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Temporal trends in incidence rates of herpes zoster among patients treated in primary care centers in Madrid (Spain), 2005—2012

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Summary *Objectives:* This study aimed to estimate total and age-specific incidence rates of HZ with data from electronic clinical records in primary care (ECRPC) and to analyze trends by sex and age.
Methods: Descriptive cross-sectional study covering the incident HZ episodes registered in the ECRPC of the Madrid Regional Public Health System in 2005—2012. Annual crude and age-adjusted incidence rates were calculated. Differences by sex and age were assessed by poisson regression. The annual percentage of change (APC) of incidence rates and 'breakthrough points' of the time trends were determined with the Joinpoint Regression Program.
Results: 211,650 episodes of HZ were identified (60.6% women, 52.2% > 55 years). The incidence rate increased from 363.21 to 481.92 per 100,000 person-year in 2005—2012. Rates were higher among women and increased with age. The APC for the period was 3.59% in men and 3.67% in women ($p < 0.05$). Age-specific rates increased in patients over 14 years. The APC in the 25—44 age group was 7.4% since 2007. The incidence rate ratio (women/men) was highest in this group.
Conclusions: The incidence of HZ presents an upward trend in 2005—2012 in adults and the elderly. Monitoring the incidence and age-specific rates, will help to detect changes in trends.

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Introduction

Herpes zoster (HZ) results from the reactivation of latent varicella zoster virus (VZV). The triggers for reactivation of VZV have not been identified and probably involve multiple factors. However, specific components of cell-mediated immunity (CMI) have an important role in controlling the development of zoster by preventing reactivation within the neuron or the full clinical expression of reactivated VZV as zoster. The effectiveness of these protective components of CMI is well maintained in immunocompetent persons during childhood and early adulthood. These CMI components are believed to be partially or substantially maintained by periodic immunologic boosting.[1]

A recent literature review of population-based studies of HZ incidence in Europe published between 1960 and 2010, showed similar HZ incidence across the included countries for which data was available.[2] Overall annual incidence varied from 2.0 to 4.6/1000 person-years depending on the country,[2] which is consistent with previous published estimates.[3] The lifetime risk of zoster is estimated to be 10—30% and incidence increases markedly with age, affecting up to 50% of people who live to 85 years.[4,5] The risk approximately doubles for each decade after 50 years of age.[6] This age-related increase in HZ is due to a varicella zoster virus-specific decline in CMI with increasing age.[7] About 5—18% of persons with HZ develop post-herpetic neuralgia, a disabling pain syndrome that can last months or even years with no consistently effective treatments.[8—10] HZ imposes a significant burden of hospitalizations and results in large cost expenses, especially in population older than 50 years of age, with an annual hospitalization rate of 10.0 per 100,000 habitants and an average cost per hospitalization of more than 3500 €.[11,12]

It has been speculated that a universal varicella vaccination program might alter the epidemiology of HZ due to the expected decline of the boosting of CMI caused by the reduced varicella circulation.[13] The mechanism of exogenous boosting exists, although not for all persons, nor in all situations.[14] Studies modeling the impact of a varicella vaccination program have predicted that cases of zoster may significantly increase in the first 50 years following vaccination.[15—17] However, other model-based evaluations show that, after varicella immunization, an increase of HZ incidence is not a certainty. Rather, it depends on the presence or absence of factors promoting a strong boosting intensity, which may or may not be heavily affected by changes in varicella circulation due to mass immunization.[18] In 2006 the Madrid Autonomous Region included universal varicella vaccination in its systematic vaccination schedule for children aged 15 months.[19]

The objectives of this study were to estimate total and age-specific incidence rates of herpes zoster on the basis of data drawn from electronic clinical records in primary care (ECRPC), and to analyze their temporal trends by sex and age.

Materials and methods

We performed a descriptive cross-sectional study covering all the HZ episodes registered in the ECRPC of the Madrid Regional Public Health System (MRPHS) for the period 2005—2012.

The target study population was defined as all persons included in the MRPHS, and therefore registered in the Individualized Health Card (IHC) database, from 1st January 2005 to 31st December 2012. IHC coverage was close to 95% of the population.

Health care data were drawn from ECRPC, implemented for 99% of primary care (PC) physicians in 2005, and with full implementation since 2006. In our region, health care episodes are registered in electronic clinical records by health professionals, coded as per the International Classification for Primary Care (ICPC), issued by the World Organization of Family Doctors (WONCA). For data extraction purposes, the strategy adopted was to select all episodes coded as S70, which corresponds to herpes zoster. For each episode, the following information was obtained: accompanying descriptive text, onset date and recording date of the episode; sex, birth date and clinical history number of the patient; and health center code. Age was calculated at the episode onset. When the year of onset of the episode and the recording year were coincident, the episode was considered as incident in that year.

The descriptive clinical text accompanying the ICPC code S70 was used to discard episodes that clearly did not correspond to herpes zoster or when an HZ code was given for a diagnosis of history of HZ or family history of HZ in a person with no evidence of an acute HZ episode. After this depuration, all remaining incident episodes were considered for the analysis. When a patient had more than one incident episode registered in the ECRPC, these were considered different cases of the disease.

Descriptive analysis of patients' characteristics was performed stratified by sex. Differences in continuous variables were assessed by Student's *t* test.

Annual crude and age-adjusted incidence rates were calculated for new cases of herpes zoster consulting in PC. The denominator used was population included in the MRPHS in the middle of the year (30 June of each year). For 2005, the denominator was the population at year-end 2005, excluding the proportion assigned to physicians having no records that year: a total of 52 physicians did not have electronic clinical records, accounting for 1% of the IHC population. Rates were adjusted by age using the direct method (European standard population).

Poisson regression was used to assess differences by sex and age in annual incidence rates during the study period. Age-specific annual incidence rate ratios, and global incidence rate ratio by sex (women/men) were calculated. Joinpoint models and the Joinpoint Regression Program were used to analyze time trends of the incidence rates and identify points where a significant change in the linear slope of the trend occurred. This method, which uses straight broken-line regression, allows for determining 'breakthrough points' of the time trends. The annual percentage of change (ACP) of incidence rates for each segment of the straight broken-lines was also calculated, together with corresponding 95% confidence intervals.[20]

The significance level used was $p < 0.05$. Statistical analyses were performed using Epidat 3.1, Stata 10.0 software and the *Joinpoint* program version 4.0.4 from the *Surveillance Research Program* of the *US National Cancer Institute*.