

INFLUENZA SYNDROMIC SURVEILLANCE BASED ON SENTINEL PHARMACIES IN CATALONIA (SPAIN) IN 2017–2020

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ABSTRACT

Objective: To analyse influenza surveillance data obtained from sentinel pharmacies of Catalonia, Spain, in 2017–18, 2018–19 and 2019–20 influenza seasons. **Methods:** Influenza surveillance information was collected from a representative sample of community pharmacies of Catalonia. Influenza-like cases were identified based on the ECDC criteria. The Chi-square test and Odds ratios were used to compare percentages between different population groups, with a $p < 0.05$ considered as statistically significant. The screening method was used to assess influenza vaccination effectiveness. The moving epidemic method (MEM) was used to assess influenza epidemics in the three influenza seasons. **Results:** A total of 836, 1,000 and 587 influenza-like cases were reported in 2017–18, 2018–19 and 2019–20. Sentinel pharmacies dispensed medications to 94–98% of patients. Paracetamol, cough medication, ibuprofen and antihistamines were dispensed to more than 25% of patients. Dispensation of antibiotics decreased by 57% from 2017–18 to 2019–20 (OR = 0.45, 95% CI: 0.28–0.74, $p < 0.001$). Physicians prescribed medications to 30–38% of influenza-like patients. The influenza vaccination effectiveness in individuals aged 65 or more years was 51.4% (95% CI: 41.9–60.7) in 2018–19 and 67% (95% CI: 53.4–79.8) in 2019–20 influenza seasons. Influenza epidemics occurred from week 50 of 2017 to week 7 of 2018; from week 51 of 2017 to week 8 of 2019; and from week 2 to week 7 of 2020. **Conclusion:** The influenza surveillance system based on sentinel pharmacies provided consistent information on the influenza epidemic, influenza morbidity not assisted in health centres and medications used to treat influenza-like cases during 2017–2019.

KEYWORDS: Influenza surveillance, influenza morbidity, influenza medications dispensed, sentinel pharmacies, influenza vaccination.

INTRODUCTION

Influenza is responsible for a seasonal epidemic every winter in the Northern hemisphere, with a great impact on then health system due to morbidity, mortality and health services use. Influenza surveillance include monitoring annual epidemics, detection of the start and duration of the epidemic in order to alert health services to reduce morbidity and economic impact. Influenza surveillance based on drug dispensation, health services utilisation and no clinical data is a recent practice.^[1,2]

Since 1988, in Catalonia, a region of Spain with 7.5 million inhabitants, influenza surveillance is carried out using the information obtained from an influenza surveillance system based on sentinel physicians, and from medical visits and hospitalizations due to influenza.^[3,4] Traditional influenza surveillance

information systems provide information on the week of start and duration of the influenza epidemic, and influenza morbidity. Nevertheless, traditional influenza surveillance systems do not provide information about influenza morbidity not attended in health centres and medications used to treat influenza-like cases.

In 2017, a new influenza syndromic surveillance system based on sentinel pharmacies was developed in Catalonia.^[5] The objective of this new sentinel surveillance system was to obtain information about the influenza epidemic and medications dispensed to patients with influenza-like illness during the influenza season. The aim of this study was to analyse influenza surveillance data obtained using a new influenza sentinel surveillance system based on sentinel pharmacies of Catalonia during the 2017–2018, 2018–2019 and 2019–2020 influenza seasons.

METHOD

Influenza syndromic surveillance

Influenza surveillance information was collected from a representative sample of community pharmacies of Catalonia, a region of Spain with 7.5 million inhabitants. Fifty pharmacies were selected randomly from the list of community pharmacies located in the four provinces of Catalonia: 33 (66%) pharmacies were selected from Barcelona, 7 (14%) from Tarragona, 7 (14%) from Girona, and 3 (6%) from Lleida. The distribution of pharmacies by province was proportional to the distribution of the population of Catalonia by province: 73.8% from Barcelona, 10% from Tarragona, 10.6% from Girona, and 5.6% from Lleida.^[6]

Influenza syndromic surveillance activity developed by sentinel pharmacies participating in the study consisted in: 1) to detect influenza-like patients among individuals attended during the 2017-18, 2018-19 and 2019-20 influenza seasons, and 2) to collect socio-demographic and health information from influenza-like patients.

Sentinel pharmacies declared and collected health information from all patients with influenza-like illness attended from week 40 to week 20 of next year during 2017-18, 2018-19 and 2019-20 influenza seasons. Influenza-like cases were detected by active epidemiological surveillance based on the four criterion of the European Centre for the Prevention and the Control of Illnesses (ECDC):^[7] 1) sudden onset of symptoms, 2) fever, 3) at least one of the four systemic symptoms: malaise, headache, myalgia, 4) at least one of three respiratory symptoms: cough, sore throat, shortness of breath.

Data collection

A new surveillance system was developed by the Public Health Agency of Catalonia to obtain information on influenza epidemic from a representative sample of pharmacies of Catalonia. An anonymous questionnaire without any personal information was used to collect socio-demographic and health information from all influenza-like patients attended by pharmacies participating in the study. The questionnaire was accessible on-line.^[7] Sociodemographic information included the age and sex. Health information collected included: 1) symptoms of influenza used to detect influenza-like cases, 2) detection of cases by sentinel pharmacies or in a previous medical visit, 3) medications dispensed by sentinel pharmacies to influenza-like patients, 3) medications prescribed by physicians, 4) derivation of patients to primary health care centres, and 5) influenza vaccination ≥ 14 days before symptoms onset (2018-19 and 2019-20).

Statistical analysis

Sociodemographic characteristics of influenza-like cases, detection of influenza by sentinel pharmacies and medical visits, medications dispensed by pharmacies, medications prescribed by physicians, derivation to

health centres, and influenza vaccination status were assessed in the three influenza seasons. Percentages and 95% confidence intervals were determined for qualitative variables. The Chi-square test (Fisher's exact test when necessary) and the odds ratios were used to compare percentages in different groups, considering a $p < 0.05$ as statistically significant. The t-test was used to compare means between different population groups, with a $p < 0.05$ considered as statistically significant. The statistical analysis of the results was carried out using IBM-SPSS Version 18 (IBM-SPSS, Chicago, IL, USA).

The effectiveness of influenza vaccination (VE) in 2018-19 and 2019-20 among individuals aged ≥ 65 years and 95% confidence intervals were calculated using the screening method.^[8] The influenza vaccination effectiveness (VE) was determined using the formula: $VE = (PV - PCV)/(PV(1 - PCV))$. In this formula, PV is the proportion population vaccinated, and PCV is the proportion of cases aged ≥ 65 years vaccinated against influenza.

Influenza epidemics during 2017-18, 2018-19 and 2019-20 were analysed using the information on the number of influenza-like cases reported per week by sentinel pharmacies. The moving epidemic method (MEM)^[9] was used to analyse influenza epidemics. Firstly, the start and duration of influenza epidemics in 2017-18 and 2018-19 were determined splitting the season in three periods based on the MEM: pre-epidemic, epidemic, and post-epidemic. Secondly, the epidemic threshold (cases declared per week) for detecting the start and duration of the 2019-20 influenza epidemic was determined using the MEM method from the pre-epidemic and post-epidemic values in 2017-18 and 2018-19 influenza seasons.

Ethics approval

The study was approved by the Public Health Agency of Catalonia and the Consell de Col·legis de Farmacèutics de Catalunya. Verbal informed consent was obtained from all influenza-like patients or their parents to participate in the study and collect sociodemographic and influenza-related health information.

RESULTS

Forty one pharmacies participated during the 2017-18 and 2018-19 influenza seasons, and 35 participated in the 2019-20 influenza season. The participation rate was 82% 2017-18 and 2018-19 and 70% 2019-20. The distribution of sentinel pharmacies by province in 2017-18 and 2018-19 was: 25 (61%) from Barcelona, 7 (17.1%) from Tarragona, 6 (14.6%) from Girona and 3 (7.3%) from Lleida. The distribution of sentinel pharmacies by province in 2019-20 was: 21 (60%) from Barcelona, 6 (17.1%) from Tarragona, 5 (14.2%) from Girona and 3 (8.6%) from Lleida. There were not statistical differences between the distribution of pharmacies by province obtained in the study and the

distribution of pharmacies according to the population of Catalonia.^[6]

Eight hundred thirty six, 1,000 and 587 influenza-like cases were reported by sentinel pharmacies to the influenza syndromic surveillance system during 2017–18, 2018–19 and 2019–20 influenza seasons, respectively (Table 1). The mean age of influenza-like cases was 44 years (44.4 years in men and 43.7 years in women) in 2017–2018; 40.9 years (39.9 years in men and 41.9 years in women) in 2018–19; and 44 years (36.8 years in men and 39 years in women) in 2019–20. The percentages of male and female cases were 46.7 and 53.3% in 2017–18; 48% and 52% in 2018–19; and 46.7% and 53.3% in 2019–20. Seventy seven percent of cases in 2017–18, 79% in 2018–19 and 73.1% in 2019–20 had 15 to 64 years (Table 1).

The percentage of cases aged 15–64 years declared by sentinel pharmacies in 2017–18 was higher than in 2018–19 and 2019–20, but differences were not statistically significant (Table 1). The percentage of cases aged ≥ 65 years declared by sentinel pharmacies in 2019–20 was lower than in 2017–18 and 2018–19, but differences were not statistically significant. The percentage of cases aged 0–4 years declared by sentinel pharmacies in 2019–20 was significantly higher ($p < 0.001$) than in 2017–18 (OR = 6.16; 95% CI: 2.87–13.2) and 2018–19 (OR = 2.78; 95% CI: 1.60–4.81).

The percentage of cases aged 15–64 years declared by sentinel pharmacies was significantly higher than the percentage of cases in other age groups for both sexes, men and women in the three influenza seasons (Table 1). The Odds ratios for influenza cases aged 15–64 years versus influenza cases in other age groups were: 14.90 (95% CI: 11.75–18.89, $p < 0.001$) in 2017–18; 11.59 (95% CI: 9.40–14.29, $p < 0.001$) in 2018–19; and 7.37 (95% CI: 5.70–9.59, $p < 0.001$) in 2019–20. The percentage of cases aged 5–14 years declared by sentinel pharmacies was significantly higher than the percentage of cases aged 0–4 years for both sexes, men and women in the three influenza seasons (Table 1). The Odds ratios for influenza cases aged 5–14 years versus influenza cases aged 0–4 years were: 5.47 (95% CI: 2.60–11.55, $p < 0.001$) in 2017–18; 4.44 (95% CI: 2.75–7.18, $p < 0.001$) in 2018–19; and 2.19 (95% CI: 1.43–3.38, $p < 0.005$) in 2019–20. The percentage of cases aged ≥ 65 years declared by sentinel pharmacies was significantly higher than the percentage of cases aged 0–4 years for both sexes, men and women in the three influenza seasons (Table 1). The Odds ratios for influenza cases aged ≥ 65 years versus influenza cases aged 0–4 years were: 16.23 (95% CI: 7.98–33.0, $p < 0.001$) in 2017–18; 6.29 (95% CI: 3.94–10.06, $p < 0.001$) in 2018–19; and 1.80 (95% CI: 1.16–2.81, $p < 0.01$) in 2019–20.

Figure 1 presents the 2017–18 and 2018–19 influenza curves and the results of the MEM analysis. Based on the MEM method, the influenza epidemic started on week 50

of 2017 and ended on week 7 of 2018 in the 2017–18 influenza season, and started on week 51 of 2018 and ended on week 8 of 2019 in the 2018–19 influenza season. The influenza epidemic peaks were achieved on week 2 of 2018 and week of 2019 in the 2017–18 and 2018–19 influenza seasons, respectively. The thresholds for influenza epidemic intensity in terms of influenza-like cases declared per week by sentinel pharmacies obtained for the 2019–20 influenza season using the influenza syndromic surveillance information obtained in the 2017–18 and 2018–19 influenza seasons were: 29.79 cases for basal influenza epidemic; 51.63 for medium influenza epidemic intensity; 133.8 for high influenza epidemic intensity; and 203.7 for very high influenza epidemic intensity. In the 2019–20 influenza season, the influenza epidemic started on week 2 (> 29 cases) and ended on week 7 (> 29 cases) of 2020 (Figure 2). The influenza epidemic peak was achieved on week 5 of 2020 in the 2019–20 influenza season.

In the three influenza seasons, most influenza-like cases declared by sentinel pharmacies had not been detected previously in a medical visit (Table 2). Seventy seven percent of influenza-like cases in 2017–2018, 68.7% in 2018–2019 and 61.8% in 2019–2020 were detected by sentinel pharmacies (Table 2). The Odds ratios for influenza detection by sentinel pharmacies versus influenza detection by physicians in a medical visits were: 4.80 (95% CI: 3.90–5.90, $p < 0.001$) in 2017–18; 4.27 (95% CI: 3.54–5.15, $p < 0.001$) in 2018–19; and 2.62 (95% CI: 2.07–3.32, $p < 0.005$) in 2019–20. In the three influenza seasons, the percentage of influenza detection by sentinel pharmacies was higher in individuals aged 15–64 years than in individuals aged 5–14 years and ≥ 65 years, but differences were not statistically significant. The percentage of influenza detection by sentinel pharmacies in individuals aged 0–4 years was significantly lower ($p < 0.001$) than in individuals aged 15–64 years in the three influenza seasons, and it was significantly lower ($p < 0.05$) than in individuals aged ≥ 65 years in 2017–18 and 2018–19.

Sentinel pharmacies dispensed medications to 787 (94.1%) patients in 2017–18, 953 (95.3%) patients in 2018–19 and 578 (98.5%) patients in 2019–20 (Table 3). The four medications more frequently dispensed to influenza-like patients in the three studied influenza seasons were paracetamol, cough medications, ibuprofen and antihistamines (Table 4). Paracetamol was dispensed to 72.4% of influenza-like patients in 2017–18, 75% of patients in 2018–19 and 83.8% of patients in 2019–20. Cough medications were dispensed to 44.7% of patients in 2017–18, 32.8% of patients in 2018–19 and 38.5% of patients in 2019–20. Ibuprofen was dispensed to 27.6% of patients in 2017–18, 27% of patients in 2018–19 and 29% of patients in 2019–20. Antihistamines were dispensed to 31.9% of patients in 2017–18, 23.7% of patients in 2018–19 and 19.4% of patients in 2019–20. Other medications were dispensed to 0.2–13% of patients (Table 4). Antibiotics were dispensed to 7.9% of patients

in 2017-18, 7.2% of patients in 2018-19 and 3.7% of patients in 2019-20.

The dispensation of medications to influenza-like patients was quite similar in 2017-18, 2018-19 and 2019-20 influenza seasons, except for antibiotics, paracetamol, cough medication and antihistamines (Table 4). Dispensation of antibiotics decreased by 57% from 2017-18 to 2019-20; dispensation of paracetamol increased 15.7% from 2017-18 to 2019-20; dispensation of cough medication decreased by 13.9% from 2017-18 to 2019-20; and dispensation of antihistamines decreased by 39.2% from 2017-18 to 2019-20. The Odds Ratio comparing the dispensation of medications in 2019-20 and 2017-18 was 0.45 (95% CI: 0.28–0.74, $p < 0.005$) for antibiotics; 1.97 (95% CI: 1.51–2.98, $p < 0.001$) for paracetamol; 0.77 (95% CI: 0.62–0.96, $p < 0.05$) for cough medication; and 0.51 (95% CI: 0.40–0.66, $p < 0.001$) for antihistamines.

Physicians had prescribed medications to 253 (30.3%) patients with influenza-like illness attended by sentinel pharmacies in 2017-18, 344 (34.4%) in 2018-19 and 225 (34.3%) in 2019-20 (Table 5). The three medications more frequently prescribed by physicians in the three studied influenza seasons were paracetamol, cough medication and ibuprofen (Table 6). Paracetamol was prescribed to 21.9% of influenza-like patients in 2017-18, 24.9% of patients in 2018-19 and 30.8% of patients in 2019-20. Cough medications were prescribed to 12% of patients in 2017-18, 8.1% of patients in 2018-19 and 9.9% of patients in 2019-20. Ibuprofen was prescribed to 11.1% of patients in 2017-18, 12.8% of patients in 2018-19 and 17% of patients in 2019-20. Other medications were prescribed to 0.1-7% of patients (Table 6). The prescription of antibiotics decreased by 57% from 2017-19 to 2018-19. The prescription of antibiotics was significantly lower in 2019-20 than in 2017-18 (OR = 0.45, 95% CI: 0.28–0.74, $p < 0.005$) and 2018-19 (OR = 0.50, 95% CI: 0.31–0.82, $p < 0.005$). Oseltamivir was prescribed to 0.4% of patients in 2017-18, 1% of patients in 2018-19 and 1% of patients in 2019-20.

The prescription of medications to influenza-like patients was quite similar in 2017-18, 2018-19 and 2019-20 influenza seasons, except for antibiotics, paracetamol, ibuprofen, and antihistamines (Table 6). Prescription of antibiotics decreased by 57% from 2017-18 to 2019-20; prescription of paracetamol increased 40.6% from 2017-18 to 2019-20; prescription of ibuprofen increased by 62.2% from 2017-18 to 2019-20; and prescription of antihistamines decreased by 49.1% from 2017-18 to 2019-20. The Odds Ratio comparing the prescription of medications in 2019-20 and 2017-18 was 0.45 (95% CI: 0.28–0.74, $p < 0.005$) for antibiotics; 1.59 (95% CI: 1.25–2.02, $p < 0.005$) for paracetamol; 1.64 (95% CI: 1.21–2.20, $p < 0.005$) for ibuprofen; and 0.50 (95% CI: 0.28–0.85, $p < 0.05$) for antihistamines.

Sixty-six (6.6%) in 2018–19 influenza season and 33 (5.6%) in 2019–20 influenza season had received the current influenza vaccine during the influenza season. The average age of vaccinated patients was of 61.2 years (63 years in men and 60.3 years in women) in 2018–19, and 54.7 years (51.8 years in men and 57.2 years in women) in 2019–20. The influenza vaccination coverage increased significantly ($p < 0.001$) with age in the 2018–19 and 2019–20 influenza seasons. In the 2018–19 influenza season, the influenza vaccination coverage increased significantly from 0% in children aged 0-14 years to 33.6% in individuals aged 65 or more years. In the 2019–20 influenza season, the influenza vaccination coverage increased significantly from 0% in children aged 0-14 years to 26.3% in individuals aged 65 or more years. The influenza vaccination coverage was significantly higher ($p < 0.001$) in individuals aged 65 or more years than in other age groups in 2018–19 and 2019–20.

In the 2018–19 influenza season, 40 (60.6%) patients had received the influenza vaccine for the recommendation addressed to people of 65 or more years; 6 (9.1%) patients for the recommendation addressed to people with high risk of influenza complications; 1 (1.5%) patient for the recommendation addressed to pregnant women; 10 (15.2%) patients for the recommendation addressed to health personnel; 1 (1.5%) patient for the recommendation addressed to carers of people of high risk; and 8 (12.1%) patients had received the influenza vaccine for personal reasons. In the 2019–20 influenza season, 14 (42.4%) patients had received the influenza vaccine for the recommendation addressed to people of 65 or more years; 4 (12.1%) patients for the recommendation addressed to people with high risk of influenza complications; 3 (9.1%) patient for the recommendation addressed to pregnant women; 4 (12.1%) patients for the recommendation addressed to health personnel; and 8 (24.3%) patients had received the influenza vaccine for personal reasons.

The effectiveness of influenza vaccination obtained in this study for individuals aged ≥ 65 years in Catalonia was 51.4% (95% CI: 41.9-60.7%) during the 2018-19 influenza season and 67.1% (95% CI: 53.5-79.8%) during the 2019-20 influenza season (Table 7). Influenza vaccination effectiveness was determined in this study using the information about the vaccination coverage in individuals aged ≥ 65 years in Catalonia in 2018-19 (51%) and 2019-20 (52%) influenza seasons.^[11]

Table 1: Distribution of patients with influenza-like illness by age and sex in Catalonia (Spain) in the 2017-2018 2018-2019 and 2019-2020 influenza seasons.

Age	Total		Men		Women	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
2017-2018 influenza season						
0-4 years	8	1.0 (0.2-1.7)	4	1.0 (0.3-2.6)	4	0.9 (0.2-2.3)
5-14 years	42	5.0 (3.5-6.6) †	21	5.4 (3.0-7.7) †	21	4.7 (2.6-6.8) ¶
15-64 years	664	79.4 (76.6-82.2)*	308	79.0 (74.8-83.1)*	356	79.8 (76.0-83.7)*
≥ 65 years	122	14.6 (12.1-17.0)**; λ	57	14.6 (11.0-18.2) ‡	65	14.6 (11.2-18.0)***
Total	836	100	390	100	446	100
2018-2019 influenza season						
0-4 years	21	2.1 (1.2-3.0)	13	2.7 (1.1-4.3)	8	1.5 (0.4-2.7)
5-14 years	87	8.7 (6.9-10.5) ¶	48	10.0 (7.2-12.8) †	39	7.5 (5.1-9.9) §
15-64 years	773	77.3 (74.6-79.9)*	365	76.0 (72.5-79.1)*	408	78.5 (74.8-82.1)*
≥ 65 years	119	11.9 (9.8-14.0)**; λ	54	11.2 (8.3-14.2) **	65	12.5 (9.6-15.4)
Total	1,000	100	480	100	520	100
2019-2020 influenza season						
0-4 years	33	5.6 (3.7-7.6)	18	6.4 (3.3-9.4)	15	4.9 (2.3-7.5)
5-14 years	68	11.6 (8.9-14.3) ¶	37	13.1 (9.0-17.2) †	31	10.2 (6.6-13.9) §
15-64 years	429	73.1 (69.4-76.7)*	204	72.1 (66.7-77.5)*	225	74.0 (68.9-79.1)*
≥ 65 years	57	9.7 (7.2-12.2)**; λ	24	8.5 (5.1-11.9) ‡	33	10.9 (7.2-14.5)***
Total	587	100	283	100	304	100

Comparison of the distribution of patients with influenza-like illness in different age groups for each influenza season in both sexes, men and women: * p < 0.001 versus other age groups, ** p < 0.001 vs. 0-4

years old, λ p < 0.001 vs. 5-14 years old, *** p < 0.01 vs. 0-4 years old, ‡ p < 0.001 vs. 0-4 years and p < 0.05 vs. 5-14 years old, † p < 0.001 vs. 0-4 years old; ¶ p < 0.005 vs. 0-4 years old, § p < 0.05 vs. 0-4 years old

Table 2: Percentage of patients with influenza-like illness declared by sentinel pharmacies not previously diagnosed of influenza-like illness in Catalonia (Spain) in the 2017-2018 2018-2019 and 2019-2020 influenza seasons.

Age	2017-2018 Influenza season			2018-2019 Influenza season			2019-2020 Influenza season		
	No.	% (95% CI)	n	No.	% (95% CI)	n	No.	% (95% CI)	n
Both sexes									
0-4 years	1	12.5 (0.3-52.6)	8	5	23.8 (8.2-47.2)	21	10	30.3 (10.3-48.0)	33
5-14 years	23	54.8 (38.5-71.0)	42	47	54.0 (45.0-65.1)	87	23	33.8 (21.8-45.8)	68
15-64 years	481	72.4 (69.0-75.9)	664	553	71.5 (68.3-74.8)	773	298	69.5 (65.0-73.9)	429
≥ 65 years	69	58.6 (47.3-65.8)	122	69	58.0 (48.7-67.3)	119	32	56.1 (42.4-69.9)	57
Total	574	68.7 (65.5-71.9)	836	674	67.4 (64.4-70.3)	1,000	363	61.8 (57.8-65.8)	587
Men									
0-4 years	1	25.0 (0.6-80.6)	4	3	23.1 (5.0-53.8)	13	4	22.2 (6.4-47.6)	18
5-14 years	11	52.4 (28.6-76.1)	21	24	50.0 (34.8-65.2)	48	15	40.5 (23.4-57.7)	37
15-64 years	232	75.3 (70.3-80.3)	308	269	73.7 (69.0-78.3)	365	141	69.1 (62.5-74.7)	204
≥ 65 years	32	56.1 (42.4-69.9)	57	34	63.0 (49.1-76.8)	54	18	75.0 (53.3-90.2)	24
Total	276	70.8 (66.1-75.4)	390	330	68.8 (64.5-73.0)	480	178	62.9 (57.1-68.7)	283
Women									
0-4 years	0	0.0 (0.0-60.2)	4	2	25.0 (3.2-65.1)	8	6	40.0 (3.2-67.7)	15
5-14 years	12	57.1 (33.6-50.7)	21	23	59.0 (42.2-75.7)	39	8	25.8 (42.2-42.8)	31
15-64 years	249	69.9 (65.0-74.8)	356	284	69.6 (65.0-74.2)	408	157	69.8 (65.0-76.0)	225
≥ 65 years	37	56.9 (44.1-69.7)	65	35	53.8 (41.0-66.7)	65	14	42.4 (41.0-60.8)	33
Total	298	66.8 (62.3-71.3)	446	344	66.2 (62.0-70.3)	520	185	60.9 (62.0-66.5)	304

Table 3: Percentage of patients with influenza-like illness that sentinel pharmacies dispensed medications in Catalonia (Spain) in 2017-18, 2018-19 and 2019-20 influenza seasons.

Age	2017-2018 Influenza season			2018-2019 Influenza season			2019-2020 Influenza season		
	No.	% (95% CI)	n	No.	% (95% CI)	n	No.	% (95% CI)	n
Both sexes									
0-4 years	7	87.5 (47.3–99.7)	8	21	100.0 (83.9–100)	21	31	93.9 (79.8–99.3)	33
5-14 years	39	92.9 (80.5–98.5)	42	78	89.7 (82.7–96.6)	87	68	100.0 (94.7–100)	68
15-64 years	631	95.0 (93.3–96.8)	664	743	96.1 (94.7–97.5)	773	423	98.6 (97.4–100)	429
≥ 65 years	110	90.2 (84.5–95.9)	122	111	93.3 (88.4–98.2)	119	56	93.2 (90.6–100)	57
Total	787	94.1 (92.5–95.8)	836	953	95.3 (93.9–96.7)	1,000	578	98.5 (97.4–99.5)	587
Men									
0-4 years	3	75.0 (19.4–99.4)	4	13	100.0 (75.3–100)	13	18	100.0 (81.5–100)	18
5-14 years	18	85.7 (63.6–96.9)	21	41	85.4 (74.4–86.4)	48	37	100.0 (90.5–100)	37
15-64 years	292	94.8 (92.2–97.4)	308	353	96.7 (94.7–98.7)	365	202	99.0 (96.5–99.9)	204
≥ 65 years	50	87.7 (78.3–97.1)	57	50	92.6 (82.1–97.9)	54	23	95.8 (78.9–99.9)	24
Total	363	93.1 (90.4–95.7)	390	457	95.2 (93.2–97.2)	480	280	98.9 (96.9–99.7)	283
Women									
0-4 years	4	100.0 (39.8–100)	4	8	100.0 (63.1–100)	8	13	86.7 (59.5–98.3)	15
5-14 years	21	100.0 (83.9–100)	21	37	94.9 (82.7–99.4)	39	31	100.0 (88.8–100)	31
15-64 years	339	95.2 (92.9–97.6)	356	390	95.6 (93.5–97.7)	408	221	98.2 (95.5–99.5)	225
≥ 65 years	60	92.3 (82.9–97.4)	65	61	93.8 (85.0–98.3)	65	33	100.0 (89.4–100)	33
Total	424	95.1 (92.9–97.2)	446	495	95.4 (93.5–97.3)	520	298	98.0 (96.4–99.7)	304

Table 4: Drugs dispended by sentinel pharmacies to cases of influenza-like illness in Catalonia (Spain) in 2017-2018, 2018-2019 and 2019-2020 influenza seasons.

Drug	2017-2018 Influenza season (n = 836)		2018-2019 Influenza season (n = 1000)		2019-2020 Influenza season (n = 587)		2019-20 vs. 2017-18 OR (95% CI)
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	
Paracetamol	605	72.4 (69.3–75.5)	750	75.0 (72.3–77.7)	492	83.8 (80.7–86.9)	1.97 (1.51–2.58)*
Ibuprofen	231	27.6 (24.5–30.7)	270	27.0 (24.2–29.8)	170	29.0 (25.2–32.7)	n. s.
Acetil salicylic acid	32	3.8 (2.5–5.2)	30	3.0 (1.9–4.1)	12	2.0 (0.8–3.3)	n. s.
Cough medication	374	44.7 (41.3–48.2)	329	32.9 (29.9–35.9)	226	38.5(34.5–42.5)	0.77(0.62–0.96)***
Antihistamines	267	31.9 (28.7–35.2)	237	23.7 (21.0–26.4)	114	19.4 (16.1–22.7)	0.51(0.40–0.66)***
Ephedrine	111	13.2 (10.9–15.6)	126	12.6 (10.5–14.7)	68	11.6 (8.9–14.3)	n. s.
Antibiotic	66	7.9 (6.0–9.8)	72	7.2 (5.4–8.8)	22	3.7 (2.1–5.4)	0.45(0.28–0.74)**
Antiseptic	35	4.2 (2.8–5.6)	41	4.1 (5.5–8.8)	20	3.4 (1.8–5.0)	n. s.
Mucolitic	73	8.7 (6.8–10.7)	67	6.7 (5.1–8.3)	53	9.0 (6.6–11.4)	n. s.
Homeopathic	5	0.6 (0.2–1.4)	2	2.0 (0.0–0.7)	1	0.2 (0.0–0.9)	n. s.
Medicinal plants	34	4.1 (2.7–5.5)	34	3.4 (2.2–4.6)	22	3.7 (2.1–5.4)	n. s.
Bronco-dilator	24	2.9 (1.7–4.1)	21	2.1 (1.2–3.0)	18	3.1 (0.0–0.6)	n. s.
Trypsin	1	0.1 (0.0–0.7)	1	1.0 (0.0–0.6)	1	0.2 (0.0–0.9)	n. s.
Oseltamivir	3	0.4 (0.1–1.0)	1	1.0 (0.0–0.6)	6	1.0 (0.1–1.9)	n. s.
Anti-inflammatory	5	0.6 (0.2–1.4)	14	1.4 (0.6–2.2)	10	1.7 (0.6–2.8)	n. s.

OR: Odds Ratio, CI: confidence interval, n. s.: not significant OR

* p < 0.001, ** p < 0.005, *** p < 0.05

Table 5: Percentage of patients with influenza-like illness that physicians prescribed medications in Catalonia (Spain) in 2017-18, 2018-19 and 2019-20 influenza seasons.

Age	2017-2018 Influenza season			2018-2019 Influenza season			2019-2020 Influenza season		
	No.	% (95% CI)	n	No.	% (95% CI)	n	No.	% (95% CI)	n
Both sexes									
0-4 years	7	87.5 (47.3–99.7)	8	15	71.4 (47.5–88.7)	21	23	69.7 (52.5–86.9)	33
5-14 years	18	42.9 (26.7–59.0)	42	41	47.1 (36.1–58.2)	87	44	64.7 (51.7–75.8)	68
15-64 years	175	26.4 (22.9–29.8)	664	237	30.7 (27.3–34.0)	773	133	31.0 (26.5–35.5)	429
≥ 65 years	53	43.3 (34.2–52.6)	122	51	42.9 (33.5–52.2)	119	25	43.9 (30.1–57.6)	57
Total	253	30.3 (27.1–33.4)	836	344	34.4 (31.4–37.4)	1,000	225	38.3 (34.3–42.3)	587
Men									

0-4 years	3	75.5 (19.4–99.4)	4	9	69.2 (69.2–90.9)	13	14	77.8 (52.4–93.6)	18
5-14 years	9	42.9 (19.3–66.4)	21	23	47.9 (32.7–63.1)	48	21	56.8 (39.4–74.1)	37
15-64 years	73	23.7 (18.8–28.6)	308	108	29.6 (24.8–34.4)	365	66	32.4 (25.7–39.0)	204
≥ 65 years	26	45.6 (31.8–59.4)	57	21	38.9 (24.8–52.8)	54	6	25.0 (9.8–46.7)	24
Total	111	28.5 (23.8–33.1)	390	161	33.5 (29.2–37.9)	480	107	37.8 (32.0–43.6)	283
Women									
0-4 years	4	100.0 (39.8–100)	4	6	75.0 (34.9–96.8)	8	6	60.0 (16.3–67.7)	15
5-14 years	9	42.9 (19.3–66.4)	21	18	46.2 (29.2–63.1)	39	8	74.2 (64.0–76.4)	31
15-64 years	102	28.7 (23.8–33.5)	356	129	31.6 (27.0–36.2)	408	158	29.8 (8.8–42.8)	225
≥ 65 years	27	41.5 (28.8–54.3)	65	30	46.2 (24.6–46.0)	65	19	57.6 (39.2–75.9)	33
Total	142	31.8 (27.4–36.3)	446	183	35.2 (31.0–39.4)	520	118	39.8 (33.2–44.5)	304

Table 6: Drugs prescribed by physicians to reported cases of influenza-like illness cases in Catalonia (Spain) in 2017-2018, 2018-2019 and 2019-2020 influenza seasons.

Drug	2017-2018 Influenza season (n = 836)		2018-2019 Influenza season (n = 1000)		2019-2020 Influenza season (n = 587)		2019-20 vs.2017-18 OR (95% CI)
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	
Paracetamol	183	21.9 (19.0–24.7)	249	24.9 (22.2–27.6)	181	30.8 (27.7–34.7)	1.59 (1.25–2.02)*
Ibuprofen	93	11.1 (8.9–13.3)	128	12.8 (10.7–14.9)	100	17.0 (13.9–20.2)	1.64 (1.21–2.22)**
Acetil salicylic acid	2	0.2 (0.0–0.9)	2	0.2 (0.0–0.7)	2	0.3 (0.0–1.2)	n. s.
Cough medication	100	12.0 (9.7–14.2)	81	8.1 (6.8–9.8)	58	9.9(7.4–12.4)	n. s.
Antihistamines	48	5.7 (4.1–7.4)	37	3.7 (2.4–4.9)	17	2.9 (1.4–4.3)	0.50(0.28–0.85)***
Ephedrine	3	0.3 (0.1–1.0)	15	1.5 (0.7–2.3)	4	0.7 (0.2–1.7)	n. s.
Antibiotic	66	7.9 (5.5–9.1)	72	7.2 (5.5–8.8)	22	3.7 (2.1–5.4)	0.45 (0.28–0.74)*
Antiseptic	3	0.4 (0.1–1.0)	6	0.6 (0.1–1.1)	4	0.7 (0.2–1.7)	n. s.
Mucolytic	27	3.2 (2.0–4.5)	27	2.7 (1.6–3.7)	14	2.3 (1.1–3.7)	n. s.
Homeopathic	0	0.0 (0.0–0.4)	0	0.0 (0.0–0.4)	0	0.0 (0.0–0.6)	n. s.
Medicinal plants	1	0.1 (0.0–0.7)	0	0.0 (1.0–2.8)	3	0.5 (0.1–1.5)	n. s.
Bronco-dilator	22	2.6 (1.5–3.8)	19	1.9 (0.0–0.4)	12	2.0 (0.8–3.3)	n. s.
Trypsin	0	0.0 (0.0–0.4)	1	0.1 (0.0–0.6)	0	0.0 (0.0–0.6)	n. s.
Oseltamivir	3	0.4 (0.1–1.0)	1	0.1 (0.0–0.6)	6	1.0 (0.1–1.9)	n. s.
Anti-inflammatori	2	0.2 (0.2–1.4)	11	1.1 (0.4–1.8)	6	1.0 (0.1–1.9)	n. s.

OR: Odds Ratio, CI: confidence interval, n. s.: not significant OR * p < 0.001, ** p < 0.005, *** p < 0.05

Table 7: Percentage of cases of influenza-like illness vaccinated against influenza during 2018-19 and 2019-20 influenza campaigns.

	Percentage of cases vaccinated against influenza					
	2018-19 Influenza campaign			2019-20 Influenza campaign		
Age	No.	% (IC 95%)	n	No.	% (IC 95%)	n
0-4 years	0	0.0 (0.0–16.1)	21	0	0.0 (0.0–10.6)	33
5-14 years	0	0.0 (0.0–4.1)	87	3	4.4 (0.9–12.4)	68
15-64 years	26	3.4 (2.0–4.7)	773	15	3.5 (1.6–5.3)	429
≥ 65 years	40	33.6 (24.7–42.5)	119	15	26.3 (14.0–38.6)	57
Total	66	6.6 (5.0–8.2)	1,000	33	5.6 (3.7–7.6)	587
Vaccine Effectiveness (≥ 65 years)		51.4 (41.9–60.7)			67.1 (53.5–79.8)	

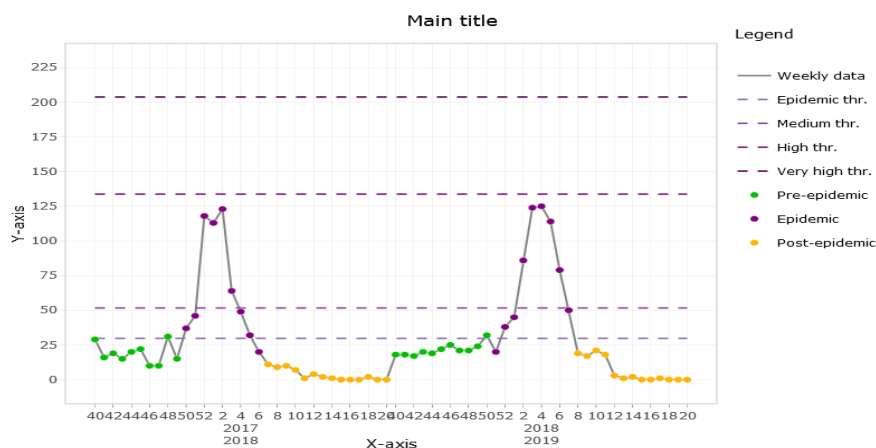


Figure 1: Assessment of influenza epidemic curves in Catalonia (Spain) in 2017-18 and 2018-19 using the MEM method.

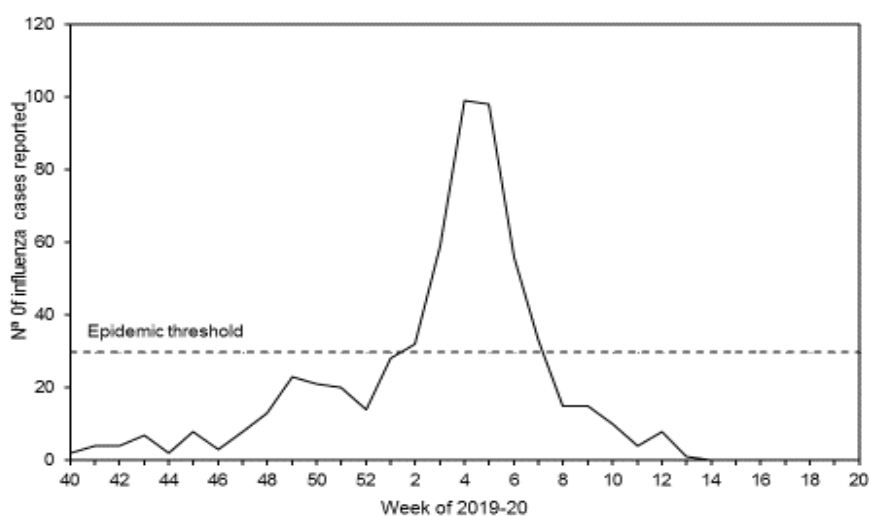


Figure 2: Influenza epidemic curve in Catalonia (Spain) in 2019-20.

DISCUSSION

The study found that influenza surveillance system based on sentinel pharmacies of Catalonia provided consistent information on influenza-like patients, medications dispensed and influenza epidemics in the three influenza seasons studied (2017-18, 2018-19 and 2019-20). The information obtained from sentinel pharmacies is complementary of the information provided by the network of sentinel physicians.

The study found that 79-80% of influenza-like cases reported by sentinel pharmacies had 15-64 years of age and that less than 1% of cases had 0-5 years of age. In addition, only 12-14% of influenza-like cases reported by sentinel pharmacies in the three studied influenza seasons were derived to health centres for clinical assistance. These data indicate that most influenza-like patients attended by sentinel pharmacies were adults of working age with mild or moderate influenza-like illness, who were looking for influenza medication.

The study found that 68.7% of influenza-like cases reported by sentinel pharmacies in 2017–18, 67.4% of patients reported in 2018–19 and 61.8% of patients reported in 2019–20 had not been detected previously in a medical visit. This data indicates that influenza morbidity and social and health impact of influenza could be underestimated based on the information obtained by current influenza surveillance systems. In addition, the fact that many patients with mild or moderate influenza-like illness solved the health problem with medications dispensed by pharmacies without drug prescriptions showed that community pharmacies were acting as health managers and gatekeepers of the health system, reducing the impact of influenza on health services use and reducing public health resources for treating influenza patients.

Sentinel pharmacies dispensed medications 94-98% of patients with influenza like-illness attended by sentinel pharmacies during 2017-20. Medications dispensed to more than 25% of patients included paracetamol, cough medications, ibuprofen and antihistamines. Other medications dispensed to less than 25% of patients

included antibiotics and oseltamivir. The dispensation of medications was quite similar in the three influenza seasons studied, except for antibiotics, paracetamol, cough medication and antihistamines. The variation in the dispensation of paracetamol, cough and antihistamines between 2017-18 and 2019-20 could be explained by a variation in patients preferences for influenza medication. The lower dispensation of antibiotics in 2019-20 than in 2017-18 is explained by the lower prescription of antibiotics to influenza patients in 2019-20.

Physicians had prescribed medications to 30-38% of patients with influenza like-illness attended by sentinel pharmacies during 2017-20. Medications prescribed to more than 8% of patients included paracetamol, cough medications and ibuprofen. Other medications prescribed to less than 8% of patients included antibiotics, antihistamines and oseltamivir. The prescription of medications was quite similar in the three influenza seasons studied, except for antibiotics, paracetamol, ibuprofen, and antihistamines. The variation in the dispensation of paracetamol, ibuprofen and antihistamines between 2017-18 and 2019-20 could be explained by a variation in physician or patient preferences for influenza treatment. The reduction in the prescription of antibiotics between 2017-18 and 2019-20 could be explained by a lower frequency of influenza complications in 2019-20 than in 2017-18 and 2018-19.

The study found that 6.6% of influenza-like patients reported by sentinel pharmacies in 2018-19 and 5.6% of patients reported in 2019-20 had received influenza vaccines. Sixty per cent of vaccinated patients in 2018-19 and 45% in 2019-20 had received influenza vaccine for the recommendation addressed to people of 65 or more years. Influenza vaccination effectiveness in individuals aged 65 or more years obtained in this study using the screening method was 51.4% in 2018-19 and 67.1% in 2019-20. The influenza vaccination effectiveness obtained in this study for 2018-19 was not statistically different than the effectiveness of influenza vaccination in preventing influenza-like illness obtained by Vua *et al.*^[12] (35%; 95% CI: 19-47%) obtained in a meta-analysis carried out in 2002. By contrast, the influenza vaccination effectiveness obtained for 2019-20 was higher than the effectiveness obtained by Vua *et al.*^[12] Nevertheless, it is difficult to compare the influenza vaccination effectiveness obtained in this study with the effectiveness obtained in the meta-analysis carried out by Vua *et al.* because the studies included in the meta-analysis assessed influenza vaccination effectiveness in patents with influenza-like illness attended in health centres.

The influenza epidemic curves in 2017-18 and 2018-19 obtained from sentinel pharmacies were quite similar to those obtained from sentinel physicians-based influenza surveillance, although the sentinel pharmacies-based influenza surveillance was able to detect the start of the

influenza epidemic one week before in 2017-18 and two weeks before in 2018-19, compared with sentinel physicians-based influenza surveillance. The start and end of the influenza epidemics detected by sentinel pharmacies surveillance were from week 50 of 2017 to week 7 of 2018 and from week 51 of 2018 to week 8 of 2019, while sentinel physicians surveillance detected start and end of the epidemic from week 53 of 2017 to week 9 of 2018 and from week 2 of 2019 to week 9 of 2019. Nevertheless, it is difficult to compare the start and end of influenza epidemics obtained for sentinel pharmacies surveillance and sentinel physicians surveillance because the sentinel physicians surveillance decided the start and end of the influenza epidemics when the influenza incidence estimated from declared influenza-like cases was above and below 278.2 per 100.000 habitants in 2017-18¹³ and when it was above and below 110,7 per 100.000 habitants in 2018-19.³

The information provided by the influenza surveillance system based on sentinel pharmacies was complementary of the information provided sentinel physicians. The influenza surveillance system based on sentinel physicians can obtain consistent information about influenza epidemics, while sentinel pharmacies can provide information about influenza-like patients who are looking for influenza medication but are not willing to receive medical assistance.

The study has several limitations. Firstly, 41 sentinel pharmacies were selected and reported cases to the influenza surveillance information in the 2017-18 and 2018-19 influenza seasons. A higher number of cases of influenza-illness could have been reported with a higher number of sentinel pharmacies participating in the study. Nevertheless, the analysis of the information collected from the sentinel pharmacies in 2017-18 and 2018-19 showed that the information provided by the 41 sentinel pharmacies was sufficient to analyse the influenza epidemic and to assess influenza morbidity not assisted in health centres and medications used to treat influenza-like cases during 2017-2019. Secondly, the number of influenza-like cases detected per week by sentinel pharmacies could be lower than the real number of cases if pharmacies were not able to detect all cases of influenza-like illness among attended persons. Nevertheless, to know these data it is necessary to develop a complex and costly study.

In the last years, several syndromic surveillance systems have been developed for influenza and for other illnesses. The Triple project-S-AGE used qualitative and quantitative indicators of success to evaluate nine influenza syndromic surveillance systems developed in Europe.^[14] The quantitative indicators included the advancement in the detection of the start of the influenza epidemic and the validity of the system and the qualitative indicators included the flexibility and acceptability of the surveillance system. The study evaluated influenza syndromic surveillance systems

based in data collected in medical visits, urgent medical visits, queries in websites and telephonic queries. The study found that influenza syndromic surveillance systems were able to detect the start of the influenza epidemic a mean of 0.75 weeks before the traditional influenza surveillance. The success of the influenza syndromic surveillance systems could explain by the following factors: 1) utilization of preclinical information collection that was collected before confirming influenza cases; 2) subnational range of the influenza syndromic surveillance systems; and 3) utilization of no clinical information. Dailey *et al.*¹⁵ compared different surveillance systems and sources of data for influenza surveillance, finding that the early detection of the start of the influenza epidemic required to use no clinical data rated to influenza as well as clinical data collected in primary health care centers and urgencies. The success of influenza syndromic surveillance systems can be explained by the facts that they use the information on patients not attended by health centers due to mild or moderate influenza illness, and the information on influenza patients without microbiological confirmation.

The results obtained in the studies assessing influenza syndromic surveillance systems suggest that the new influenza syndromic surveillance system developed in Catalonia (Spain) can improve the influenza surveillance and control because it is more rapid than the traditional influenza surveillance systems, and because it obtain information that could not be collected using traditional influenza surveillance systems.

CONCLUSIONS

The study found that influenza surveillance system based on sentinel pharmacies of Catalonia provided consistent information on influenza-like patients, medications dispensed and influenza epidemics in the three influenza seasons studied.

Contribution of the authors: P. P., AM. J., G. C., M. R., M. J. and P. R. designed the study. AM. J., M. R. and P. R. selected and coordinated sentinel pharmacies. P.P., G. C. and M. J. managed the collection of influenza surveillance information. P. P. carried out the statistical analysis. All authors participated in the interpretation of data; took part in revising the article; and gave final approval of the version to be published.

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