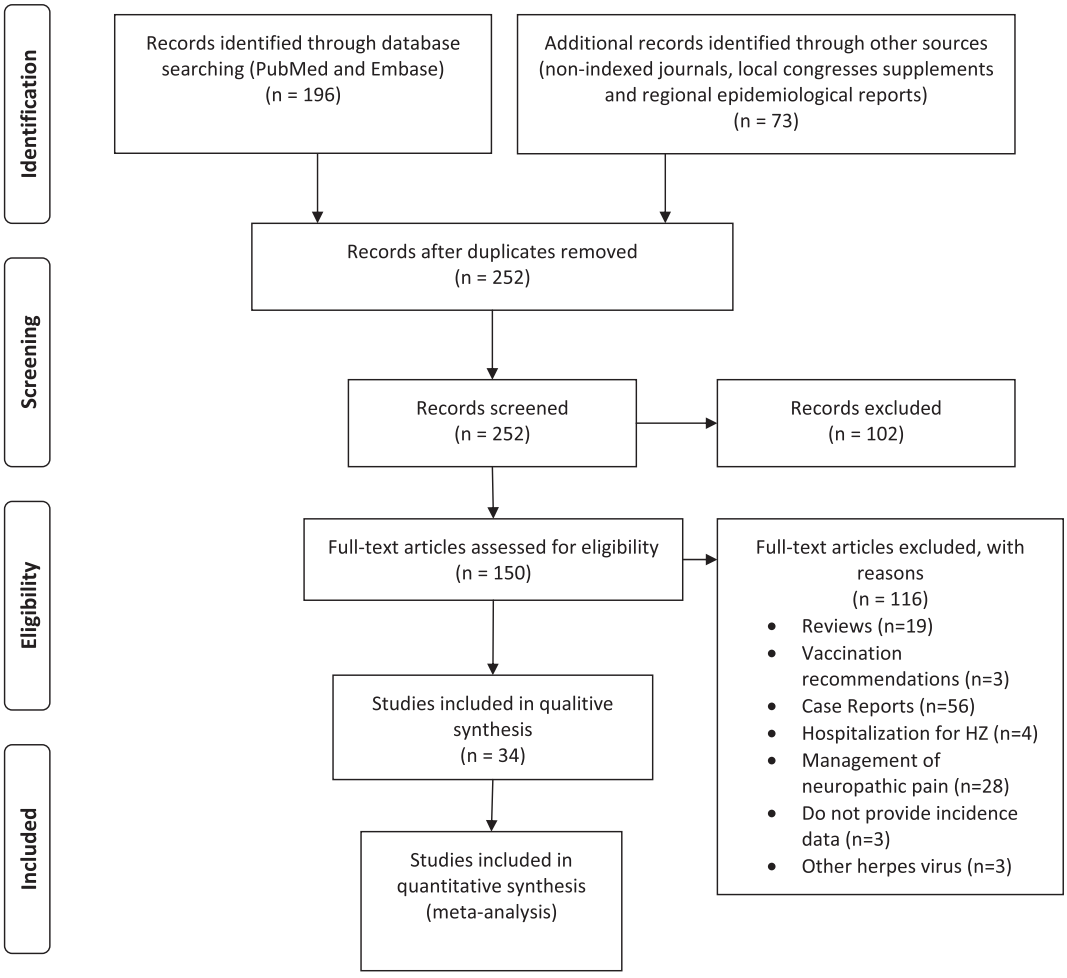

Fig. 1 – Flow diagram describing the selection and exclusion process used in the review according to the PRISMA criteria. HZ, herpes zoster; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

reviews ($n = 19$), vaccination recommendations ($n = 3$), case reports ($n = 56$), referred to the treatment of neuropathic pain ($n = 28$), HZ hospitalisations ($n = 4$), did not provide incidence rates ($n = 3$) or referred to another herpes virus ($n = 3$).

Finally, a total of 34 studies meeting the selection criteria were included, of which 14 provided epidemiological data on the incidence of HZ in the general population, and 20 evaluated the incidence of HZ in specific subpopulations.

Fig. 1 shows the flow diagram describing the selection and exclusion process used in the review according to the PRISMA criteria.[34]

Characteristics of studies

From the total number of selected publications ($n = 34$), 21 (62%) were written in Spanish.

Focussing on the study design, the vast majority of the publications concerned retrospective studies (68%), followed by prospective studies (15%), regional epidemiological (15%) and one ambispective study (i.e. having both, retrospective and prospective data collection).

In total, 68% were studies performed in the general population ($n = 23$), whereas the remaining 32% of references were stratified by sex and age.

Two of the studies[35,36] were developed in a Spanish population without specifying the Autonomous Communities—using data from the Spanish BIOBADASER registry—and 32 studies were conducted at the regional level, in the following Autonomous Communities: 21% ($n = 7$) in the Valencian Community[37–43]; 18% ($n = 6$) in the Community of Madrid;[44–49] 9% ($n = 3$) in Catalonia[50–52] and Navarre;[53–55] 6% ($n = 2$) in the Basque Country,[56,57] Castile and León,[58,59] Andalusia,[60,61] Aragon[62,63] and the Canary Islands;[64,65] and 3% ($n = 1$) in the Balearic Islands,[66] Galicia[67] and the Principality of Asturias.[68]

Among the selected publications, 47% were presented as communications to national scientific congresses, and the rest were full-text articles published in national and international peer-reviewed journals (indexed and non-indexed) ($n = 13$) or official regional epidemiological reports ($n = 5$).

The specific characteristics and details of the selected articles are shown in Table 1.

Incidence of HZ in the general population

Of the 14 publications that analysed the incidence of HZ in the general population in different Autonomous Communities in Spain, eight were presented as communications to scientific congresses.

The annual incidence rate reported by these publications ranged from 2.08[56] to 5.46[58] cases/1000 person-years, based on the retrospective and prospective studies that used data collected from the Sentinel Network of General Practitioners or through the review of medical records in primary care settings (Fig. 2).

In those studies, in which the population was stratified by age groups,[37,38,44,47,56,58,59,62] it was observed that the HZ incidence was higher as the age of patients increased. Although the age groups differed from one study to another, the incidence of HZ by age remained stable during the review period, being approximately 2/1000 in the population aged 15–49 years, 5–8/1000 in patients older than 50 years and up to 11/1000 in patients older than 75 years.

Only one study[47] reported that the incidence of HZ decreases as the age of patients increases, with incidence rate of HZ of 11.89 and 10.89/1000 inhabitants in the 65- to 74-year age group and 75- to 84-year age group, respectively.

Several studies found higher HZ incidence in the oldest population (>70 years)[37,44,47,59,62] and also among women.[44,47,58,59] In the article by Vega et al.,[59] the incidence rate of HZ was significantly higher in women (5.92/1000 person-years) than in men (3.72/1000 person-years). Similarly, in another study,[44] the incidence of HZ in women was higher than in men, with rates of 3.18 and 2.91 cases/1000 population, respectively.

Some studies observed that the HZ incidence increased over time within the same region. The reported incidence of HZ in the Community of Madrid[44] rose from 2.82 cases/1000 inhabitants in 2001–2003 to 3.86 cases/1000 inhabitants in 2007–2010. Similarly, the Autonomous Community of Castile and Leon[58] saw a rise in the incidence rate from 3.78/1000 person-years in 2009 to 5.46 cases/1000 persons-years in 2014.

Two studies[44,47] described the evolution of the incidence of HZ after the introduction of the varicella vaccine in 2006 in childhood vaccination schedules. One of them[44] performed a comparison of the incidence of HZ in the years before the vaccine (2001–2006) versus the HZ incidence during the systematic vaccination period (from 2007 to 2010), being of 2.82/1000 inhabitants and 3.86/1000 inhabitants, respectively. The other study[47] analysed the incidence of HZ during the period 2007–2010, which presented the HZ incidence rate of 3.90/1000 inhabitants for the year 2007 and 4.84/1000 inhabitants for the year 2010. Therefore, both studies reported an increase in the incidence of HZ, despite the introduction of the varicella vaccine in childhood vaccination schedules.

After manually searching the websites for the Autonomous Communities, a total of five official regional epidemiological reports were identified for the Autonomous Communities of Aragon, Balearic Islands, Galicia, Madrid and Navarre. The most recent annual incidence rate of HZ for each region was 5.2/1000 persons in Aragon (year 2016), 3.7/1000 persons in the Balearic Islands (year 2016), 1.5/1000 persons in Galicia (year 2012), 2.6/1000 persons in the Community of Madrid (year 2014) and 4.0/1000 persons in Navarre (year 2016).

Incidence of HZ in specific subpopulations

Twenty studies reported the incidence of HZ in certain subgroups of high-risk patients. Of these publications, 12 were full-text articles published in the national and international journals, and the rest were communications to scientific congresses.

Most of these publications ($n = 17$) analysed the incidence of HZ in subpopulations of immunocompromised patients. The causes of immunosuppression in these patients were organ transplantation, cancer, AIDS and rheumatic diseases.

In three studies,[40,48,53] HZ incidence rates ranging from 9.4 to 15.3/1000 patient-years with DM were reported.

Two studies evaluated the incidence rates of HZ in patients with COPD,[41,48] which were 11.0 and 11.4/1000 patient-years,

Table 1 – Characteristics of selected studies.

Author, year of publication	Type of study	Years	Type of population	Age ranges	HZ cases	HZ incidence[c] (incidence rates or incidence proportion)	95% CI
Sancho Martínez et al. 2010[56,a]	Retrospective	2008–2009	General	All ages	233	2.1 HZ cases/1000 person-years	NA
Vega et al. 2012[59,a]	Retrospective	2011	General	>14 years	NA	4.9 HZ cases/1000 person-years	NA
Cebollada et al. 2016[62,a]	Retrospective	2014	General	Mean: 57.5 years	6298	4.9 HZ cases/1000 person-years 12.0 HZ cases/1000 person-years (70–74 years) 10.1 HZ cases/1000 person-years (>75 years)	4.8–5.0
Ruiz Sopeña et al. 2015[58,a]	Retrospective	2009–2014	General	All ages	68,814	5.5 HZ cases/1000 person-years	NA
Cebrián-Cuenca et al. 2011[37,b]	Prospective	2006–2007	General	>14 years	146	4.1 HZ cases/1000 persons (general) 1.3 HZ cases/1000 persons (<50 years) 6.7 HZ cases/1000 persons (50–59 years) 5.2 HZ cases/1000 persons (60–69 years) 11.1 HZ cases/1000 persons (≥70 years)	3.4–4.7
Cabrera Miranda et al. 2012[47,a]	Retrospective	2007–2011	General	All ages	1897	4.8 HZ cases/1000 persons (all ages) 6.2 HZ cases/1000 persons (45–65 years) 11.9 HZ cases/1000 persons (65–74 years) 10.9 HZ cases/1000 persons (75–84 years)	4.4–5.2
Gutiérrez et al. 2011[44,a]	Retrospective	2001–2010	General	NA	NA	4.2 HZ cases/1000 persons	3.8–4.6
Gutiérrez-Gimeno et al. 2010[39,a]	Retrospective	2007–2009	General	15–100 years	20,343	4.8 HZ cases/1000 person-years	4.8–4.9
Gutiérrez-Gimeno et al. 2010[38,a,d]	Ambispective	2006–2007	General	15–100 years	NA	2.4 HZ cases/1000 persons (15–49 years) 6.5 HZ cases/1000 persons (50–59 years) 8.7 HZ cases/1000 persons (60–69 years) 8.3 HZ cases/1000 persons (70–100 years)	2.37–2.52 6.27–6.77 8.39–9.01 8.06–8.58
Regional epidemiological report of Navarre, 2016[55]	Regional registry	2010–2015	General	All ages	NA	3.9 HZ cases/1000 persons	NA
Regional epidemiological report of Galicia, 2012[67,e]	Regional registry	2012	General	All ages	NA	1.5 HZ cases/1000 persons (all ages) 1.7 HZ cases/1000 persons (50–59 years) 2.7 HZ cases/1000 persons (60–69 years) 3.3 HZ cases/1000 persons (70–79 years) 3.6 HZ cases/1000 persons (>80 years)	NA
Regional epidemiological report of Madrid, 2014[49,e]	Regional registry	2001–2013	General	All ages	NA	2.6 HZ cases/1000 persons (all ages) 3.3 HZ cases/1000 persons (45–64 years) 6.8 HZ cases/1000 persons (65–84 years) 6.5 HZ cases/1000 persons (≥85 years)	NA
Regional epidemiological report of Aragon, 2016[63]	Regional registry	2015	General	All ages	NA	5.2 HZ cases/1000 persons (all ages)	NA
Regional epidemiological report of Balearic Islands, 2016[66]	Regional registry	2015	General	All ages	NA	3.7 HZ cases/1000 persons	NA
Muñoz-Quiles et al. 2016[41,b]	Prospective	2009–2014	COPD	≥50 years	NA	11.0 HZ cases/1000 person-years	NA
Muñoz-Quiles et al. 2016[40,a,f]	Retrospective	2009–2014	DM	≥50 years	NA	9.4 HZ cases/1000 person-years	9.1–9.4

Esteban-Vasallo et al. 2014[48,b]	Prospective	2009–2012	DM, COPD, asthma, cardiovascular diseases, AIDS and cancer	≥18 years	81,541	DM: 9.4 HZ cases/1000 person-years COPD:11.4 HZ cases/1000 person-years Asthma: 6.9 HZ cases/1000 person-years Cardiovascular diseases: 10.5–12.4 HZ cases/1000 person-years AIDS: 12.5 HZ cases/1000 person-years Cancer: 10.0 HZ cases/1000 person-years	NA
Aldaz et al. 2013[53,b]	Retrospective	2006	DM	>30 years	409	15.3 HZ cases/1000 person-years	NA
García-Doval et al. 2010[36,b]	Retrospective	2003–2006	Patients with rheumatic diseases	≥18 years	106	6.56 HZ cases/1000 person-years	5.4–7.98
Muñoz et al. 2010[45,b]	Retrospective	1988–2006	Transplanted patients	Mean: 52.92 years	17	44.3 HZ cases/1000 persons	NA
Rodríguez-Moreno et al. 2006[46,b]	Retrospective	1995–2004	Transplanted patients	Mean: 38 years	4	4.9 HZ cases/1000 persons	NA
García-Vidal et al. 2009[50,b]	Retrospective	1999–2005	Patients with rheumatic diseases	Mean: 49.3 years	1	10.6 HZ cases/1000 persons	NA
Herrero et al. 2004[54,b]	Retrospective	1990–2002	Transplanted patients	Mean: 55.5 years	25	120.0 HZ cases/1000 persons	NA
Sempere et al. 1992[42,b]	Retrospective	1989–1991	Transplanted patients	≥14 years	5	238.1 HZ cases/1000 persons	NA
Miguel et al. 2011[35,a]	Retrospective	2000–2010	Patients with rheumatic diseases	Mean: 55 years	NA	27.0 HZ cases/1000 persons	25–29
Muñoz-Pérez et al. 1998[60,b]	Prospective	1993	Immunocompromised patients	17–80 years	77	70.0 HZ cases/1000 persons	NA
Jiménez-Pérez et al. 2006[61,b]	Retrospective	1998–2003	Transplanted patients	Mean: 62 years	1	58.8 HZ cases/1.000 persons	NA
Adell et al. 2004[51,b]	Prospective	1998–2000	Transplanted patients	>14 years	NA	NA	NA
Fernández et al. 2015[43,a]	Retrospective	NA	Immunocompromised patients	All years	900	60.0 HZ cases/1000 persons	NA
Álvarez-Argüelles et al. 2015[68,a]	Retrospective	2006–2014	Immunocompromised patients	Mean: 38.2 years	3	1.3 HZ cases/1000 persons	NA
Gilarranz et al. 2014[64,a]	Retrospective	2001–2013	Patients with CNS infections	Mean: 44.5–67.3 years	NA	400.0 HZ cases/1000 persons	NA
Catalán Eraso et al. 2012[52,a]	Retrospective	2006–2012	Patients with CNS infections	Mean: 51 years	14	357.14 HZ cases/1000 persons	NA
López Soria et al. 2012[57,a]	Retrospective	2000–2011	Patients with CNS infections	2–90 years	50	260.0 HZ cases/1000 persons	NA
López Méndez et al. 2010[65,a]	Retrospective	2000–2009	Patients with CNS infections	NA	NA	NA	NA

AIDS, acquired immunodeficiency syndrome; CI, confidence interval; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; NA, not available; HZ, herpes zoster.

[a] Abstract.

[b] Full article.

[c] Incidence rate (n/person-years) and incidence proportion (n/persons).

[d] This study partially includes results from reference Cebrián-Cuenca, 2010. Here is presented additional data not included in reference Cebrián-Cuenca, 2010.

[e] HZ incidence showed for population >50 years, additional information for other age ranges is available in the report.

[f] Subsequently, the study was found as full article.[72]

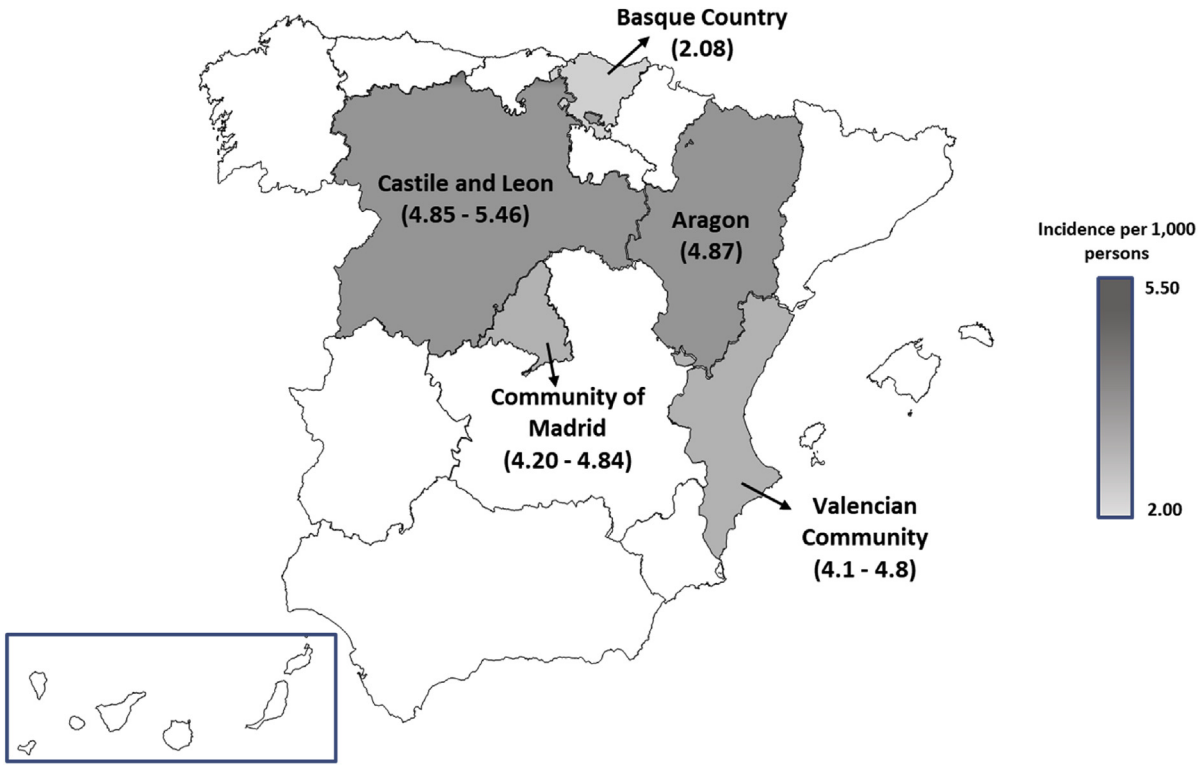

Fig. 2 – Incidence proportion of HZ in the general population by Autonomous Communities. The figure shows the HZ incidence proportions reported for some regions which were found during the review. Differences on the values (incidence per 1000 persons) between regions were highlighted using a coloured scale, from higher values in dark grey to lower incidences in light grey. HZ, herpes zoster. Adapted from the figure available in http://analisisydecision.es/trucos-excel-mapa-de-espana-por-comunidades-autonomas/.

respectively. Patients with COPD who received inhaled corticosteroids (ICSs)[41] had an HZ incidence rate of 13.0/1000 patient-years.

In patients with cardiovascular diseases (cardiopulmonary disease, ischaemic heart disease, heart failure, atrial fibrillation, and valvular pathology),[48] the incidence rate of HZ ranged from 10.5 to 12.4/1000 patient-years.

Only one study[48] evaluated the incidence rate of HZ in patients with asthma, which was 6.9/1000 patient-years.

Seventeen studies[35,36,42,43,45,46,48,50–52,54,57,60,61,64,65,68] showed the incidence rate of HZ in immunocompromised patients, ranging from 1.3 to 400/1000 person-years. Specifically, the incidence of HZ was 10.0/1000 cancer patient-years,[48] 12.5/1000 AIDS patient-years,[48] between 5 and 240/1000 transplant patients[42,45,46,54,61] and for rheumatic diseases of 6.6/1000 patient-years,[36] 10.6/1000 patients[50] and 27/1000 patient-years.[35]

Regarding the incidence of HZ in immunocompromised patients, only one study evaluating a cohort of 12 patients with neurological complications[65] concluded that immunosuppression was not a determining factor in patients with central nervous system involvement resulting from VZV infection because most of the patients progressed favourably after treatment with acyclovir.

Fig. 3 shows the incidence rates of HZ for each subgroup of patients.

Finally, three studies[40,41,53] determined that patients with DM or COPD have an increased risk of HZ compared with the general population. Muñoz-Quiles et al.[40] reported a 24% risk of acquiring HZ in patients with DM. Aldaz et al.[53] reported that patients with DM have a relative risk of 2.1% (95% CI: 1.9–2.4) compared with the general population, reaching 3.7 (95% CI: 2.0–6.8) in people aged 30–44 years. In the study by Muñoz-Quiles et al.,[41] the risk was 39% in patients with COPD and 61% in patients with COPD who received ICSs.

Discussion

To our knowledge, this is the first systematic review that evaluates the incidence of HZ in the general population and in specific subpopulations in Spain.

Our review shows annual HZ incidence rates in the general Spanish population that range from 2.08 to 5.46/1000 person-years and increases in women and older patients.

The results we obtained in relation to the incidence of HZ in the general population are very similar to those published in other systematic reviews.[9,18,69] For Spain, Kawai et al.[69] reported that the incidence rates of HZ ranged from 3.59 to 4.82/1000 inhabitants in the general population, and Pinchinat et al.[18] estimated an incidence of HZ to be 4/1000 inhabitants. The annual incidence of HZ in the adult population reported

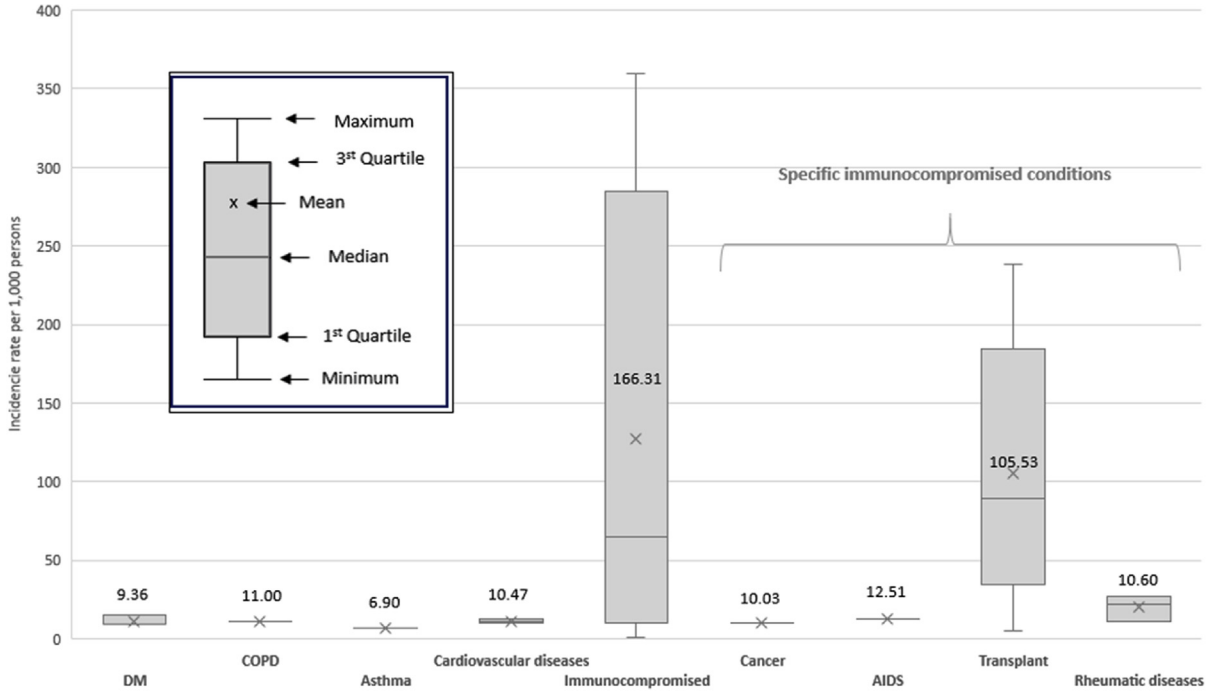

Fig. 3 – Incidence figures of HZ in the specific subpopulation. This figure is a box-and-whisker plot representing the incidence of HZ in the specific subpopulations. The two lines outside the box (whiskers) represent the maximum and minimum values of HZ incidence identified in the review for each subpopulation. The box spans the interquartile range of data, as the ends of the box correspond to the first and third quartile. Median value is indicated by a vertical line within the box. Mean value is showed by a cross and also is numerically specified in the figure. AIDS, acquired immunodeficiency syndrome; HZ, herpes zoster; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease.

for USA and other European countries[9] ranged from 3.6 to 14.2/1000 inhabitants.

For the specific subpopulations, the review shows that the highest incidence rates were associated with immunocompromised patients, followed by patients with cardiovascular diseases, patients with COPD and patients with DM.

The main limitation of the present study is the small number of localised publications as the literature regarding the incidence rates of HZ in the general population and specific subpopulations in Spain is scarce. Furthermore, it should be noted that the methodological heterogeneity (study population, observation period, data collection, age groups, geographical location and specific subpopulations) of the studies made it difficult to compare the results among studies. Additionally, data concerned only a few Spanish regions, making the extrapolation of conclusions more complex.

Half of the publications are communications to scientific congresses,[35,38,39,41,43,44,47,52,56–59,62,64,65,68] which limits the information available and hampers data extraction. Only one communication to scientific congresses was subsequently localised as a full-text article.[70]

One of the sources of incidence data is the official regional epidemiological reports issued by the Health Councils of the Autonomous Communities, which provides robust and standardised information. However, these documents are not indexed in bibliographic databases, making them difficult to find and extract data. It would be of great interest if health authorities promoted the routine publication of epidemiological data in scientific journals, which would lead to greater dissemination and facilitate the identification and localisation of these data.

The sustainability objective of health systems, which have been established in some countries including Spain,[71] requires the efficient allocation of the scarce available healthcare resources.[72] In terms of health policy related to preventive measures—such as vaccination—any information that helps determine the groups most likely to benefit is valuable to establish priorities for the implementation of public health programmes.

The present study, despite its limitations, aims to shed light on the available evidence of the epidemiological situation of HZ in Spain, focussed on the existence of specific subpopulations. The limitations described here have prevented quantitative data analysis of the information, although conclusions can be drawn from the qualitative analysis. There is a need for further research and publication of data to increase knowledge of HZ epidemiology and to improve understanding of patient populations with specific conditions that may be potential risk factors for HZ. This will help improve the reliability and robustness of the evidence base.

To date, figures for the impact of HZ vaccination programme in Spain are not available. Despite the heterogeneity of the reviewed studies, this review identified high-risk population subgroups for HZ compared with the general population.

Until now, figures about repercussion of HZ vaccination programme in Spain are not available.

The implementation of a future non-routine HZ vaccination programme would require definition of priority groups for vaccine administration. The results here could be helpful for decision makers to establish recommendations based on the existence of potential risk factors for HZ. The possibility of using a vaccine in the immunocompromised population and the duration of protection may be important factors in assessing the maximum benefit of the HZ vaccination programme.

Author statements

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Author contributions

R.M. and M.A.C. conceived this systematic review. M.M. and I.O. identified the eligible studies, analysed the data, did the literature search and wrote the initial draft of the manuscript. M.M prepared the tables. M.M., I.O., M.A.C. and R.M. interpreted the results. All authors had full access to the data and approved the final version of the article for submission.

Ethical approval

None declared.

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Competing interests

R.M. is an employee of the GSK group of companies and holds shares in this entity. M.M., I.O. and M.A.C. are employees of PORIB that received consultancy fees for the conduct of this study.

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Appendix A. Supplementary data

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