

Impact of Penicillin Allergy Label on Length of Stay and Mortality in Hospitalized Patients through a Clinical Administrative National Dataset

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Keywords

Penicillin allergy · Length of stay · Electronic medical record · Healthcare resources

Abstract

Background: Penicillin allergy is a common problem in the management of infectious diseases. The aim of this study was to determine the impact of penicillin allergy on length of hospital stay (LOHS) among hospitalized adult patients and on in-hospital mortality at a national level. **Methods:** A retrospective cohort study of adult patients discharged from the Spanish Hospital System between 2006 and 2015 was conducted using the Minimum Basic Data Set (MBDS). We compared LOHS and in-hospital mortality of adult patients whose records contained penicillin allergy code V14.0 (International Classification of Diseases, Ninth Revision, Clinical Modification) as a secondary diagnosis, with a random sample without such a code. **Results:** We identified 981,291 admissions with code V14.0, which corresponded to 2.63% of all hospitalizations. Adults patients with a penicillin allergy label were significantly older than patients without such a

label, with a median of 70 years (interquartile range [IQR]: 51–80) versus 63 years (IQR: 40–77). The proportion of women and the prevalence of infectious diseases were higher in the group with a penicillin allergy label (61.40% vs. 53.84%; 34.04% vs. 30.01%; respectively). We found a higher median Elixhauser-Van Walraven score in hospitalized patients with an allergy label. The median LOHS for hospitalizations with a penicillin allergy label (5 [IQR: 2–9]) was significantly longer than that in those without such a label (4 [IQR: 2–9]). Multivariate analysis showed an increase in LOHS due to the penicillin allergy label (odds ratio [OR] [95% confidence interval [CI]: 1.061 [1.057–1.065]) and a decrease in mortality in penicillin allergy records (OR [95% CI]: 0.834 [0.825–0.844]). **Conclusion:** In our study, the prevalence of a penicillin allergy label in hospitalized patients, using the MBDS, is low. Hospitalizations with an allergy label was associated with a longer LOHS. However, penicillin-allergic patients did not show higher mortality rates. Inaccurate reporting of penicillin allergies may have an impact on healthcare resources.

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Introduction

Drug allergy is a common problem in clinical practice. However, an accurate true frequency is unknown. Allergy to beta-lactams is considered one of the most reported drug allergies in our environment, with a prevalence that ranges from 5% to 10% of the population [1] and reaches 15% in hospitalized patients [2, 3]. Nevertheless, after performing an allergic workup of patients with a suspected diagnosis of allergy to beta-lactams, >80% turned out to be negative [4, 5] and, therefore, had been incorrectly labeled as penicillin-allergic [6].

In hospitalized patients with a personal history of allergy to beta-lactams, an overuse and overprescription of broad-spectrum antibiotics, such as vancomycin and fluoroquinolones [7], have been observed. Several authors have demonstrated that the prescription of second-line antibiotics has a positive effect on the emergence of resistant strains [8]. Thus, over time, the excessive intake of fluoroquinolones is associated with the onset of multiresistant strains of *Pseudomonas aeruginosa* [9], whereas the overprescription of vancomycin is associated with outbreaks of vancomycin-resistant *Enterococcus sp.* or methicillin-resistant *Staphylococcus aureus* [10]. In addition, the increase in cases of colitis due to *Clostridioides difficile*, associated with the use of fluoroquinolones [11], must be considered.

Last, some studies have shown that costs are 4 times higher when the treatment of hospitalized patients is changed to second-line antibiotics as a consequence of misdiagnosed hypersensitivity reactions [12]. Other studies of patients with beta-lactam allergy have also shown an increase in healthcare costs compared to nonallergic patients [13]. The impact of mislabeling patients as allergic to beta-lactams is also displayed in the consensus article between several scientific societies and in antibiotic stewardship in Spanish hospitals, as well as, recently, in primary care [14].

While observational studies regarding the incidence of suspected allergy to antibiotics and, especially, to beta-lactams in hospitalized patients exist, there are none in Spain that allow us to ascertain the effect of labeling a patient as allergic to penicillin nor the morbidity and mortality based on the use of hospital resources. The aim of this study was to determine the impact of penicillin allergy on length of the hospital stay (LOHS) and mortality in hospitalized adult patients at a national level.

Materials and Methods

Study Design and the Setting

A retrospective cohort study of adult patients discharged from the hospitals of the Spanish Hospital System between 2006 and 2015, using the administrative records of the Minimum Basic Data Set (MBDS), was conducted. The MBDS [15] is the largest administrative database maintained in Spain that contains standardized clinical data of hospitalized patients and is the main source of information on morbidity. It includes, for each hospitalization, information about the patient's demographics, coding of the main diagnosis, up to 14 secondary diagnoses, and 20 procedures – according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) until 2015 [16], as well as information about LOHS, reasons for discharge, and costs, among others.

In addition, various studies have used this registry or similar ones, at a national or international level, to estimate the incidence of allergic reactions to drugs among hospitalized patients, as well as for studies on different allergic diseases [17, 18]. However, such studies have identified underreporting and possible errors in the coding as some of the disadvantages of these registers, even though this tool provides valuable information based on the mandatory nature of its completion, either private or public hospital activity [19].

Population (or Selection of Cases)

A case is defined as any record of hospitalization of patients over 17 years of age that contains, as a secondary diagnosis in its MBDS, the code described as penicillin allergy: V14.0 (ICD-9-CM). A random sample of adult patients from the total national cohort submitted was taken to perform the selection of controls, and the episodes that included a secondary diagnosis with code V14.0 were excluded.

Data Analysis

We defined LOHS as the number of days between the discharge date and the hospital admission date. Mortality was defined as the number of hospitalization episodes in which death was the reason for hospital discharge.

The influence of comorbidities in each admission was determined by applying the Elixhauser score – modified by Van Walraven – to all hospitalization records. This score is associated with longer hospital stays, higher hospital costs, and death [20]. The Elixhauser comorbidity index score [21] includes 30 types of comorbidities from different groups of diseases, including cardiovascular system (6), neurological (2), pulmonary (1), endocrinological and nutritional diseases (5); kidney failure (1); digestive disease (2); HIV infection (1); cancer (3); connective tissue disease (1); hematological disease (3); alteration of the fluid and electrolyte balance (1); substance abuse (2); and psychiatric illness (2).

We assessed the influence of an infectious disease diagnostics among hospitalized patients in Spain [22] by using the ICD-9-CM codes related to the most prevalent infections, such as respiratory infection, urinary infection, intra-abdominal infection, post-surgery infection, skin and soft tissue infection, bacteremia, and obstetric-gynecologic infection [16]. The same analysis was performed with all records that included at least one infectious disease code.

Table 1. Demographic and clinical characteristics in hospitalized adults with and without a penicillin allergy label

Variable	Hospitalizations with a penicillin allergy label (n = 969,916)	Hospitalizations without a penicillin allergy label (n = 3,309,006)	p value
Age, years			
Median (IQR)	70 (51–80)	63 (40–77)	<0.001 ^a
Sex, n (%)			
Men	374,388 (38.60)	1,527,437 (46.16)	<0.001 ^b
Women	595,528 (61.40)	1,781,569 (53.84)	<0.001 ^b
Secondary diagnoses, n			
Median (IQR)	6 (4–9)	4 (2–7)	<0.001 ^a
Elixhauser-Van Walraven score			
Median (IQR)	3 (0–9)	2 (0–9)	<0.001 ^a
Infectious diagnosis, n (%)	330,195 (34.04)	993,344 (30.01)	<0.001 ^b
Respiratory infection	159,493 (16.44)	414,320 (12.52)	<0.001 ^b
Intra-abdominal infection	61,390 (6.32)	184,686 (5.58)	<0.001 ^b
Urinary infection	55,778 (5.75)	171,579 (5.18)	<0.001 ^b
Gynecol-obstetric infection	25,232 (2.60)	127,751 (3.86)	<0.001 ^b
Skin and soft tissue infection	14,632 (1.51)	46,824 (1.42)	<0.001 ^b
Post-surgery infection	10,771 (1.11)	30,282 (0.91)	<0.001 ^b

IQR, interquartile range. ^a Mann-Whitney U test (Prob >z). ^b χ^2 test.

Statistical Analysis

Categorical variables were reported as counts and percentages and were compared with the χ^2 test or Fisher's exact test. Quantitative variables were described by the mean and standard deviation or by the median and interquartile range (IQR). The normal distribution of the quantitative variables was checked with the Shapiro-Wilk test, using the Student's *t* test or the Mann-Whitney U test.

A univariate regression analysis was performed to identify variables to assess their connection to LOHS. Age was organized into 2 groups: older or younger than the median age (years). The Elixhauser-Van Walraven score was divided into 4 quartiles depending on the outcome (strata 1: from –9 to –1; strata 2: from 0 to 4; strata 3: from 5 to 9; and strata 4: from 10 to 30). The year of admission was categorized into 5 periods. Subsequently, a multivariate logistic regression model, which included the penicillin allergy label, was built. Regarding mortality, several simple logistic regression models with the same covariates were used. The odds ratio (OR) was estimated to be at 95% confidence interval (CI). Statistical analysis was performed using Stata/MP v16.1.

Results

Study Data

The number of hospitalizations in Spain recorded in the national MBDS from 2006 to 2015 was 36,856,032 [23]. According to the request made to the Spanish Ministry of Health on July 30, 2018, we received a cohort that included all hospitalizations with code V14.0 in any of the 14 secondary diagnoses (981,291 records)

and 10% of the remaining hospitalizations during that same period, which were randomly selected (3,685,612 records).

The records with code V14.0 represented 2.63% of all hospitalizations in Spain between 2006 and 2015. Regarding the distribution of the penicillin allergy label performed by the autonomous communities (the first administrative division in Spain), the percentages ranged from 1.41% in the Basque Country to 3.32% in Asturias. For each autonomous community, the median percentage of records with code V14.0 was 2.45% (IQR: 1.88–3.01; $p < 0.001$). The total number of childhood hospitalizations (under 18 years of age) was 386,685, which represented 1.03% of the hospitalizations with code V14.0 and 10.21% of those without a label.

Demographic and Clinical Characteristics of the Records

The demographic and clinical characteristics in hospitalized adults with and without code V14.0 are shown in Table 1. Patients with a penicillin allergy label were significantly older than patients without such a label, median 70 years (IQR: 51–80) versus 63 years (IQR: 40–77) ($p < 0.001$), respectively. The number of women in the group of penicillin-allergic patients was higher (61.40% vs. 53.84%, $p < 0.001$). Patients with a penicillin allergy label had a higher prevalence of infectious diseases (34.04% vs. 30.01%, $p < 0.001$). Hospitalized patients with

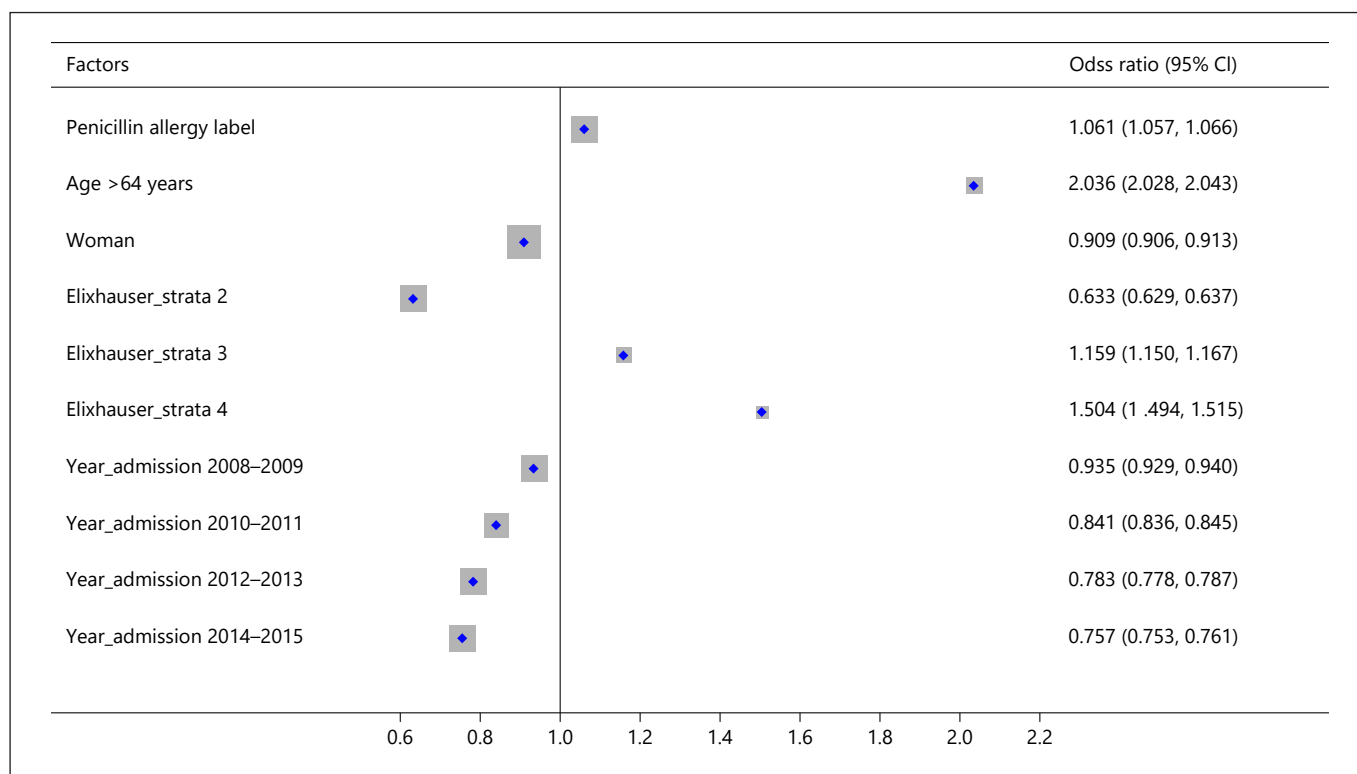


Fig. 1. Risk factors associated with LOHS. Results of the multivariate logistic analysis. LOHS, length of the hospital stay; OR, odds ratio; CI, confidence interval.

a penicillin allergy label had a significantly higher median Elixhauser score ($p < 0.001$).

Crude Analysis for Outcome Variables

Overall, the median LOHS of hospitalizations with a penicillin allergy label (5 [IQR: 2–9]) was significantly longer than that in those hospitalizations without a penicillin allergy record (4 [IQR: 2–9]), according to the Mann-Whitney U test ($p < 0.001$). Mortality was lower in the group with a penicillin allergy label (4.35%) versus that without a label (4.61%) ($p < 0.001$).

Univariate and Multivariate Logistic Regression Models

To estimate the risk factors associated with a longer LOHS, we calculated the OR from univariate logistic regression models. Age older than 64 years (OR: 2.531 [95% CI: 2.522–2.539]) and comorbidities by the Elixhauser score (strata 3 OR: 1.414 [95% CI: 1.404–1.424] and strata 4 OR: 1.917 [95% CI: 1.903–1.939]) were associated with higher risk of a longer LOHS, while to be a woman (OR: 1.414 [95% CI: 1.404–1.424]) and the

admission year were associated with lower risk of LOHS.

The multivariate logistic regression model, which included the penicillin allergy label covariate and the other variables, showed that this label increased LOHS (OR: 1.061, 95% CI: 1.057–1.065), age to over 64 years of age (OR: 2.035, 95% CI: 2.028–2.043), and Elixhauser score strata 3 and 4. On the other hand, the factors that decreased LOHS were the most recent periods of the year of admission, sex (female), and Elixhauser score strata 2 (shown in Fig. 1). Regarding mortality (Table 2), we obtained that a penicillin allergy label protects against death during admission (OR: 0.834, 95% CI: 0.825–0.844).

Analysis of Infectious Disease Hospitalizations

Out of the records, 30.93% of hospitalizations had at least one code of infectious disease diagnostics. Patients with an infectious disease code were significantly older than patients without such codes, with a median age of 72 years (IQR: 52–81) versus 64 years (IQR: 43–78) ($p < 0.001$). The median age among infected patients was also significantly higher in the group with a penicillin allergy

Table 2. Analysis adjusted for mortality by covariates: penicillin allergy label, age, woman, Elixhauser score, and year of admission

Covariate	Mortality			
	adjusted OR	<i>p</i> > <i>z</i>	95% CI, lower limit	95% CI, upper limit
Penicillin allergy label	0.834	0.000	0.825	0.844
Woman	0.942	0.000	0.933	0.951
Age >64 years	3.417	0.000	3.374	3.461
Elixhauser score				
Strata 1	1			
Strata 2	1.180	0.000	1.142	1.219
Strata 3	3.210	0.000	3.108	3.315
Strata 4	7.294	0.000	7.069	7.526
Year of admission				
2006–2007	1			
2008–2009	0.978	0.004	0.963	0.992
2010–2011	0.936	0.000	0.922	0.950
2012–2013	0.904	0.000	0.891	0.918
2014–2015	0.894	0.083	0.880	0.907

Elixhauser score: strata 1: –9 to –1; strata 2: 0–4; strata 3: 5–9; and strata 4: 10–33. OR, odds ratio; CI, confidence interval.

Table 3. Analysis adjusted for mortality and length of the stay by covariates: penicillin allergy label, age, sex, Elixhauser score, and year of admission, in records with infectious disease codes

Covariate	Length of stay				Mortality			
	adjusted OR	<i>p</i> > <i>z</i>	95% CI, lower limit	95% CI, upper limit	adjusted OR	<i>p</i> > <i>z</i>	95% CI, lower limit	95% CI, upper limit
Penicillin allergy label	0.984	0.000	0.991	1.001	0.800	0.000	0.787	0.814
Woman	0.749	0.000	0.745	0.754	0.910	0.000	0.898	0.923
Age >72 years	1.634	0.000	1.623	1.644	2.368	0.000	2.330	2.406
Elixhauser score								
Strata 1	1				1			
Strata 2	0.728	0.000	0.719	0.736	1.177	0.000	1.123	1.234
Strata 3	1.371	0.000	1.353	1.389	3.211	0.000	3.064	3.364
Strata 4	1.748	0.000	1.725	1.770	6.013	0.000	5.745	6.293
Year of admission								
2004–2005	1				1			
2006–2007	0.930	0.000	0.921	0.940	0.966	0.003	0.944	0.988
2008–2010	0.840	0.000	0.832	0.849	0.941	0.096	0.920	0.962
2011–2012	0.780	0.000	0.772	0.787	0.915	0.180	0.895	0.936
2013–2015	0.759	0.000	0.751	0.766	0.891	0.083	0.872	0.911

Elixhauser score: strata 1: –9 to –1; strata 2: 0–4; strata 3: 5–9; and strata 4: 10–33. OR, odds ratio; CI, confidence interval.

label, being 74 years (IQR: 59–82) versus 70 years (IQR: 49–81) in that without such a label ($p < 0.001$); additionally, there was also a higher proportion of women (58.12% vs. 51.18%, respectively). The median Elixhauser comorbidity index score was 2 (IQR: 1–4).

Concerning LOHS, in the multivariate regression analysis, the OR for the penicillin allergy label was 0.984 (95% CI: 0.977–0.991). Regarding mortality, in the subgroup with several infectious disease codes, we found, in the multivariate regression logistic model, that a penicil-

Table 4. Analysis adjusted for length of the stay by covariates: penicillin allergy label, age, sex, Elixhauser score, and year of admission, in records with infectious disease codes

Infection/covariate	Hospitalizations, <i>n</i>	Length of stay			
		adjusted OR	<i>p</i> > <i>z</i>	95% CI, lower limit	95% CI, upper limit
Respiratory	573,813				
Penicillin allergy label		0.839	0.000	0.830	0.848
Woman		1.090	0.000	1.079	1.101
Age > median years		0.993	0.194	0.983	1.003
Elixhauser score		1.184	0.000	1.179	1.189
Year of admission		0.935	0.000	0.932	0.938
Intra-abdominal	246,076				
Penicillin allergy label		0.929	0.000	0.914	0.945
Woman		0.736	0.000	0.725	0.747
Age > median years		2.088	0.000	2.057	2.119
Elixhauser score		1.304	0.000	1.295	1.312
Year of admission		0.897	0.000	0.892	0.901
Urinary	227,357				
Penicillin allergy label		0.901	0.000	0.886	0.917
Woman		1.077	0.000	1.060	1.093
Age > median years		1.387	0.000	1.366	1.409
Elixhauser score		1.300	0.000	1.291	1.309
Year of admission		0.921	0.000	0.916	0.926
Gynecol-obstetric	152,983				
Penicillin allergy label		1.156	0.000	1.127	1.186
Woman		0.825	0.365	0.544	1.251
Age > median years		1.096	0.000	1.075	1.117
Elixhauser score		0.886	0.000	0.875	0.898
Year of admission		0.999	0.795	0.992	1.005
Skin and soft tissue	61,456				
Penicillin allergy label		0.984	0.369	0.951	1.018
Woman		1.000	0.969	0.970	1.031
Age > median years		1.959	0.000	1.900	2.021
Elixhauser score		1.231	0.000	1.215	1.248
Year of admission		0.951	0.000	0.941	0.961
Post-surgery	41,053				
Penicillin allergy label		0.928	0.003	0.884	0.975
Woman		0.968	0.145	0.926	1.011
Age > median years		1.607	0.000	1.539	1.679
Elixhauser score		1.415	0.000	1.387	1.443
Year of admission		0.894	0.000	0.880	0.908
Bacteremia	27,150				
Penicillin allergy label		0.833	0.000	0.785	0.883
Woman		0.901	0.000	0.859	0.945
Age > median years		0.846	0.000	0.807	0.887
Elixhauser score		1.224	0.000	1.199	1.250
Year of admission		0.921	0.000	0.906	0.937
Ear, nose, throat	9,545				
Penicillin allergy label		1.236	0.000	1.135	1.347
Woman		1.065	0.085	0.991	1.145
Age > median years		2.308	0.000	2.140	2.489
Elixhauser score		1.748	0.000	1.674	1.825
Year of admission		0.930	0.000	0.906	0.954

OR, odds ratio; CI, confidence interval.

lin allergy label acted as a protector (OR: 0.800, 95% CI: 0.787–0.814); as shown in Table 3.

Table 4 summarizes the OR for LOHS of the most prevalent infectious diseases. LOHS was longer in the records with codes related to obstetric infections and in those records that contained ear, eye, or nose infection codes.

Discussion

In this large cohort study designed to explore the impact on LOHS and in-hospital mortality of labeling patients as penicillin-allergic in the Spanish Hospital System, we found that a penicillin allergy label was associated with an increase in LOHS. On the other hand, we observed lower in-hospital mortality in hospitalizations with a penicillin allergy label.

Based on the registry of patients that were admitted to the Spanish Hospital System (MBDS) between 2006 and 2015, we identified a lower prevalence of a penicillin allergy label in hospitalized patients than that described by other authors [24, 25], as well as significant differences depending on the region of Spain. It is difficult to determine the true prevalence of penicillin allergy in hospitalized patients through different studies because the methodology is not common. Macy and Contreras [10], in a retrospective study that used a clinical administrative database, reported a cohort with 51,807 cases (penicillin allergy-labeled) that represented 11.2% of all hospitalized patients. A small study of hospitalized patients in internal medicine wards, based on the computerized database, discovered an estimated prevalence of 6.12%; however, the authors concluded that in-hospital prevalence was much higher due to an observed under-registration [26]. On the other hand, a recent Portuguese study, from 2000 to 2014, which also used the MBDS, identified 102,872 hospitalizations with the penicillin allergy code, according to the ICD-9-CM, which corresponded to 0.9% of all adult hospitalizations in public hospitals (<1% admissions) [27]. Although the prevalence in our study can be considered low, it was almost 3 times higher than that of the Portuguese study, which only included adults and public hospitals.

The validity of the MBDS depends on the availability of a full clinical report and the high quality of the coding of the administrative and clinical variables. An audit that took place in 8 public hospitals of the Region of Murcia in Spain, in which 796 records were reviewed, found inconsistencies regarding the percentages as these were

higher for clinical data and variables [28]. In 2011, another study in Spain, with the main objective to evaluate the reliability of the MBDS in terms of cerebrovascular disease, in a sample of 11,209 medical records, showed through coding, a concordance of 81.87% between the assessed MBDS and the original hospital's MBDS [29].

In our study, patients with a penicillin allergy label were older, and there was a greater proportion of women as in other authors' studies [30]. In our total cohort, we identified that hospitalizations with records of penicillin allergy had a longer LOHS than that in those without such a label (median value 5 days vs. 4 days); although with the Elixhauser score, comorbidities were also higher in the patients with a penicillin allergy label. An American study by Macy and Contreras [10] discovered that LOHS in patients with a penicillin allergy label was significantly longer than that in those without such a label, an average of 0.59 days since admission. Furthermore, in the Portuguese study, which also used the MBDS as in our study, a difference in LOHS was identified as it was approximately 8% longer in the group with a penicillin allergy label [27]. In this last study, comorbidity, according to the Charlson Comorbidity Index, was also higher in the penicillin-allergic group. Similarly, in our analysis which was adjusted for sex (women), over 64 years of age, comorbidity, and year of admission, we observed that LOHS was longer in the group with a penicillin allergy label, as shown in Figure 1.

On the other hand, when the dependent variable was mortality, the multivariate analysis showed that a penicillin allergy label could be a protective factor. In this regard, the Macy and Contreras [10] study did not find statistically significant differences regarding in-hospital deaths. In the homologous Portuguese study, the frequency of in-hospital deaths was lower in the labeled group despite its higher morbidity, according to the Charlson Comorbidity Index [27]. Mortality was not adjusted for covariates in logistic regression in either of the 2 studies (the American and the Portuguese), although both databases were matched for demographics and main diagnosis or system. In our study, in which the logistic regression analysis carried out for mortality was adjusted for the same confounding variables, we observed an even more protective effect of labeling that was also maintained in all groups of patients. Blumenthal et al. [31] recently investigated the impact of recorded penicillin allergy and the risk of mortality in a population-based matched cohort study, using an electronic database and selecting a period of 20 years. They identified, through a multivariable-adjusted hazard ratio for all-cause mortality, an overall in-

crease in death of 14% in patients with a recorded penicillin allergy compared to those without a recorded penicillin allergy. This study was different from ours as the cases and controls in it were patients from hospitalization records and that had a 6-year follow-up for all-cause death.

Last, we analyzed the behavior of a penicillin allergy label in those records with a code related to the most prevalent infectious diseases in Spain [22]. The longer LOHS in patients with diagnoses associated with obstetric infection and suspected allergy to penicillin should be highlighted. This outcome further supports the importance of penicillin allergy testing in pregnant women who report an allergy. Different authors already recommend this as beta-lactam antibiotics are a first-line regimen for the prevention and treatment of infection during pregnancy [32].

Different studies have demonstrated how the incomplete codification of the secondary diagnoses can bias the estimation of the risk of in-hospital death based on the MBDS. Librero and Peiro [33] discovered conditions associated with a reduced risk of death, such as diabetes mellitus, myocardial infarction, or hypertension. They concluded that it was probably due to an information bias in the MBDS due to the tendency to register less information about the persons who die [33]. It seems that there is a tendency to register the more severe and marked comorbidities and adverse events at the expense of those that are more mild, frequent, and easy to handle [34]. In our study, the weak association between a penicillin allergy label and LOHS could be partially explained due to the underreporting of certain health problems, such as allergies or adverse effects. It is a known fact that a low-risk code is more likely to be registered if there is no other factor of greater severity to be registered. Thus, regarding in-hospital mortality, suspected penicillin allergy using the MBDS could have a nonreporting bias.

Some limitations have already been mentioned throughout this section. The most evident is the fact that it is a retrospective study. The long period of analysis (2006–2015) could also have led to variability in the quality of the data. However, the issue was able to be resolved, partly, by the model. The year of admission is one of the covariates.

In conclusion, our study does not show that there is higher mortality in patients labeled “penicillin-allergic,” although we suspect it was due to a reporting bias. On the other hand, LOHS seems to be longer in the group of penicillin-allergic patients, according to a multivariate analysis adjusted for age, sex, comorbidities, and year of admission.

The MBDS can be a very useful tool for clinical research. The Eleventh Revision of the International Classification of Diseases will soon be released. The Eleventh Revision of the International Classification of Diseases has deeply updated the classification of allergic disorders and might provide a better tool to analyze allergic patients' hospitalizations [35].

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Statement of Ethics

This study was approved by the research Ethics Committee of the Hospital Universitario Fundación Alcorcón, Madrid, Spain (number 20/94, May 15, 2020). Informed consent was not needed, given the anonymization of the MBDS.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M.P. collected and analyzed the data and wrote the manuscript as a part of her thesis. M.A.T. conceived the study design and critically supervised the study. S.L. contributed to the interpretation of the clinical administrative national dataset. J.E.L. conceived the research question and checked the infectious aspects of the investigation. S.W. contributed to the design and the statistical analysis. All the authors reviewed and gave their final approval of the version to be submitted.

Data Availability Statement

The data that support the findings of this study are available from corresponding author (M.P.) and may be requested by editors, reviewers, and readers if so considered.

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