

Risk factors and effectiveness of preventive measures against influenza in the community

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Background The role of different risk exposures and preventive measures against influenza has not been well established.

Objective The aim of this study was to evaluate risk factors and measures to prevent influenza infection in the community.

Methods We conducted a multicenter case-control study. Cases were 481 outpatients aged 18 years or older with laboratory-confirmed influenza A(H1N1)09 in the 2009-2010 season in Spain. A control was selected for each case from outpatients from the same area matched by age and date of consultation. Information on risk situations, preventive measures and other variables was obtained by interview and review of the medical record.

Results In the multivariate conditional logistic regression analysis, the risk of a diagnosis of influenza increased with the number of cohabitants (compared with <3 cohabitants, three

cohabitants had an OR = 1.80, 95% CI 1.12-2.89, and ≥5 cohabitants had an OR = 2.66, 95% CI 1.31-5.41) and for health care workers (OR = 2.94, 95% CI 1.53-5.66). The use of metropolitan public transport was associated with a lower frequency of a diagnosis of influenza (OR = 0.45, 95% CI 0.30-0.68) but not the use of taxis or long-distance transport. The influenza A(H1N1)09 vaccine had a protective effect (OR = 0.13, 95% CI 0.04-0.48), unlike hand washing after touching contaminated surfaces or the use of alcohol-based hand sanitizers.

Conclusion The home environment appears to play an important role in the spread of influenza in adults, but not the use of public transport. Health care workers have a higher risk of contracting influenza. Vaccination was the most effective preventive measure.

Keywords Epidemiology, infection control, influenza, public health, transmission, vaccine.

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Introduction

The influenza virus is transmitted in the community by infected people with or without symptoms, mostly by aerosol, but also by hand contact.¹⁻³ Propagation is favoured by large numbers of people in enclosed places, home, educational and occupational environments and public transport.⁴⁻¹³ Various measures have proven efficacy in preventing influenza. However, the role of different risk exposures and preventive measures against influenza in the community has not been well established. The principal preventive measure is influenza vaccination, but the

protective effect sought is not always achieved, either because there is not a good match between the vaccine and the circulating viral strain or owing to the emergence of a new pandemic virus.¹⁴⁻¹⁶ Some intervention studies have reported that hand washing or alcohol-based hand sanitizers may reduce the risk of influenza.¹⁷⁻²⁰ The usefulness of these measures in the general public depends on their acceptance, their systematic application and how easily they can be assimilated into normal social functions.^{5,21}

During the pandemic influenza A(H1N1)09 wave in Spain, an exhaustive campaign was carried out, with the participation of institutions, the mass media, civil bodies,

educational centres and health care professionals, with the objective of informing the public about non-pharmacological influenza prevention measures, and with an emphasis on simple measures such as covering the mouth when sneezing or coughing, and hand washing. The pandemic vaccine was first used in Spain on November 16, 2009 and was offered to persons with medical conditions that increased the risk of complications and health care professionals.

This study evaluated the effect of various situations that could lead to a greater risk of infection, including the number of cohabitants, being a health care worker and the use of public transport, on the risk of contracting influenza. We also evaluated the effectiveness of preventive measures such as influenza vaccination, hand washing and the use of alcohol-based hand sanitizers.

Methods

Study population and design

This case-control study analysed ambulatory primary health care (PHC) patients enrolled in a larger study of cases with pandemic influenza A(H1N1)09 and matched controls treated by 36 Spanish hospitals or their respective PHC areas between July 2009 and February 2010. The larger study aimed to evaluate the effectiveness of pharmacological and non-pharmacological measures in preventing influenza. Hospitalized cases were matched with patients with the same age (± 5 years), date of consultation (± 10 days with respect to the symptom onset of the case) and province of residence. Each matched group included, among others, two PHC patients: one with confirmed influenza virus A(H1N1)09 infection and another who had consulted for other reasons.²² The study was approved by the Ethics Committee of the hospitals involved.

Only ambulatory PHC patients from the larger study were considered for the present case-control analysis. Cases were defined as PHC patients aged ≥ 18 years with influenza virus A(H1N1)09 infection confirmed by real-time RT-PCR. Controls were PHC patients from the same matched group as cases who had consulted for reasons other than influenza-like syndrome, acute respiratory infection or gastroenteritis. Pandemic influenza had been confirmed in nasopharyngeal swabs from a systematic sample of the first two patients with influenza-like illness diagnosed by PHC physicians each week. Exclusion criteria were documented previous diagnosis of influenza A(H1N1)09 and inability to respond to the interview.

Data collection

This case-control study analysed data that were collected in the context of the large study. After giving written informed consent, cases and controls were interviewed by specifically trained health professionals. Using a structured

questionnaire, we collected information on sociodemographic variables (age, sex and educational level), pre-existing medical conditions (smoking, pregnancy and the following major risk conditions: lung disease, cardiovascular disease, renal failure, diabetes, immunodeficiency, disabling neurological disease, neoplasia, transplantation, body mass index ≥ 40 kg/m², asthma and treatment with systemic or inhaled corticosteroids), exposure to social environments that could favour influenza infection, and influenza prevention measures. The social environments studied that could favour influenza infection included: the number of cohabitants, being a health care worker and the use of metropolitan public transport (bus, metro, tram or local train), long-distance transport (train or plane), and taxi in the 7 days before the onset of symptoms in cases or the medical consultation in controls. The influenza prevention measures evaluated were vaccination with pandemic vaccine more than 7 days before the onset of symptoms in cases or consultation in controls, hand washing after touching contaminated surfaces, the frequency of hand washing and the use of alcohol-based hand sanitizers in the previous 7 days.

Participants chose whether to carry out the interview in a health centre or by telephone. Information on pre-existing medical conditions and vaccination was completed and verified by review of the medical record.

Statistical analysis

A bivariate comparison was made between cases and controls for demographic variables and medical conditions using McNemar's chi-square test for categorical variables and the Student's *t*-test for continuous variables.

A multivariate conditional logistic regression analysis was carried out, which included all the variables assessed and potential confounding factors. The crude and adjusted odds ratio (OR) and their 95% confidence intervals (CI) were used as the measure of association. Analysis of the effect of the pandemic vaccine was repeated for the period after November 16, 2009, when vaccination began.

Results

A total of 481 outpatients with confirmed influenza A(H1N1)09 and 481 controls were included. In spite of matching, cases were slightly younger than controls and more often had secondary or higher education, were pregnant women, or had more than one major risk condition (Table 1). A total of 93.3% of cases and 80.5% of controls were interviewed by telephone ($P < 0.001$).

A total of 42.9% of cases had ≥ 3 cohabitants compared with 31.1% of controls ($P < 0.001$), and a higher proportion were health care workers (18.5% versus 6.2%, $P < 0.001$). Only 0.8% of cases and 3.7% of controls

Table 1. Characteristics of cases and controls

	Cases (n = 481) n (%)	Controls (n = 481) n (%)	Crude OR (95% CI)	P value
Age in years, mean ± SD	43.2 ± 13.7	47.0 ± 15.9		<0.001
Age group				
<45 years	273 (56.8)	225 (46.8)	Reference	
45–64 years	175 (36.4)	186 (38.7)	0.27 (0.15–0.48)	<0.001
65 or more years	33 (6.9)	70 (14.6)	0.06 (0.02–0.16)	<0.001
Sex				
Male	180 (37.5)	180 (37.4)	Reference	
Female	300 (62.5)	301 (62.6)	0.98 (0.74–1.30)	0.886
Educational level				
No education or primary	90 (18.8)	144 (30.3)	Reference	
Secondary or higher	388 (81.2)	332 (69.7)	2.26 (1.57–3.25)	<0.001
Pregnancy				
No	426 (88.6)	468 (97.3)	Reference	
Yes	55 (11.4)	13 (2.7)	5.67 (2.79–11.51)	<0.001
Major risk conditions				
0	358 (74.4)	358 (74.4)	Reference	
1	65 (13.5)	86 (17.9)	0.77 (0.53–1.11)	0.163
2 or more	58 (12.1)	37 (7.7)	1.60 (1.01–2.53)	0.047
Smoking				
Non-smoker	271 (57.2)	266 (55.9)	Reference	
Smoker/former smoker	203 (42.8)	210 (44.1)	0.96 (0.73–1.25)	0.734

($P < 0.001$) had received the monovalent influenza A(H1N1)09 vaccine more than 7 days before symptom onset. There was no difference in vaccination coverage between health care worker controls and other controls (3.3% versus 4.4%, $P = 1$). There was less use of metropolitan public transport in the 7 days before symptom onset in cases compared with controls. However, there were no differences between groups in the use of taxis or long-distance transport in the 7 days before symptom onset (Table 2).

Both the unadjusted and adjusted conditional logistic regression analyses found that the same variables were associated with a greater probability of having a laboratory-confirmed diagnosis of influenza. The risk of a diagnosis of influenza increased with the number of cohabitants, with three cohabitants having an OR = 1.80 compared with >3, four cohabitants an OR = 2.03 and ≥ 5 cohabitants an OR = 2.66, and this trend was statistically significant ($P = 0.002$). Health care workers were almost three times more likely to have a diagnosis of influenza than the rest of the study population (OR = 2.94, 95% CI 1.53–5.66) (Table 2). The use of public transport during the previous 7 days was associated with a lower frequency of influenza (OR = 0.45, 95% CI 0.30–0.68). The use of taxis or long-distance transport during the previous 7 days had no significant effect.

The monovalent influenza A(H1N1)09 vaccine had a protective effect of 87% (OR = 0.13, 95% CI 0.04–0.48)

in the analysis of the entire study period and 96% (OR = 0.04, 95% CI 0.003–0.66, $P = 0.024$) when the analysis was restricted to the period after the vaccine became available. Habitual hand washing after touching contaminated surfaces was associated with a non-significantly lower risk of influenza. The frequency of hand washing and the use of alcohol-based hand sanitizers had no significant protective effect (Table 2). In the adjusted model, the 2009–2010 seasonal influenza vaccine did not show any effect in preventing laboratory-confirmed influenza.

Discussion

The results of this study suggest that, during the 2009–2010 influenza pandemic, the home environment was of great importance in the transmission of influenza in adults, with an increase in the probability of a diagnosis of influenza when there were three or more cohabitants. However, the use of different modes of public transport was either not significant or showed a lower probability of a diagnosis of influenza. Of the preventive measures studied, pandemic influenza vaccination had a protective effect similar to that reported in other studies using different methods.^{23–28} Hand washing after touching contaminated surfaces had a non-significant protective effect, while frequent hand washing or using alcohol-based hand sanitizers had no influence. Health care workers had a higher risk of

Table 2. Association between risk exposures, preventive measures and the diagnosis of laboratory-confirmed influenza in the bivariate and multivariate analyses

	Cases* (n = 481) n (%)	Controls* (n = 481) n (%)	Crude OR (95% CI)**	P value	Adjusted OR (95% CI)***	P value
No. cohabitants						
1–2	136 (28.9)	204 (43.5)	Reference		Reference	
3	133 (28.2)	119 (25.4)	1.95 (1.35–2.82)	<0.001	1.80 (1.12–2.89)	0.015
4	154 (32.7)	114 (24.3)	2.27 (1.59–3.22)	<0.001	2.03 (1.28–3.20)	0.002
5 or more	48 (10.2)	32 (6.8)	3.02 (1.74–5.24)	<0.001	2.66 (1.31–5.41)	0.007
Health care worker						
No	392 (81.5)	451 (93.8)	Reference		Reference	
Yes	89 (18.5)	30 (6.2)	3.81 (2.36–6.16)	<0.001	2.94 (1.53–5.66)	0.001
Use of transportation						
Metro, bus, tram or local train [†]						
No	257 (54.0)	201 (42.0)	Reference		Reference	
Yes	219 (46.0)	278 (58.0)	0.55 (0.41–0.74)	<0.001	0.45 (0.30–0.68)	<0.001
Train or plane [†]						
No	388 (82.4)	391 (82.0)	Reference		Reference	
Yes	83 (17.6)	86 (18.0)	0.97 (0.58–1.37)	0.859	0.80 (0.50–1.28)	0.346
Taxi**						
No	403 (85.2)	400 (83.5)	Reference		Reference	
Yes	70 (14.8)	79 (16.5)	0.86 (0.59–1.26)	0.446	1.19 (0.70–2.04)	0.522
Preventive measures						
Influenza A(H1N1)2009 vaccination						
No	477 (99.2)	463 (96.3)	Reference		Reference	
Yes	4 (0.8)	18 (3.7)	0.24 (0.08–0.70)	0.009	0.13 (0.04–0.48)	0.002
Hand washing [†]						
4 or less times/day						
	122 (25.6)	123 (25.6)	Reference		Reference	
5–10 times/day						
	161 (33.8)	185 (38.5)	0.91 (0.64–1.28)	0.574	0.87 (0.54–1.39)	0.555
More than 10 times/day						
	193 (40.5)	173 (36.0)	1.13 (0.79–1.60)	0.514	0.98 (0.59–1.64)	0.936
Hand washing after touching contaminated surfaces [†]						
Never–occasional						
	197 (41.4)	174 (36.4)	Reference		Reference	
Frequently–always						
	279 (58.6)	304 (63.6)	0.72 (0.52–0.99)	0.044	0.70 (0.44–1.11)	0.132
Alcohol-based hand sanitizers [†]						
Never–occasional						
	350 (73.4)	398 (82.9)	Reference		Reference	
Frequently–always						
	127 (26.6)	82 (17.1)	1.80 (1.30–2.50)	<0.001	1.36 (0.85–2.19)	0.197

*Some variables had missing values.

**Odds ratio and confidence intervals obtained by crude conditional logistic regression.

***Odds ratio and confidence intervals obtained by conditional logistic regression adjusted for sex, age, educational level, pregnancy, smoking, major risk conditions, type of interview and the variables shown in the table. After excluding missing values, 441 case–control pairs were included in the multivariate analysis.

[†]Refers to 7 days prior to symptom onset in cases or medical consultation in controls.

influenza infection than the rest of the study population, which may have been due to occupational exposure.⁷

The association between the number of cohabitants and the risk of influenza has been reported by other studies and supports the idea that the home environment may play an important role in the spread of influenza.^{5–7}

Health care workers are more often exposed to influenza at work, and if they acquire the infection can spread it to patients.^{8,9} This supports the recommendation for annual influenza vaccination in this group. In the season studied, the specific vaccine against the circulating virus was late and many of the cases occurred before it became available.

In other seasons, the greater risk in health care workers may have been combated by a higher vaccination coverage, but no specific vaccine was available during the largest part of the pandemic, and only a low vaccination coverage was achieved in Spanish health care workers.²⁹

Interestingly, the use of public transport was associated with a lower frequency of a diagnosis of influenza. Public transport users probably have a better health status and may consult the physician less. Troko *et al.*¹⁰ found that regular users of public transport may have less risk of acute respiratory infections, perhaps due to the development of protective antibodies attributable to repeated exposure to

the influenza virus. Williams *et al.*⁷ found no difference in the probability of a diagnosis of influenza in regular users of public transport, but an increased risk in adults with their own cars, and Mardani *et al.*¹³ described limited transmission in prolonged periods of close contact during travel.

As in other studies, influenza vaccination was the most effective preventive measure against influenza, especially when, as in this case, the vaccine was a good match with the circulating virus.^{23–28} Habitual hand washing after touching contaminated surfaces was associated with a lower probability of a diagnosis of influenza, although the difference was not significant, possibly because of the low power of the study in demonstrating small-scale effects. Hand washing has been shown to have a preventive effect against influenza in controlled^{30,31} and observational studies in specific groups.^{32,33} In our study, conducted in the community during an epidemic, it is possible that aerosol transmission had greater relevance and the impact of measures to prevent transmission through the hands was lower.³⁴ Alcohol-based hand sanitizers have also proven effective in preventing the transmission of infections, but their effect in adults who habitually wash their hands may be marginal.³⁵ The quality of hand washing or disinfection by alcohol-based sanitizers was not evaluated, and poor cleaning techniques might also explain these findings.

This study had some limitations. To correctly interpret the results, it should be remembered that the cases presented with influenza and had consulted the physician. Therefore, it might be expected that a significant association would be found not only with variables representing risk factors for having influenza but also the variables that influenced the frequency of medical consultation in case of influenza. Second, information on the use of transport, hand washing and the use of alcohol-based hand sanitizers was collected by personal interview, which may have been affected by memory bias and other reporting biases. Nevertheless, we attempted to reduce the effect of such biases by including controls who consulted for other reasons, by training of interviewers and by the use of the same procedures and questionnaire for cases and controls. Third, it is possible that some controls may have had asymptomatic influenza, which would bias the results towards the null hypothesis, underestimating the effect of preventive measures. Fourth, the study was conducted in the 2009–2010 pandemic season, which had some special characteristics and therefore the results may not be generalizable to other influenza seasons, where part of the population may have immunity owing to past exposure and where the seasonal vaccine is normally available from the start of the season. Finally, the power of the study may be insufficient to demonstrate small effects, and therefore we can not rule out the protective effect of some of the measures assessed even when they did not reach statistical significance.

Conclusion

Our results show that, during the 2009–2010 pandemic influenza, the home environment played an important role in the transmission of influenza, while the use of public transport had no appreciable risk. Vaccination was the most effective preventive measure in the community. Frequent hand washing and alcohol-based hand sanitizers may be useful, although our results suggest a limited utility in preventing influenza transmission in the community. Health care workers had a higher risk of influenza than other groups, underlining the importance of routine annual vaccination of this risk group.

Addendum

The other members of the CIBERESP Cases and Controls in Influenza Working Group are: *Andalusia*: E Azor, J Carrillo, R Moyano, J A Navarro, M Vázquez, F Zafra (Sentinel physicians), M A Bueno, M L Gómez, M Mariscal, B Martínez, J P Quesada, M Sillero (Complejo Hospitalario de Jaén), M Carnero, J Fernández-Crehuet, J del Diego Salas (Hospital Virgen de la Victoria), V Fuentes (Hospital Costa del Sol), V Gallardo, E Pérez (Servicio de Epidemiología), R López (Hospital Infanta Elena de Huelva), J R Maldonado (Hospital de Torrecárdenas), A Morillo (Hospital Virgen del Rocío), J M Navarro, M Pérez (Laboratorio de Referencia de Gripe), S Oña (Hospital Carlos Haya), M J Pérez (Hospital Virgen de Valme), M C Ubago (Hospital Virgen de las Nieves), M Zarzuela (Hospital Puerta del Mar). *Valencia Community*: J Blanquer (Hospital Clínico de Valencia), M Morales (Hospital Doctor Peset). *Castile and Leon*: D Carriero, F Díez, I Fernández, S Fernández, M P Sanz (Complejo Asistencial Universitario de León), J J Castrodeza, A Pérez (Dirección General de Salud Pública e Investigación, Desarrollo e Innovación), R Ortiz de Lejarazu (Centro Nacional de Gripe de Valladolid), J Ortiz (Hospital de El Bierzo), A Pueyo, J L Viejo (Complejo Asistencial de Burgos), P Redondo (Servicio Territorial de Sanidad y Bienestar Social de León), A Molina (Instituto de Biomedicina, Universidad de León) *Catalonia*: A Agustí, A Torres, A Trilla, A Vilella (Hospital Clínic); F Barbé (Hospital Arnau de Vilanova); L Blanch, G Navarro (Hospital de Sabadell); X Bonfill, J López-Contreras, V Pomar, M T Puig (Hospital de Sant Pau); E Borràs, A Martínez, N Torner (Dirección General de Salud Pública); C Bravo, F Moraga (Hospital Vall d'Hebrón); F Calafell (Universitat Pompeu Fabra); J Caylà, C Tortajada (Agencia de Salud Pública de Barcelona); I García, J Ruiz (Hospital Germans Trias i Pujol); J J García (Hospital Sant Joan de Deu); O Garín (CIBERESP-Universitat Pompeu Fabra), J Gea, J P Horcajada (Hospital del Mar); N Hayes (Hospital Clínic_CRESIB); A Rosell (Hospital de Bellvitge). *Madrid*: C Álvarez, M Enríquez, F Pozo

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Competing interest

None.

Patient consent

Obtained.

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