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CLINICAL AND EPIDEMIOLOGICAL STUDY

Adherence and factors associated with influenza vaccination among subjects with asthma in Spain

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Abstract
Purpose Influenza has a high morbidity and mortality rate and an increased risk of complications in vulnerable individuals. Children and adults with asthma have a high risk of complications, hospitalisation and even death. The objectives of this study were as follows: to compare influenza vaccination coverage in Spain in a population of asthmatics aged ≥16 years with an equivalent population of non-asthmatics; to identify the factors that influence vaccination coverage among patients with asthma; and to compare coverage during the period 2006/2007 with that of 2009/2010.
Methods We used data from the 2009 European Health Survey (EHS), which included a population of 22,188 individuals (≥16 years of age), of whom 1,669 [7.5 %; 95 % confidence interval (CI), 7.13–7.98] had asthma. The dependent variable was the answer (yes/no) to a question asking whether or not the interviewed person had been vaccinated against seasonal (not pandemic) influenza in the previous season. As independent variables, we analysed socio-demographic characteristics, health-related variables and the use of health care services.
Results Vaccination coverage was 35.2 % (95 % CI, 32.5–37.9) among asthmatics and 22.1 % (95 % CI, 21.4–22.7) among non-asthmatics ($p < 0.001$). The probability of being vaccinated is almost twice as high for asthmatics as it is for non-asthmatics [odds ratio (OR), 1.92; 95 % CI, 1.69–2.17]. Among asthmatics, vaccination coverage increased with age, worse self-rated health status and not smoking. No significant change in coverage was observed between the study periods.
Conclusions Seasonal influenza vaccination coverage among Spanish asthmatics is lower than desired and has not improved in recent years. Urgent strategies are necessary in order to increase vaccination coverage among asthmatics.

Keywords Adherence · Asthma · Coverage · Influenza · Vaccine

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Introduction

Influenza has a high rate of morbidity and mortality and an increased risk of complications in vulnerable individuals, including asthmatics [1–3]. The National Asthma Education and Prevention Program (NAEPP), which is coordinated by the National Heart, Lung, and Blood Institute (NHLBI) of the USA, recommends annual influenza vaccination as one of the principal measures in asthma care [4]. The safety of this vaccination in asthma patients is well documented [5–7], and exacerbations do not occur after vaccination [6]. Other studies report that the frequency of hospitalisation and the number of complications decrease after vaccination [8, 9]. In most European countries, health

authorities recommend vaccination against influenza for asthmatics [3, 10]. In Spain, the Spanish Ministry of Health, Social Policy and Equality has recommended an annual flu vaccination for asthmatics since 1992. This vaccination is free of charge [11]. Despite these recommendations, fewer than 50 % of asthmatics have been vaccinated against influenza [12–16], possibly because of the fear of a potential exacerbation of their illness [17].

The objectives of our study were as follows:

1. To compare influenza vaccination coverage among asthmatics aged ≥16 years with an equivalent population of non-asthmatics using data from the European Health Survey (EHS) in Spain.
2. To identify factors influencing the vaccination coverage among asthmatics.
3. To compare coverage during the 2009 National Health Survey (NHS) in Spain with that of the 2006/2007 NHS.

Methods

We conducted a descriptive cross-sectional epidemiological study based on data obtained from the EHS in Spain. The information was compiled between April 2009 and March 2010 using a representative sample of non-institutionalised residents in Spain aged ≥16 years. A structured questionnaire was administered during personal interviews in the respondents' homes. Details of the EHS methodology are available elsewhere [18]. Subjects were classified as having asthma if the disease had been diagnosed by a doctor. The dependent variable was whether or not the respondent had been vaccinated against influenza during the previous influenza season.

Vaccination information refers exclusively to seasonal influenza vaccine (pandemic influenza vaccine has been available in Spain since November 2009); this distinction was explained explicitly to the respondent. The independent variables were as follows: (a) socio-demographic characteristics (age, gender, age at completion of formal education and monthly income); (b) variables related to health (self-rated health status, diabetes, heart disease and/or stroke, depression and/or anxiety, obesity, smoking, alcohol consumption and physical exercise); and (c) use of health care services (visits to the doctor in the last 4 weeks, hospital admissions in the last 12 months, emergency room visits in the last 12 months). Finally, we compared coverage with that reported in the 2006/2007 NHS by age group.

Statistical analysis

We performed a descriptive statistical analysis [percentage and 95 % confidence interval (CI)] of influenza vaccination coverage according to the study variables. We compared coverage by age group from the 2009/2010 NHS with that of the 2006/2007 NHS. We used Pearson's χ^2 test for the bivariate comparison of proportions. To analyse the independent association of each of the independent variables with the dependent variable (influenza vaccination) among asthmatics, the corresponding odds ratio (OR) was obtained using multivariate logistic regression analysis.

The multivariate logistic regression model was built using the "enter modelling" method. The process included four steps: (1) Bivariate analysis of each variable; (2) Selection of variables for the multivariate analysis. We included all variables whose bivariate test results were statistically significant ($p < 0.20$) and those we considered scientifically relevant according to the references reviewed; (3) In order to ensure the fit of the multivariate model, the importance of each variable included was verified by examining the Wald statistic and comparing each estimated coefficient with the coefficient from the bivariate model containing only that variable. Variables that did not contribute to the model based on these criteria were eliminated and a new model was fitted. The new model was compared with the old model using the log-rank test. This process of deleting, refitting and verifying continued until all the important variables were included in the model; (4) Once the model was constructed, we looked more closely at the variables included (linearity) and checked for interactions. Estimates were made using the "svy" function (survey commands) of Stata 9.1, which enabled our sampling design and the weights for all our statistical calculations (descriptive, Pearson's χ^2, logistic regression) to be incorporated. A p-value <0.05 (two-tailed) was considered to be significant. According to Spanish legislation, ethics committee approval was not required, as this analysis was conducted on de-identified, public-use datasets.

Results

Using 2009 EHS data, we analysed the records of 22,188 people aged ≥16 years. Asthma was physician-diagnosed in 7.5 % of patients ($n = 1{,}669$; 95 % CI, 7.13–7.98). Table 1 shows the distribution of our study variables in asthmatics and non-asthmatics. Tables 2 and 3 show influenza vaccination coverage according to the different variables analysed. More asthmatics than non-asthmatics had been vaccinated during the previous season (35.2 %, 95 % CI, 32.5–37.9 % vs. 22.1 %, 95 % CI, 21.4–22.7; $p < 0.001$). Coverage increased among asthmatics from 15.6 % in those aged 16–39 years to 77.5 % to those aged ≥65 years. The figures for the same age groups in the 2006/2007 NHS were 16.1 % (95 % CI, 12.5–20.4), 36.5 % (95 % CI, 31.3–41.9) and 77.8 % (95 % CI, 73.1–81.9). No significant

Table 1 Distribution according to the study variables of asthmatics and non-asthmatics included in the European Health Survey (EHS) for Spain 2009

Variable	Categories	Asthma		Total
		Yes (n = 1,669)% (95 % CI)	No (n = 20,519)% (95 % CI)	(N = 22,188)% (95 % CI)
Age (mean, 95 % CI)	Years	45.8 (44.6–46.9)	46.6 (46.3–46.9)	46.6 (46.3–46.9)
Gender[a]	Female	56.9 (53.9–59.8)	50.5 (49.7–51.4)	51 (50.2–51.8)
Age at completion of formal education	≤16 years	53.8 (50.9–56.7)	55.1 (54.2–55.9)	55 (54.2–55.8)
Monthly income[a]	>€1,400	57.1 (54–60.2)	60.9 (60–61.8)	60.6 (59.7–61.4)
Self-rated health status[a]	Excellent, good	57 (54.1–59.8)	72 (71.3–72.7)	70.9 (70.1–71.6)
Smoking[a]	Smoker	25.4 (22.9–28.1)	30.2 (29.4–31)	29.9 (29.1–30.6)
	Ex-smoker	22.2 (19.8–24.8)	20.2 (19.6–20.9)	20.4 (19.8–21.1)
	Non-smoker	52.3 (49.4–55.3)	49.5 (48.7–50.4)	49.7 (48.9–50.6)
Obesity[a]	Yes	19.9 (17.7–22.3)	15.3 (14.7–16)	15.7 (15.1–16.3)
Alcohol consumption	Yes	21.9 (19.6–24.4)	25.9 (25.1–26.6)	25.6 (24.9–26.3)
Physical exercise	Yes	49.5 (46.6–52.4)	52.4 (51.6–53.3)	52.2 (51.4–53)
Cardiovascular disease[a]	Yes	9.9 (8.4–11.6)	6.5 (6.1–6.9)	6.7 (6.4–7.1)
Diabetes[a]	Yes	8.3 (6.9–10)	6.6 (6.3–7)	6.8 (6.4–7.1)
Depression[a]	Yes	11.7 (10.1–13.5)	7.1 (6.7–7.5)	7.4 (7–7.8)
Visits to the doctor during the previous month[a]	Yes	41.5 (38.7–44.4)	27.4 (26.7–28.2)	28.5 (27.8–29.2)
Hospital admissions during the previous 12 months[a]	Yes	13.5 (11.7–15.5)	8.8 (8.3–9.3)	9.1 (8.7–9.6)
Emergency room visits during the previous 12 months[a]	Yes	13.6 (11.9–15.7)	8.9 (8.4–9.4)	9.3 (8.8–9.7)
Total		7.5 (7.1–8)	92.5 (92–92.9)	100

[a] Statistically significant association when comparing the distribution of variables in asthmatics and non-asthmatics

Table 2 Influenza vaccination coverage in asthmatics and non-asthmatics according to socio-demographic variables, self-rated health and smoking. European Health Survey for Spain, 2009

Variable	Categories	Influenza vaccination coverage	
		With asthma, % (95 % CI)	Without asthma, % (95 % CI)
Age[a,b] (years)	16–39	15.6 (12.4–19.5)	7 (6–7.4)
	40–64	34.1 (29.7–38.9)	16.4 (15.6–17.4)
	≥65	77.5 (72.6–81.7)	65.4 (63.9–66.9)
Gender[a,b]	Female	37.9 (34.5–41.5)	23.2 (22.3–24.1)
	Male	31.6 (27.5–35.9)	20.9 (20–21.9)
Age at completion of formal education [a,b] (years)	≤16	45.6 (41.8–49.4)	28.4 (27.5–29.3)
	>16	22.8 (19.3–26.8)	14.3 (13.4–15.2)
Monthly income[a,b]	≤€1,400	42.5 (38.2–46.9)	29.1 (28–30.4)
	>€1,400	27.5 (23.8–31.4)	18 (17.2–19)
Self-rated health status[a,b]	Excellent, good	21.5 (18.5–25)	15 (14.3–15.7)
	Fair, poor, very poor	53.2 (49.1–57.3)	40.2 (38.4–41.6)
Smoking[a,b]	Smoker	17 (13–22.1)	11.7 (10.7–12.6)
	Ex-smoker	43 (37–49.3)	27.1 (25.6–28.7)
	Non-smoker	38.9 (35.1–43)	24.4 (23.5–25.4)
Total		35.2 (32.5–37.9)	22.1 (21.4–22.7)

[a] Statistically significant association when analysing influenza vaccination coverage among asthmatics

[b] Statistically significant association when analysing influenza vaccination coverage among non-asthmatics

Table 3 Influenza vaccination coverage according to lifestyle variables, concomitant diseases and use of health care services in asthmatics and non-asthmatics. European Health Survey for Spain, 2009

Variable	Influenza vaccination coverage	
	With asthma, % (95 % CI)	Without asthma, % (95 % CI)
Obesity[a,b]		
No	30.4 (27.5–33.5)	19.7 (19–20.4)
Yes	47.5 (41.1–53.9)	30.1 (28.3–32.1)
Alcohol consumption[b]		
No	34.6 (31.5–37.9)	20.7 (19.9–21.4)
Yes	32.2 (27–37.9)	22.5 (21.2–23.8)
Physical exercise[a,b]		
No	43.7 (39.8–47.7)	27 (26.1–28)
Yes	26.5 (23.1–30.2)	17.5 (16.7–18.4)
Chronic obstructive pulmonary disease[a,b]		
No	27 (24.1–30.1)	21 (20.3–21.6)
Yes	53.9 (48.6–59)	46.8 (42.9–50.6)
Cardiovascular disease[a,b]		
No	31.3 (28.6–34.2)	19.4 (18.8–20.1)
Yes	70.2 (61.8–77.4)	60.3 (57.4–63.2)
Diabetes[a,b]		
No	32.3 (29.6–35.2)	19.4 (18.8–20.1)
Yes	66.3 (56.9–74.6)	59.4 (56.5–62.3)
Depression[a,b]		
No	32.3 (29.5–32.3)	20.8 (20.2–21.5)
Yes	56.2 (48.6–63.5)	38 (35.3–40.8)
Visits to the doctor during the previous month[a,b]		
No	26.9 (23.7–30.4)	16.9 (16.2–17.6)
Yes	46.8 (42.4–51.2)	35.7 (34.3–37.2)
Hospital admissions during the previous 12 months[a,b]		
No	33 (30.2–35.9)	20.9 (20.2–21.5)
Yes	48.5 (41.1–55.9)	34.3 (31.8–36.8)
Emergency room visits during the previous 12 months[a,b]		
No	33 (30.1–35.9)	20.8 (20.2–21.5)
Yes	49.2 (41.9–56.6)	34.4 (32–37)

[a] Statistically significant association when analysing influenza vaccination coverage among asthmatics

[b] Statistically significant association when analysing influenza vaccination coverage among non-asthmatics

differences were observed in coverage by age group between the study periods. The probability of being vaccinated is almost two times higher among patients with asthma (crude OR, 1.92; 95 % CI, 1.69–2.17).

The bivariate analysis revealed the socio-demographic variables that were significantly associated with a higher vaccine coverage to be female sex, lower educational level and lower monthly income. With regard to health-related variables, not smoking, worse self-rated health status, obesity and not taking regular physical exercise were significantly associated with higher coverage.

Finally, vaccination was also significantly more frequent among asthmatics who reported concomitant comorbidities such as chronic obstructive pulmonary disease, heart disease, and/or stroke or diabetes, and among those who had recently sought medical attention.

The results of the multivariate analysis are shown in Table 4. The factors that were independently and significantly associated with a greater probability of being vaccinated (predictors) among asthmatics were as follows: (1) Age $\geq$65 years [the vaccination rate for this age group is 12 times (OR, 12.12) that of patients aged between 16 and 39 years]; (2) Self-rated health status as fair or poor. Almost twice as many people in this category were vaccinated compared to those who did not perceive their health as fair or poor (OR, 1.86); (3) Being a non-smoker or ex-smoker. Twice as many people in this category were vaccinated than smokers (OR, 0.45).

Table 4 Predictors for influenza vaccination coverage among Spanish asthmatics. European Health Survey for Spain, 2009

	Adjusted OR	95 % CI
Age (years)		
16–39	1	–
40–64	2.42	1.69–3.47
≥65	12.12	7.97–18.44
Gender		
Male	1	–
Female	1.03	(0.75–1.41)
Smoking		
Non-smoker	1	–
Ex-smoker	1.03	(0.73–1.45)
Smoker	0.45	(0.3–0.68)
Self-rated health status		
Excellent, good	1	–
Fair, poor, very poor	1.86	(1.36–2.54)

The variables initially selected and included from the bi-variate analysis in the multivariate model were all those shown in Tables 2 and 3, except for "alcohol consumption"

Discussion

The most relevant finding of this study is that influenza vaccination coverage among Spanish asthmatics aged ≥16 years (35.2 %) is below desirable levels. Several studies have investigated the prevalence and predictors of influenza vaccination among asthmatics [13, 16, 19–23].

Our results are similar to those reported in Canada (36.3 %) [16] and the USA [19], where 39.9 % of adults aged 18–64 years had been vaccinated, with coverage of 33.9 % for people aged 18–49 years and 54.7 % for those aged 50–64 years.

Few European studies have described influenza vaccine coverage among asthmatics [7, 20–23]. Keenan et al. [20] reported coverage of 40.2 % among asthmatic patients for the year 2003. Ten years previously, based on data from elderly individuals with asthma in a cohort from the UK General Practice Research Database [7], coverage of 43 % (1991–1992), 39 % (1992–1993) and 41 % (1993–1994) was reported.

In the 2003–2004 campaign in the Netherlands, the results from two medical information sources [the Great Influenza Survey (an Internet-based survey of influenza-like illness) and the official data obtained by Dutch GPs participating in the Dutch Sentinel Practice Network] revealed coverage rates of 73 and 68 %, respectively [21]. A study from Portugal based on a telephone survey reported 34.3 % coverage among persons with self-reported asthma [22].

Another relevant finding of our investigation was that no change was observed in vaccination coverage among Spanish asthmatics between 2006 and 2010. A similar observation was made in the USA for the period 2000–2007 [13, 19].

Our multivariate analysis showed that older age (especially age >65 years) was a positive predictor for vaccination among asthmatics. The fact that vaccination coverage is higher as age increases in populations with asthma or other chronic lung diseases has already been described in Spain and elsewhere [12–14, 16, 19, 23].

We found vaccination coverage to be lower among smokers, as did Jiménez-García et al. [23]. This finding is important, as smokers who also have chronic respiratory diseases are at a higher risk of suffering from respiratory complications [24]. Tobacco usage has also been found to be a negative predictor for vaccination in previous studies examining people who suffer from chronic lung diseases [14, 16].

Our results showed that asthmatics who perceived their health to be bad or very bad were 1.86 times more likely to be vaccinated than those who perceived their health to be good, a finding that was similar to Ford et al. [13]. One possible explanation is that asthmatics visit health care professionals more frequently and, therefore, are more likely to be vaccinated.

The reasons for low vaccination coverage among asthmatics are mixed and involve both patients and health care professionals. Vaccination may be refused by people who are already sick, because they think that they will develop influenza or because they do not perceive any benefit from vaccination [25]. Younger people may not be aware of the need for vaccination to prevent complications of asthma or they may feel that being vaccinated could cause them to have adverse reactions because of their existing disease [13].

Health care professionals play a significant role in encouraging patients to be vaccinated. By providing adequate information about immunization, they could improve coverage among asthmatics [13]. In addition, urgent action must be taken to inform asthmatics of the potential dangers of influenza and of the effectiveness and safety of the vaccine [26].

Our study has several limitations. First, the validity of the questions used by the EHS to classify vaccination status has not been evaluated. As data from the EHS are de-identified, it is not feasible to cross the self-reported information with medical records. In Spain, the only study to assess the validity of the self-reporting of influenza vaccination [27] was conducted among health care professionals over four influenza campaigns and found that sensitivity ranged from 73 to 91 % and specificity ranged from 73 to 94 %. Our literature review revealed eight studies comparing self-reporting with influenza vaccination records in high-risk populations. In all cases, the sensitivity

was very high, ranging from 92 to 100 % and the specificity ranged from 38 to 96 %. In addition, the overall agreement determined using Cohen's kappa ranged from 0.36 to 0.88 [28–35]. Therefore, we believe that self-reporting is a valid source for the assessment of influenza vaccination coverage. Furthermore, many other authors from different countries have published papers on vaccination coverages using population surveys with self-report data and without validating their answers with medical records [12–14, 16, 19, 23, 36–39]. Second, the timing of the survey with respect to the availability of the vaccination may affect recall bias, and the information obtained may be affected by the subjects' desire to provide socially acceptable answers. Third, information on relevant variables, such as pharmacological treatment, use of other recommended vaccinations (pneumococcal vaccine), and the duration and severity of asthma are not included in the EHS and may act as confounders. And, lastly, the response rate to the NHS was 64 %, with the result that a non-response bias may exist [18].

In conclusion, influenza vaccination coverage among Spanish asthmatics is lower than desired and has not improved in recent years. Urgent strategies for increasing vaccination coverage among asthma sufferers are necessary and must target young adults, smokers and those who perceive their health to be good, as these are the groups who least follow vaccination recommendations.

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Conflict of interest None of the authors have any conflicts of interest to declare.

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