



Short communication

## Varicella vaccination coverage inverse correlation with varicella hospitalizations in Spain

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### ABSTRACT

Varicella vaccines available in Spain were marketed in 1998 and 2003 for non-routine use. Since 2006 some regions included universal varicella vaccination in their regional routine vaccination programs at 15–18 months of age. Regions without universal vaccination in toddlers, but instead with the strategy of vaccinating susceptible adolescents, reached different varicella vaccination coverage through private market.

This study shows the correlation between severe varicella zoster virus infections requiring hospitalization and the varicella vaccination coverage by region.

A total of 3009 hospital discharges related to varicella were reported in 2009–2010. The overall annual rate of hospitalization was 3.27 cases per 100,000. In children younger than 5 years old varicella hospitalization rate was 30.73 cases per 100,000.

Varicella related hospitalizations were significantly lower in the regions with universal vaccination. In those regions without universal vaccination at 15–18 months of age, those with higher coverage in private market showed lower hospitalization rates.

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In the absence of vaccination, varicella affects almost all children in the course of their childhood [1]. Varicella is usually mild in immunocompetent children, but can cause severe complications and even fatalities [2]. In the United States, a major reduction in the varicella incidence was observed after the introduction of varicella vaccination, not only of cases of varicella but also of hospitalizations due to its complications [3]. In other countries like Australia [4], Germany [5], Canada [6], or Italy (Region of Veneto) [7] universal childhood vaccination against varicella has reached similar effects.

Varicella is a notifiable disease in Spain. 141,339 and 157,914 cases were reported to the National System of Notifiable Diseases (EDO) in 2009 and 2010, respectively (<http://www.isciii.es/ISCIII/es/contenidos/fd-servicios-cientifico-tecnicos/fd-vigilancias-alertas/fd-enfermedades/enfermedades-declaracion-obligatoria-series-temporales.shtml>).

The Advisory Committee on Vaccines (CAV) of the Spanish Association of Paediatrics (AEP), taking into account epidemiological data as well as evidence on the safety, effectiveness and efficiency of vaccines, recommends the administration of the first dose of the

varicella vaccine at age 12 months and the second dose at age 2–3 years [8].

Starting in late 2006, four regions of Spain – Madrid (1-dose) and Navarra, Ceuta and Melilla (2 doses since 2007) – included varicella vaccination in their routine childhood schedule at 15–18 months of age [9]. The other 15 autonomous regions vaccinate susceptible children at 10–14 years with one or two doses but, in these 15 regions, infant vaccination is neither financed nor reimbursed by the public health care system. Following the recommendations of the AEP, paediatricians prescribe varicella vaccination at 12–18 months of age with an important number of children being vaccinated with the parents paying the full cost of vaccination. The estimated vaccination coverage in these regions was 32% in 2009–2010, ranging from 13% to 64% (vaccine distribution data provided by IMS Health).

This epidemiological study aimed to describe population-based data on the burden of hospitalization for varicella in 2009–2010 according to the varicella vaccination coverage in the different Regions in Spain.

The Spanish centralized hospital discharge database (CMBD: Conjunto Mínimo Básico de Datos) includes more than 98% of hospitalizations in the Spanish health care system, which covers 99.5% of the population [10]. It has been used for research purposes including epidemiological studies on varicella [11].

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All varicella related hospitalizations reported from January 1st, 2009 through December 31st, 2010 were analyzed. The 9th International Classification of Diseases ICD-9-CM codes for varicella (052.X) were selected.

The annual incidences of hospitalizations both in the general population and in children under 5 years old were calculated. Data were also obtained by Autonomous Region.

Spearman correlation was used for assessing the association between the hospitalization rates and the vaccination coverage. Data on vaccination coverage by region were obtained from distribution data provided by IMS Health.

In all test the significance level used was  $p < 0.05$ . Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS/PASW, version 19.0; Chicago, IL) and R, version 2.15.3 (R Core Team, 2013, Vienna, Austria).

A total of 3009 hospital discharges related to varicella were reported in 2009–2010. The overall annual rate of hospitalization was 3.27 (CI 95%: 3.16–3.39) cases per 100,000. Of those, 1472 hospitalizations occurred in children up to 5 years old with a rate of hospitalization of 30.73 (CI 95%: 29.16–32.30) cases per 100,000. Six percent of the patients hospitalized were immunocompromised.

Varicella was coded as principal diagnosis in 66% of the hospitalizations, of those, 45.8% were coded as varicella, 26.8% as hemorrhagic pneumonitis, 22.6% complications of varicella, 4.5% encephalitis and 0.3 myelitis.

There were 42 deaths related to varicella infection during the study period, all of them occurred in immunocompromised patients.

In Table 1, the 17 Autonomous Regions and the 2 Autonomous Cities are grouped regarding the varicella vaccination coverage and their hospitalization rates during the period. There is an inverse linear correlation between vaccination coverage and hospitalization rates during the 2009–2010 period, both for all age population ( $Rho = -0.850$ ,  $p < 0.001$ ) and for children up to 5 years old ( $Rho = -0.496$ ,  $p = 0.036$ ). If we only consider non-routine

vaccination regions (Madrid, Navarra, Ceuta and Melilla excluded) the inverse linear correlation for all age population remains significant ( $Rho = -0.717$ ,  $p < 0.001$ ). It is not the case for children up to 5 years old ( $Rho = -0.148$ ,  $p = 0.597$ ).

Fig. 1 shows the hospitalization rates related to varicella in the different autonomous regions. Navarra, Madrid, Ceuta, Melilla, Castilla León and Canary Islands showed lower hospitalization rates in the 2009–2010 period (1.37, 1.99, 1.29, 2.73, 1.91 and 1.93 per 100,000, respectively). The first four regions had universal coverage with vaccination coverage of nearly 90%, Castilla-León and Canary Islands do not have universal infant vaccination programs, but reached the highest coverage in the non-routine vaccination (64% and 46%, respectively). Among the rest of the regions, Cantabria and Murcia registered the highest hospitalizations rate (5.70 and 5.20 per 100,000, respectively (Fig. 1). These regions were among those with the lowest vaccination coverage (16% and 21% in the period 2009–2010, respectively).

This retrospective epidemiology study shows the hospitalization rates in the different regions of Spain. Importantly it highlights the inverse correlation between the varicella vaccination coverage in Spain and the incidence of hospitalizations.

The main finding of this study is that the hospitalization rates related to VZV infection in Spain are lower in the regions with universal vaccination and among those with non-routine vaccination but reaching high coverage compared to the regions with non-routine vaccination and low coverage. This pattern can also be observed in 2010 for hospitalizations occurred in children <5 years old, where more than 50% of the hospitalization occurred and which is the age group directly benefited by the vaccination. Our results show a potential beneficial effect from herd protection in older children and adolescents due to some reduction in the varicella circulation in the community. Important point to consider as the global prevalence of antibodies for varicella-zoster virus among young adults in a recent study in Spain was 92.8% [12].

**Table 1**  
Hospitalization rates by Autonomous Regions in Spain regarding the vaccination coverage.

Vaccination coverage <sup>a</sup>	Regions	Hospitalization rates (per 100,000)		
		2009 <sup>**</sup>	2010 <sup>***</sup>	2009–2010
<25%	Asturias, Baleares, Cantabria, Murcia	4.84	4.83	4.84
25–34%	Andalucía, Aragón, Castilla la Mancha, Cataluña, Galicia, P. Vasco	3.89	3.55	3.72
35–44%	Valencia, Extremadura, La Rioja	3.66	2.48	3.07
45–54%	Canarias	2.91	0.96	1.93
>55%	C. León <sup>****</sup>	2.67	1.16	1.91
Universal vaccination	Madrid, Navarra, Ceuta and Melilla	2.41	1.46	1.93
Vaccination coverage <sup>a</sup>	Regions	Hospitalization rates in children <5 (per 100,000)		
		2009 <sup>**</sup>	2010 <sup>***</sup>	2009–2010
<25%	Asturias, Baleares, Cantabria, Murcia	50.81	41.97	46.35
25–34%	Andalucía, Aragón, Castilla la Mancha, Cataluña, Galicia, P. Vasco	26.99	31.84	29.44
35–44%	Valencia, Extremadura, La Rioja	33.11	22.87	27.94
45–54%	Canarias	42.90	60.02	51.55
>55%	C. León <sup>****</sup>	36.87	53.55	45.33
Universal vaccination	Madrid <sup>b</sup> , Navarra, Ceuta and Melilla	17.30	7.04	12.08

<sup>a</sup> Distribution data provided by IMS Health.

Spearman correlation was used for assessing the association between the hospitalization rates and the vaccination coverage.

<sup>b</sup> A vaccine coverage of 92.7% has been considered for Madrid [García Comas L, Ordobás Gavín M, Cañellas Llabrés S, Gutiérrez Rodríguez A, Servicio de Epidemiología. Subdirección General de Promoción de la Salud y Prevención. Dirección General de Atención Primaria. Comunidad de Madrid. Boletín Epidemiológico de la Comunidad de Madrid. 2010; 7 (16) ISSN 1695-7059 <http://www.madrid.org/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobheadername1=Content-disposition&blobheadername2=cadena&blobheadervalue1=filename%3DJulio2010.pdf&blobheadervalue2=language%3Des%26site%3DPortalSalud&blobkey=id&blobtable=MungoBlobs&blobwhere=1271908141371&ssbinary=true>].

<sup>\*</sup> A vaccine coverage of 90% has been considered for Ceuta, Melilla and Navarra.

<sup>\*\*</sup> Coverage groups 2009: <25% (Asturias, Baleares, Cantabria, Murcia). 25–34% (Andalucía, Aragón, Castilla la Mancha, Catalonia, Galicia, Basque Country). 35–44% (Valencia, Extremadura, La Rioja). 45–54% (Canary Islands). >54% (Castilla Leon) and Systematic vaccination (Madrid, Navarra, Ceuta, Melilla).

<sup>\*\*\*</sup> 2010: <25% (Asturias, Baleares, Cantabria, Murcia). 25–34% (Andalucía, Castilla la Mancha, Catalonia, Galicia, Basque Country). 35–44% (Aragón, Valencia, Extremadura, Canary Islands). 45–54% (La Rioja). >54% (Castilla Leon) and Systematic vaccination (Madrid, Navarra, Ceuta, Melilla).

<sup>\*\*\*\*</sup> Vaccination coverage in Castilla y León for the study period (2009–2010) was 64%.

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