

## Social class based on occupation is associated with hospitalization for A(H1N1)pdm09 infection. Comparison between hospitalized and ambulatory cases

J. PUJOL<sup>1,2\*</sup>, P. GODOY<sup>1,3,4</sup>, N. SOLDEVILA<sup>4</sup>, J. CASTILLA<sup>4,5</sup>, F. GONZÁLEZ-CANDELAS<sup>4,6</sup>, J. M. MAYORAL<sup>4,7</sup>, J. ASTRAY<sup>4,8</sup>, S. GARCIA<sup>9</sup>, V. MARTIN<sup>4,10</sup>, S. TAMAMES<sup>4,11</sup>, M. DELGADO<sup>4,12</sup> AND A. DOMÍNGUEZ<sup>2,4</sup> and the CIBERESP Cases and Controls in Pandemic Influenza Working Group†

<sup>1</sup> *Universitat de Lleida, Departament de Cirurgia, Lleida, Spain;* <sup>2</sup> *Departament de Salut Pública, Universitat de Barcelona, Barcelona, Spain;* <sup>3</sup> *Public Health Agency, Generalitat de Catalunya, Barcelona, Spain;* <sup>4</sup> *CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain;* <sup>5</sup> *Instituto de Salud Pública de Navarra, Pamplona, Spain;* <sup>6</sup> *Unidad Mixta 'Infección y Salud Pública' FISABIO-Universidad de Valencia, Spain;* <sup>7</sup> *Servicio de Vigilancia de Andalucía, Sevilla, Spain;* <sup>8</sup> *Área de Epidemiología, Comunidad de Madrid, Madrid, Spain;* <sup>9</sup> *Unidad de Investigación, Hospital Galdakao-Usansolo, Bizkaia, REDISSEC, Spain;* <sup>10</sup> *Instituto de Biomedicina, Universidad de León, León, Spain;* <sup>11</sup> *Dirección General de Salud Pública e Investigación, Desarrollo e Innovación, Junta de Castilla y León, Spain;* <sup>12</sup> *Universidad de Jaen, Jaen, Spain*

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### SUMMARY

This study aimed to analyse the existence of an association between social class (categorized by type of occupation) and the occurrence of A(H1N1)pmd09 infection and hospitalization for two seasons (2009–2010 and 2010–2011). This multicentre study compared ambulatory A(H1N1)pmd09 confirmed cases with ambulatory controls to measure risk of infection, and with hospitalized A(H1N1)pmd09 confirmed cases to assess hospitalization risk. Study variables were: age, marital status, tobacco and alcohol use, pregnancy, chronic obstructive pulmonary disease, chronic respiratory failure, cardiovascular disease, diabetes, chronic liver disease, body mass index >40, systemic corticosteroid treatment and influenza vaccination status. Occupation was registered literally and coded into manual and non-manual worker occupational social class groups. A conditional logistic regression analysis was performed. There were 720 hospitalized cases, 996 ambulatory cases and 1062 ambulatory controls included in the study. No relationship between occupational social class and A(H1N1)pmd09 infection was found [adjusted odds ratio (aOR) 0·97, 95% confidence interval (CI) 0·74–1·27], but an association (aOR 1·53, 95% CI 1·01–2·31) between occupational class and hospitalization for A(H1N1)pmd09 was observed. Influenza vaccination was a protective factor for A(H1N1)pmd09 infection (aOR 0·41, 95% CI 0·23–0·73) but not for hospitalization. We conclude that manual workers have the highest risk of hospitalization when infected by influenza than other occupations but they do not have a different probability of being infected by influenza.

**Key words:** Influenza A, outbreaks, public health, public health emerging infections, vaccination (immunization).

\* Author for correspondence: Dr J. Pujol, Pica d'Estats, 14, 4, 4, 25006, Lleida, Spain.  
(Email: [jesus.pujol@cirurgia.udl.cat](mailto:jesus.pujol@cirurgia.udl.cat))

† Other members of the CIBERESP Cases and Controls in Pandemic Influenza Working Group are given in the Appendix.

### INTRODUCTION

The epidemiological pattern of infectious diseases has changed throughout history [1, 2]. Explanations for these changes are usually based on different

alternatives such as the appearance of new aetiological pathogens, climate change, environmental circumstances, improper use of antibiotics and changes in society in relation to behavioural and socio-demographic characteristics [3]. One recent example of this evolution is the emergence of a new strain of influenza virus [A(H1N1)pdm09] in spring 2009, which caused the first pandemic of the 21st century [4, 5].

Socio-demographic factors are conditions that influence the behaviour of infectious diseases [6, 7]. It has been shown that social disparities influence the appearance of the disease and cause differences in its perception, progress and outcome. These differences can be explained, at least partially, by differences in social characteristics, which include many components such as education level, income, material possessions, livelihood means and occupation [8, 9]. For public health analyses, these factors are usually summarized in a single indicator variable, denoted social class [10, 11].

Social class based on occupation is an indicator of socioeconomic position and health-related behaviour. Occupation is a very useful individual feature for social theories which attempt to measure the social classes and is a better indicator than education in studies comparing variables such as mortality or lifestyle [12]. A classification based on occupation is a way of identifying inherent factors of social structure of social models [13, 14].

Following this argument, it is possible that occupation classification might differentiate between groups of individuals with similar clinical and behavioural risk factors of influenza infection, by severity of A(H1N1)pdm09 influenza infection and also to differentiate them according to utilization of health services [15].

Risk factors that lead to hospitalization from influenza can be very different from those associated with the risk of infection by influenza at the community level. Therefore, these two outcomes should be studied separately and, consequently, case-control studies should use two types of controls, influenza community cases or community non-influenza controls, respectively [16].

The aim of this study was to investigate the association between social class (categorized by type of occupation) and the occurrence of A(H1N1)pdm09 infection and hospitalization for two seasons (2009–2010 and 2010–2011).

## METHODS

A multicentre study with matched cases and controls was conducted in 36 hospitals and 22 primary-care

centres from seven Spanish regions (Andalusia, Basque Country, Catalonia, Castile & Leon, Madrid, Navarra, Valencian Community) [17]. Cases and controls were recruited between July 2009 and February 2011, and were aged >18 years at the date of inclusion. The minimum number of pairs needed to detect an odds ratio (OR) of 1.5 and assuming a prevalence of the investigated factors in controls of 0.30, a bilateral significance level  $\alpha = 0.05$  and a power of  $\beta = 0.80$  was 425 using the criteria proposed by Schlesselman [18]. To calculate the risk of infection, ambulatory cases were matched with ambulatory controls and to calculate the risk of hospitalization, hospitalized cases were matched with ambulatory cases.

### Selection and matching of ambulatory cases, ambulatory controls and hospitalized cases

An ambulatory case of A(H1N1)pdm09 was considered if reverse transcription–polymerase chain reaction (RT–PCR) was positive for this virus in a suspected case visiting a primary-care centre. Ambulatory controls were people attending a primary-care centre for any reason other than influenza-like illness. Ambulatory cases were matched with ambulatory controls taking into account age ( $\pm 5$  years), date of diagnosis of the case ( $\pm 10$  days) and residential province of the case. When several potential controls were available, the selection was made by using a table of random numbers. If an adequate control was not found, the range of the diagnosis date was expanded. A hospitalized case was defined as a patient admitted to hospital for  $\geq 24$  h with RT–PCR confirmed infection by influenza A(H1N1)pdm09 virus. Hospitalized cases excluded nosocomial infections (determined by onset of symptoms  $\geq 48$  h after admission to the hospital). Ambulatory cases were matched to hospitalized cases by age ( $\pm 5$  years), residential province and date of admission to the hospital ( $\pm 10$  days).

### Socio-demographic and pre-existing behavioural and medical variables

For all the subjects included in the study the following demographic and medical variables were obtained: age, marital status, tobacco and alcohol use, pregnancy (for women aged 15–49 years), chronic obstructive pulmonary disease (COPD), chronic respiratory failure, cardiovascular disease, diabetes, chronic liver

disease, obesity type III (body mass index >40) [19], and treatment with systemic corticosteroids.

### Occupational variables

The occupation of the studied population was registered literally and, in order to develop the analyses, it was coded using the indicators of occupational social class postulated by the Working Group of Social Determinants of the Spanish Society of Epidemiology for use in the research and practice of public health in Spain. This classification was based on the National Classification of Occupations of 2011 [20] and a neo-Weberian perspective designated CSO-SEE12 (Clase Social Ocupacional–Sociedad Española de Epidemiología 2012) [14]. The classification and categories are: (1) Directors and managers of businesses with  $\geq 10$  employees and professions traditionally associated with a university grade; (2) Directors and managers of businesses with <10 workers and professions traditionally associated with a university diploma and other as professional technical support, athletes and artists; (3) Middle occupations (administrative employees and professional support for administrative and other management services); (4) Self-employed; (5) Supervisors and workers in skilled technical occupations; (6) Workers qualified at the primary sector and other workers semi-skilled; and (7) Unskilled workers. These seven categories can be aggregated into six-, five-, three- and two-category classifications [14]. The two-category scheme aggregates categories (1)–(3) in a new category called non-manual workers, and categories (4)–(7) in a manual workers category [14].

This two-category classification was used for the main analyses presented here in order to maximize the statistical power of the study. To perform the classification, the occupation declared by all cases and controls was first assigned to one of the seven categories of the CSO-SEE12 classification and subsequently classified in the manual or non-manual class. Students, housewives and unemployed or handicapped individuals who did not report their last occupation were considered as unclassifiable and were excluded from the analyses.

Vaccination status for cases and controls was assessed by immunization records with an influenza pandemic vaccine, a monovalent vaccine with the A/California/04/2009 (H1N1) strain, in the 2009–2010 season and with a trivalent influenza vaccine

that included the A/California/04/2009 (H1N1) strain in the 2010–2011 season.

Medical variables were obtained from hospital clinical records and primary healthcare centre registers. In hospitalized cases, vaccination status was obtained from hospital records or vaccination cards. If none of these was available, primary healthcare centre registers were consulted. For ambulatory cases and controls, vaccination status was obtained from primary healthcare centre registers or vaccination cards. Behavioural and occupational information was obtained by direct or phone interviews with the patient.

### Ethical considerations

All information collected was treated as confidential, in strict compliance with the Spanish legislation on observational studies. The study was approved by Ethics Committees of the hospitals involved. Written informed consent was obtained from all patients included in the study.

### Statistical analysis

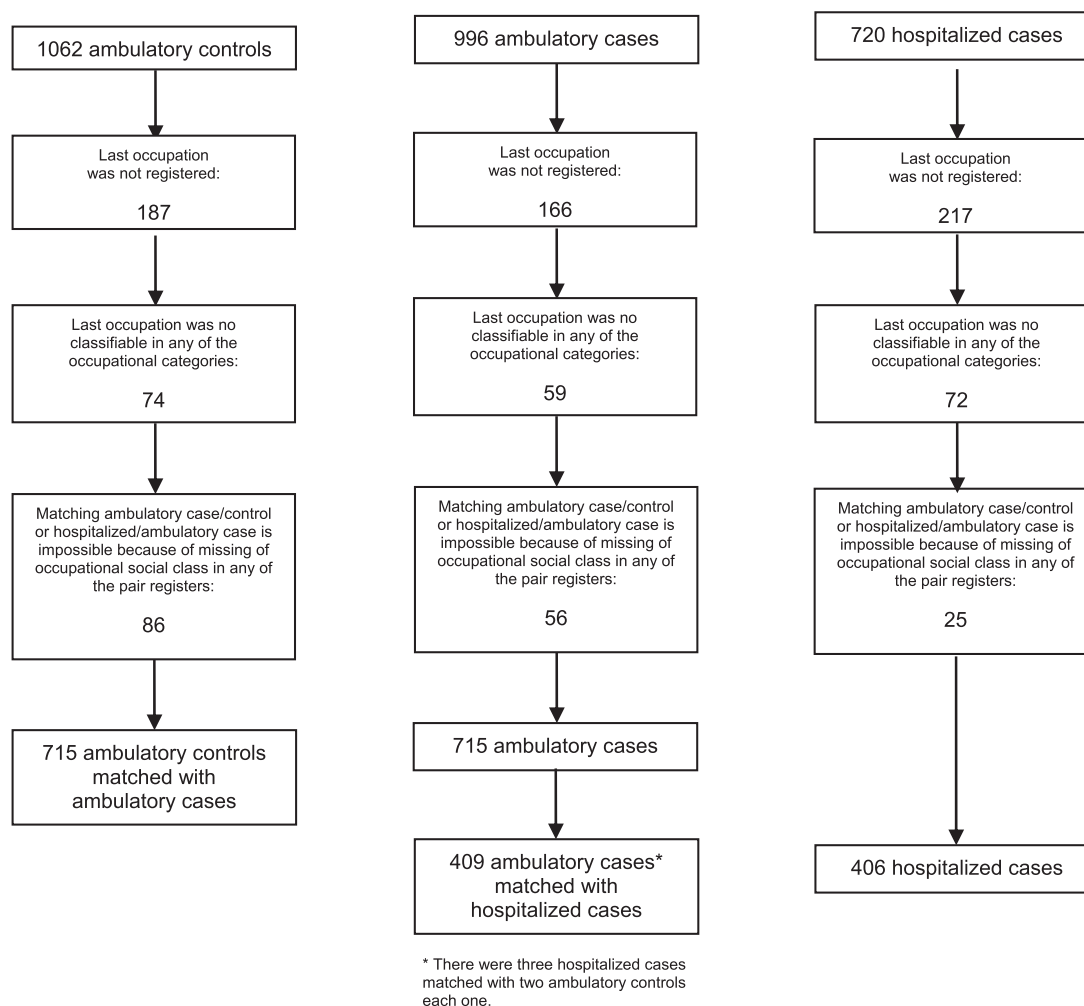
Once the field occupation was completed, each epidemic wave database was checked, correcting any detected inconsistencies.

The association of the dependent variable, infection or hospitalization, with the primary independent variable (occupational social class) was estimated by calculating the odds ratio (OR) and 95% confidence intervals (CI). Multivariate analysis was performed using conditional logistic regression adjusting for age and influenza vaccination as well as for variables that are predictive of infection or hospitalization in a model constructed by selection procedure of variables, with a cut-off point of  $P < 0.2$ .

## RESULTS

A total of 996 confirmed influenza A(H1N1)pdm09 ambulatory and 720 hospitalized cases were initially available for study. The ambulatory controls were 1062. After filtering, 715 ambulatory cases, 715 ambulatory controls and 406 hospitalized cases were retained for analysis, as shown in Figure 1.

No statistically significant differences were found in the proportion of manual and non-manual workers between ambulatory cases and ambulatory controls



**Fig. 1.** Number of ambulatory controls, ambulatory cases and hospitalized cases included in the study.

(Table 1). The occupation variable showed no association with A(H1N1)pdm09 infection (OR 0.83, 95% CI 0.68–1.02).

Despite the matching process, some differences between ambulatory cases and ambulatory controls were observed. The proportion of ambulatory cases aged >60 years was 12.8% while the proportion of ambulatory controls aged >60 years was 26.6%.

Pregnancy was much more frequent in ambulatory cases than in ambulatory controls. The prevalence of diabetes in ambulatory controls was higher than in ambulatory cases. Ambulatory cases were treated with corticoids in a higher proportion than ambulatory controls. Influenza vaccination was three times more frequent in ambulatory controls (Table 1).

In hospitalized cases, the proportion of manual workers was higher than for ambulatory cases (Table 2). Hospitalized cases aged >60 years were

almost double (24.7%) that of ambulatory cases (12.8%). In hospitalized cases pregnancy was slightly more frequent than in ambulatory cases. Major chronic conditions showed significant differences, with a higher prevalence in hospitalized cases in COPD, chronic respiratory failure, chronic liver disease, body mass index >40, and diabetes (Table 2).

In the adjusted comparison of ambulatory cases and controls using a conditional logistic regression model (Table 3), no significant relationship between A(H1N1)pdm09 infection and the main independent variable, occupational class, was observed (aOR 0.97, 95% CI 0.74–1.27). Older ages remained protective of the infection and so did the influenza pandemic vaccine. Pregnant women continued presenting a strong association with the infection.

In a similar analysis comparing hospitalized cases and ambulatory cases (Table 4), the relationship

Table 1. Distribution of ambulatory cases and controls according to demographic, behavioural factors, medical conditions and occupational class

	Ambulatory cases, <i>n</i> (%) ( <i>N</i> = 715)	Ambulatory controls, <i>n</i> (%) ( <i>N</i> = 715)	OR (95% CI)	<i>P</i> value
Occupational social class				
Non-manual workers	367 (51.3)	332 (46.4)	1	
Manual workers	348 (48.7)	383 (53.6)	0.83 (0.68–1.02)	0.08
Age group, years				
18–30	147 (20.6)	71 (9.9)	1	
31–40	187 (26.2)	138 (19.3)	0.31 (0.19–0.52)	<0.001
41–50	174 (24.3)	156 (21.8)	0.08 (0.04–0.17)	<0.001
51–60	116 (16.2)	160 (22.4)	0.02 (0.01–0.04)	<0.001
61–70	59 (8.3)	112 (15.7)	0.01 (0.002–0.02)	<0.001
>70	32 (4.5)	78 (10.9)	0.002 (0.001–0.01)	<0.001
Marital status				
Single	185 (26.2)	144 (20.3)	1	
Married/couple	462 (65.3)	474 (66.9)	0.72 (0.55–0.95)	0.02
Widow	23 (3.3)	37 (5.2)	0.45 (0.25–0.81)	0.01
Divorced/separated	37 (5.2)	53 (7.5)	0.54 (0.33–0.88)	0.01
Smoking status				
Non-smoker	401 (56.2)	364 (51.0)	1	
Smoker	180 (25.2)	183 (25.6)	0.89 (0.69–1.15)	0.37
Former smoker	133 (18.6)	167 (23.4)	0.75 (0.57–0.98)	0.03
Alcoholism	29 (4.1)	37 (5.2)	0.76 (0.46–1.26)	0.29
Pregnant women	61 (8.5)	16 (2.2)	4.49 (2.46–8.21)	<0.001
COPD	15 (2.1)	18 (2.5)	0.81 (0.39–1.69)	0.58
Chronic respiratory failure	8 (1.1)	7 (1.0)	1.14 (0.41–3.15)	0.80
Cardiovascular disease	20 (2.8)	32 (4.5)	0.61 (0.35–1.08)	0.09
Diabetes	28 (3.9)	66 (9.2)	0.35 (0.21–0.58)	<0.001
Chronic liver disease	14 (2.0)	14 (2.0)	1.00 (0.46–2.16)	1.00
Body mass index >30	84 (12.2)	103 (15.0)	0.76 (0.55–1.03)	0.08
Corticoid treatment	16 (2.2)	4 (0.6)	4.00 (1.34–11.96)	0.01
Influenza vaccination	36 (5.1)	109 (15.3)	0.24 (0.15–0.39)	<0.001

OR, Odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

between occupational class (non-manual and manual workers) and hospitalization for A(H1N1)pmd09 resulted in statistical significance (aOR 1.53, 95% CI 1.01–2.31). Older age groups were highly predisposed to hospitalization, as was the case for diabetes, COPD and pregnancy.

## DISCUSSION

Manual workers had 53% more risk of being hospitalized once they had been infected with by influenza A (H1N1)pmd09 virus. Occupational social class was not associated with infection, but the statistical power to detect differences was low in the present study. Public health policies should take these results into account in order to emphasize and adapt messages about preventive recommendations to the manual worker population and their families.

The lack of difference in the risk of infection between manual and non-manual workers is consistent with studies that highlight more infection risk is only associated with occupations with more social exposition [21].

The higher risk of hospitalization in the lower social class is congruent with a recent meta-analysis by Tricco *et al.* [22] that evidences more risk of hospitalization in socially vulnerable groups vs. non-vulnerable people. In this meta-analysis, risk of hospitalization considered conditions such as pregnancy and comorbidities such as chronic lung conditions, heart conditions, and diabetes with an adjusted OR of 2.26 (95% CI 1.53–3.32). Another study by Van Kerkhove *et al.* [23] pooled data on risk factors for A(H1N1)pmd09 severe outcome and included data from governmental surveillance programmes across 19 countries, including Spain. In that study, vulnerable social groups had a higher risk of hospitalization.

Table 2. Distribution of hospitalized cases and ambulatory cases according to demographic, behavioural factors, medical conditions and occupational class

	Hospitalized cases, n (%) (N = 406)	Ambulatory cases, n (%) (N = 409)	OR (95% CI)	P value
Occupational social class				
Non-manual workers	160 (39.4)	208 (50.9)	1	
Manual workers	246 (60.6)	201 (49.2)	1.65 (1.23–2.22)	0.001
Age group, years				
18–30	46 (11.3)	92 (22.5)	1	
31–40	81 (20.0)	99 (24.2)	4.04 (1.95–8.38)	<0.001
41–50	94 (23.2)	97 (23.7)	12.13 (5.00–29.45)	<0.001
51–60	85 (20.9)	76 (18.6)	44.10 (14.51–134.06)	<0.001
61–70	60 (14.8)	28 (6.8)	591.85 (102.00–3434.25)	<0.001
>70	40 (9.9)	17 (4.2)	2319.59 (282.91–19018.16)	<0.001
Marital status				
Single	94 (23.6)	122 (30.2)	1	
Married/couple	260 (65.3)	255 (63.1)	1.38 (0.98–1.93)	0.07
Widow	19 (4.8)	13 (3.2)	1.99 (0.89–4.46)	0.09
Divorced/separated	25 (6.3)	14 (3.5)	2.27 (1.12–4.60)	0.02
Smoking status				
Non-smoker	193 (47.9)	239 (58.4)	1	
Smoker	109 (27.0)	99 (24.2)	1.38 (0.98–1.93)	0.06
Former smoker	101 (25.1)	71 (17.4)	1.75 (1.22–2.51)	0.002
Alcoholism	40 (10.1)	30 (7.4)	1.44 (0.87–2.38)	0.15
Pregnant women	44 (11.2)	33 (8.3)	1.48 (0.87–2.51)	0.15
COPD	61 (15.0)	9 (2.2)	9.80 (4.23–22.73)	<0.001
Chronic respiratory failure	31 (7.6)	8 (2.0)	4.38 (1.92–9.99)	<0.001
Cardiovascular disease	39 (9.6)	11 (2.7)	4.59 (2.13–9.88)	<0.001
Diabetes	71 (17.5)	10 (2.4)	11.17 (4.84–25.74)	<0.001
Chronic liver disease	21 (5.2)	9 (2.2)	2.50 (1.10–5.68)	0.03
Body mass index >40	92 (22.7)	58 (14.2)	1.82 (1.25–2.65)	0.002
Corticoid treatment	17 (4.2)	11 (2.7)	1.60 (0.73–3.53)	0.24
Influenza vaccination	60 (14.8)	35 (8.6)	1.98 (1.22–3.21)	0.005

OR, Odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

considering the same demographic, behavioural factors and medical conditions that we have considered in the present study and the results about rates of hospitalization are close to ours [23].

The existence of poorer life conditions expressed throughout the lifespan and also using occupational social class has been demonstrated in Van Raalte *et al.*'s [24] cross-sectional analyses of trends in adult lifespan variation over four decades (1971–2010) by occupational social class (manual, lower non-manual, upper non-manual) using Finnish register data. One of the main findings of their study was the existence of disparities in access to new medical treatments and campaigns to discourage self-deleterious behaviour, circumstance that would not apply in our study because during the study period the Spanish public health system was universal and free.

When focusing on the influence of socioeconomic status in the clinical evolution of acute infectious diseases, a Danish population-based cohort study on bacteraemia in working patients [25] revealed that people of lower socioeconomic status had higher mortality within 30 days after bacteraemia than those of higher status.

Our study confirms that risk factors for influenza hospitalization are different from those of influenza infection. Age is probably the variable that shows this difference more clearly. While hospitalization risk markedly increased with age, as previously shown by other authors [26], older age groups are associated with a markedly lower risk of infection. This result is in line with the report by Hoschler *et al.* [27] about the large increase in antibody levels after the 2010–2011 winter in persons aged >75 years. Clinical surveillance data suggest that elderly

Table 3. Risk factors associated with A(H1N1)pdm09 infection in a conditional logistic regression model

	aOR (95% CI)	P value
Occupational social class		
Non-manual workers	1	
Manual workers	0.97 (0.74–1.27)	0.83*
Age group, years		
18–30	1	
31–40	0.30 (0.17–0.52)	<0.001
41–50	0.10 (0.05–0.20)	<0.001
51–60	0.02 (0.01–0.04)	<0.001
61–70	0.01 (0.002–0.02)	<0.001
>70	0.002 (0.001–0.008)	<0.001
Pregnant women	3.93 (1.91–8.10)	<0.001
Diabetes	0.46 (0.22–0.94)	0.03
Influenza vaccination	0.41 (0.23–0.73)	0.003

aOR, Adjusted odds ratio; CI, confidence interval.

\* Statistical power: 25.9%.

Table 4. Risk factors associated with A(H1N1)pdm09 hospitalization in a conditional logistic regression model

	aOR (95% CI)	P value
Occupational class		
Non-manual workers	1	
Manual workers	1.53 (1.01–2.31)	0.04
Age group, years		
18–30	1	
31–40	3.86 (1.74–8.56)	<0.001
41–50	9.81 (3.65–26.35)	<0.001
51–60	36.75 (10.26–131.59)	<0.001
61–70	276.34 (40.40–1890.32)	<0.001
>70	935.44 (81.49–10738.07)	<0.001
Pregnant women	2.28 (1.16–4.48)	0.02
COPD	5.87 (1.77–19.45)	0.004
Cardiovascular disease	2.48 (0.81–7.60)	0.11
Diabetes	7.46 (2.51–21.21)	<0.001
Influenza vaccination	0.89 (0.42–1.88)	0.75

aOR, Adjusted odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

\* Statistical power: 84.3%.

persons (>65 years) were relatively protected from infection with A(H1N1)pdm09 virus.

The meta-analysis by Mertz *et al.* [28] on infection and hospitalization during pregnancy concluded, in accord with our study, that pregnancy is a major risk factor for hospitalization in infected pregnant women, but not for other outcomes (community-acquired pneumonia, mortality, admission to an intensive care unit or need for ventilatory support). Their study also confirmed the importance of three

chronic diseases (COPD, cardiovascular disease, diabetes) for the risk of hospitalization by influenza infection, the same as in our study with the distinction that in the Mertz *et al.* study diabetes also increased the risk of death in A(H1N1)pdm09 patients.

The results of our study show that vaccination can prevent 59% (95% CI 23–77) of influenza infections. This value is similar to that in a European multi-centre case-control study by Kissling *et al.* [29] that found in 2010–2011 a vaccine effectiveness (VE) of 41.3% (95% CI 2.6–66.4) in people aged 15–59 years and of 59.9% (95% CI 16.7–80.7) in people aged  $\geq 60$  years. In a case-control study including all ages that was performed in the UK in 2010–2011, Pebody *et al.* [30] found a VE of 57% (95% CI 42–68). In a case-control study in England and Scotland performed in 2009–2010, Hardeid *et al.* [31] found a VE of 72% (95% CI 21–90), a point estimate higher than ours but with confidence intervals similar to those we have obtained.

This study has several strengths. It is a multicentre study that involves centres throughout Spain. All ambulatory and hospitalized cases were confirmed by RT-PCR and the vaccination and medical conditions of the participants were directly obtained from medical records. To ensure the observed association between occupational class, all co-associated variables described in other studies about the risk of infection or hospitalization by A(H1N1)pdm09 virus have been included in the analysis.

Nevertheless, the study has some limitations related to the indicator chosen to measure social class, in our case, occupation. As mentioned above, this is a highly valid indicator to measure social class, but it would have been useful to combine it with additional indicators such as home-ownership [32]. In our study, the register of the occupation has been made by encoding the last occupation declared by each individual included in the study into the occupational social-class categories. Following the recommendations of Domingo-Salvany [14] there are two ways of enquiring about occupation class, the one we have used in this study, i.e. a single open question about the actual or former occupation, and the same question with six multiple choice answers. Therefore, it was possible to encode more than the 90% of literally registered last occupation reports.

## CONCLUSION

This study adds to previous findings that occupation as an individual characteristic representing social class, is associated with poorer results in health.

Our study confirms that manual workers have a higher risk of hospitalization when they are infected by influenza A(H1N1)pdm09 virus than other occupations but they do not have a different probability of being infected by the virus. Vaccination prevents infection in 59% of vaccinated individuals and therefore vaccination programmes should be reinforced.

## APPENDIX

### Other members of the CIBERESP Cases and Controls in Pandemic Influenza Working Group

Andalusia: E. Azor, J. Carrillo, R. Moyano, J. A. Navarro, M. Vázquez, F. Zafra (Médico Centinela), M. A. Bueno, M. Delgado, M. L. Gómez, M. Mariscal, B. Martínez, J. P. Quesada, M. Sillero (Compl. Hosp. Jaén), M. Carnero, J. Fernández-Crehuet, J. del Diego Salas (Hosp. Virgen de la Victoria), V. Fuentes (Hosp. Costa del Sol), V. Gallardo, E. Pérez (Servicio de Epidemiología), R. López (Hosp. Infanta Elena de Huelva), J. R. Maldonado (Hosp. Torrecárdenas), A. Morillo (Hosp. Virgen del Rocío), I. Pedrosa Corral, M. F. Bautista, J. M. Navarro, M. Pérez (Lab. Referencia Gripe), S. Oña (Hosp. Carlos Haya), M. J. Pérez (Hosp. Virgen de Valme), M. C. Ubago (Hosp. Virgen de las Nieves), M. Zarzuela (Hosp. Puerta del Mar). Castile and Leon: P. Sanz (Universidad de León), D. Carriedo, F. Díez, I. Fernández, S. Fernández, M. P. Sanz (Compl. Asist. Universitario, León), J. J. Castrodeza, A. Pérez, R. Ortiz de Lejarazu (Centro Nacional de Gripe, Valladolid), J. Ortiz (Hosp. El Bierzo), A. Pueyo, J. L. Viejo, A. Seco (Compl. Asist. Burgos), P. Redondo (Serv. Territorial de Sanidad y Bienestar Social, León), T. Fernandez, A. Molina (Inst. Biomedicina, Universidad de León). Catalonia: A. Agustí, A. Torres, A. Trilla, A. Vilella (Hosp. Clínic); F. Barbé (Hosp. Arnau de Vilanova); L. Blanch, G. Navarro (Hosp. Sabadell); X. Bonfill, J. López-Contreras, V. Pomar, M. T. Puig (Hosp. Sant Pau); E. Borràs, A. Martínez, N. Torner; C. Bravo, F. Moraga (Hosp. Vall d'Hebrón); F. Calafell (Universitat Pompeu Fabra); J. Caylà, C. Tortajada (Agencia de Salud Publica de Barcelona); I. Garcia, J. Ruiz (Hosp. Germans Trias i Pujol); J. J. García (Hosp. Sant Joan de Deu); M. Baricot, O. Garín (CIBERESP); J. Alonso (IMIM-Hosp. del Mar), J. Gea, J. P. Horcajada (Universitat Pompeu Fabra (CIBER Enfermedades Respiratorias); T. Pumarola

(Red Esp. Inv. en Patología Infecciosa); N. Hayes (Hosp. Clínic\_CRESIB); A. Rosell, J. Dorca (Hosp. de Bellvitge), M. Saez (Universidad de Girona). Madrid: A. Castro (CIBER Enfermedades Respiratorias); C. Álvarez, M. Enríquez, A. Hernández Voth, F. Pozo (Hosp. 12 de Octubre), F. Baquero, R. Cantón, J. C. Galán, A. Robustillo, M. Valdeón (Hosp. Universitario Ramón y Cajal); E. Córdoba, F. Domínguez, M. García Barquero, J. García, R Génova, E. Gil, S. Jiménez, M. A. Lopaz, J. López, F. Martín, M. L. Martínez, M. Ordobás, E. Rodriguez, S. Sánchez, C. Valdés (Área de Epidemiología, Comunidad de Madrid), J. R. Paño, M. Romero (Hosp. Universitario La Paz). Navarre: A. Martínez, L. Martínez (Inst. de Salud Pública), M. Ruiz, P. Fanlo, F. Gil, V. Martínez-Artola (Compl. Hosp. Navarra), M. E. Ursua, M. Sota, M. T. Virto, J. Gamboa, F. Pérez-Afonso (Médico Centinelas). The Basque Country: U. Aguirre, A. Caspelastegui, P. P. España, J. M. Antoñana, I. Astigarraga, J. I. Pijoan, I. Pocheville, M. Santiago, J. I. Villate (Hosp. Cruces), J. Aristegui, A. Escobar, M. I. Garrote (Hosp. Basurto), A. Bilbao, C. Garaizar (Fundación Vasca de Innovación e Investigación Sanitarias), G. Cilla, J. Korta, E. Pérez-Trallero, C. Sarasqueta (Hosp. Donostia), F. Aizpuru, J. L. Lobo, C. Salado (Hosp. Txagorritxu), J. Alustiza (Hosp. Mendaro), F. J. Troya (Hosp. de Santiago). Valencia Community: J. Blanquer (Hosp. Clínic), M. Morales (Hosp. Doctor Peset).

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## DECLARATION OF INTEREST

None.



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