

Title: Influenza A (H1N1) at the Onset of the Winter in Buenos Aires: A time-series study

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Abstract

Background

The swine influenza pandemic continues to evolve. Measures of disease frequency, effect and impact are needed to allow us to be better prepared to respond. Data from 150000 Argentinean HMO members provides evidence on the burden of Influenza A (H1N1) on an exposed population.

Methods

Time series design compares annual rates of influenza like illness (ILI), severe acute respiratory disease (SARI) and SARI mortality from 2007 to 2009. We also describe fatality and mortality rates per 100000 for A/H1N1 influenza from May 24th to July 11th, 2009. The population database used is from Hospital Italiano de Buenos Aires' HMO.

Results

Ambulatory care demand for ILI increased 17%. SARI rates were similar for the three years while SARI mortality rate was higher when compared to year 2008 (RR 2.8; 95%CI 1.18-6.63) and similar to that of year 2007 (RR 1.05; 95%CI 0.56-1.49). However 2009 was the first year with younger than 65 years old SARI mortalities. The estimated A/H1N1 fatality rate for SARI patients was 6.2%. The estimated A/H1N1 mortality rate among middle class Argentinean HMO members was 6 per 100000 during the study period.

Conclusion

The A/H1N1 epidemic quickly dispersed at the onset of the winter. The impact in the health care system was mainly in ambulatory care with a low rate of increase in admissions. SARI mortalities for year 2009 were 3 fold higher than year 2008 and distributed in a younger age strata. The burden of the swine flu epidemic was mild.

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Introduction

In April 2009, the Mexican Ministry of Health (MoH) reported an outbreak of respiratory illness: In affected patients, a new strain of influenza A (H1N1) virus of swine origin had been isolated.[1] After documentation of human to human transmission of the virus in at least three countries in two regions the WHO raised the alert to pandemic level 6.[2]

By early June, the virus had already spread throughout Buenos Aires and surroundings. The National Surveillance System (NSS) requires physicians to report swine flu patients and to fill out a paper epidemiological form in order to obtain oseltamivir treatment for the reported patient. Mass chemoprophylaxis had not been recommended. The primary diagnostic test (Real-time PCR) was also centralised by the MoH. Initially this test was only done at one public laboratory; after June 18th other public and private laboratories, including Hospital Italiano central laboratory, performed it as well.[3-6]

The Hospital Italiano de Buenos Aires (HIBA) is a 750-bed tertiary centre with high standards in quality of health care and an advanced information system.[7-9] The HIBA is one of the sentinel centres that reports notifiable diseases to the NNS. The

HIBA Health Maintenance Organization (HMO), is a prepaid health care system with approximately 150,000 enrollees; they are middle class residents in the city of Buenos Aires and its surrounding areas.[10]

On July 16th, W.H.O. recommends a weekly report of a qualitative assessment of the geographical spread, trend of cases, intensity of A/H1N1 Influenza and its impact on the health-care system.[13] In this study we describe all these assessment criteria during the onset of the southern winter in 150.000 middle class Argentinean living in Buenos Aires and its surroundings.

Materials and methods

Design: time series

The time period analysed in this study spans from epidemiological week number 21 through 26 (May 24th to July 11th) for year 2009, and for the same period for years 2007 and 2008.

Setting

The study took place within the Health Maintenance Organization (HMO) of the Hospital Italiano de Buenos Aires. The HMO is a prepaid health system that provides services to 27 facilities in the city of Buenos Aires and surrounding areas. Most of the HMO health care system is based on primary care. Patients who require hospitalization are admitted to the Hospital Italiano; laboratory tests are

also centralised. The HMO is paperless with medical and administrative computerised records.[11, 12] The HMO electronic information system requires clinical entries of pharmacological prescriptions and physical examinations and provides reports of laboratory results. These data entries are attached to a specific medical problem controlled by the Spanish version of SNOMED CT.[9] [14, 15] As a medical problem, influenza like illnesses and pneumonia diagnoses are entered, reported and aggregated with a local thesaurus on a terminology server. Subsets of terms included as flu like illness are described in a supplementary file.

Epidemiologic Surveillance system

Case definitions

Acute respiratory illness (ARI): Acute febrile respiratory illness (fever $>38^{\circ}\text{C}$) with the spectrum of disease from influenza-like illness to pneumonia.

Influenza Like Illness (ILI): Sudden onset of fever of $>38^{\circ}\text{C}$ and cough or sore throat in the absence of other diagnoses.

Severe acute respiratory illness (SARI): Meets ILI case definition AND shortness of breath or difficulty breathing AND requiring hospital admission.[13]

Suspected Case of Swine Flu: The Ministry of Health's definition changed during the epidemic: in May, only ILI patients that had been in Mexico and USA were considered; by June, ILI patients that had been in contact with a confirmed case and by July, every person having flu like symptoms. Suspected cases were

required to be reported to national authorities. Suspected cases were treated with oseltamivir.[5, 16-19]

Confirmed H1N1 patients: Real-time PCR test was used. Virological specimens were collected in suspected cases until epidemiological week (EW) number 24. After that week only SARI cases were swabbed.[5, 16-19]

The total number of diagnoses related to ILI, ARI and SARI registered by physicians in the electronic medical record are reported weekly to the NSS:

Suspected and confirmed cases of swine flu, including personal data, were reported to the national surveillance system from the onset of the epidemic. HIBA also began an on-going epidemiological and virological monitoring process and submitted the mandated forms electronically. It has continued this oversight throughout the influenza pandemic. Characteristics of those patients are described elsewhere.[20]

Patients with ILI that visited the emergency department during the EW 21 and the first ten positive A/H1N1 cases in the same week were georeferenced using the HIBA Geographic Information System (GIS).

Measurement

Rate of ILI consultations are described by epidemiological week from fiscal year 2007 to 2009. The epidemic rate was noted when it rose over 200 per 100.000 per week. [21]

Daily ARI (ILI and Pneumonia) rates were calculated for older and younger than 15 years old to define the onset date of the epidemic in each age stratum.

Weekly ARI rate, the number of suspected cases that health national authorities asked to be reported and the proportion of positive A/H1N1 among those swabbed are compared by EW.

Rates of SARI and SARI patients requiring intensive care are compared for the last three years and SARI deaths by age strata (under and over 65 years old).

The electronic medical records from deceased SARI patients during the study period were manually checked to validate the SARI definition and diagnosis, including the nasopharyngeal swab indication to respiratory viruses.

All-cause mortality rates were calculated from the HMO mortality registry.

Rates are expressed by 100000 members with their 95% confidence intervals and from year 2007 to 2009.

Results

A total of 148.741 persons were affiliated on May 31st 2009 with a mean age of 45 years old (SD 25) with 58% females. (Population pyramids shown as supplementary data)

Impact on the Health care system

From May 24th 2009 to July 11th 2009, a total of 19095 persons (13%) had sought care for at least one unscheduled medical consultation for any cause: 48% (9127 patients) asked for home visits, 55% (10582) for unscheduled ambulatory visits and 5.3% (1020) for emergency visits.

Comparing the number of total unscheduled visits between June 2008 and June 2009, there were 4230 per 100.000 more unscheduled visits: 24113 visits per 100.000 for year 2008 vs 28343 visits per 100.000 for year 2009; 17% more unscheduled visits for any cause for year 2009.

Six thousand five hundred and sixty-six patients had sought care due to ILI. The number of ILI registries increased more than fourfold comparing year 2009 to years 2007-2008 (Figure 1).

There was similar number of SARI hospitalizations in years 2009, 2008 and 2007: (145, 121 and 119 respectively) during the same study period.

Trend of cases

The outbreak started among children with a quick onset on June 5th. The adult onset was later, on June 12th, and broader than that of pediatric patients. (Figure 2)

The number of pediatric visits due to ILI on June 6th was 63 for year 2009 while the average number of visits in previous years on the same date was 1.33.

Weekly total ILI consultation rates per 100.000 members increased from EW 21, reached epidemiological threshold on week 23, kept high till EW 26 and then

started to drop below peak observed levels (Post-peak period). However the weekly number of suspected cases requiring national notification did not increase similarly to the increase observed in the ILI rates. The proportion of confirmed A/H1N1 cases was almost 100% for EW 21 to 25 and then decreased to a 50% of positivity. (Figure 3)

The rate of patients treated with oseltamivir in our population during the onset of the epidemic was 143.7/100.000 members.

Intensity of disease

All-cause mortality rate per 100000 during the study period for younger than 65 years old was 15 (95%CI 9 to 25) for year 2007, 18 (95%CI 12 to 29) for year 2008 and 16 (95%CI 9 to 25) for year 2009; and it was 315 (95%CI 260 to 380), 287 (95%CI 237 to 49) and 340 (95%CI 286 to 403) for older than 65 years old respectively.

SARI rates for years 2007, 2008 and 2009 were similar: 84.5 (95%CI 70.4 to 111-5), 82.9 (95%CI 69.1 to 99.5) and 97.4 (95%CI 82.6 to 115) per 100.000 respectively.

SARI Mortality rate (13.4; 95%CI 8.67 to 20.84) for year 2009, was higher when compared to year 2008 (4.79; 95%CI 2.28 to 10.06) (RR 2.8; 95%CI 1.18 to 6.63) and similar to that of year 2007 (12.7; 95%CI 8.05 to 20.29) (RR 1.05; 95%CI 0.56 to 1.49).

Comparable proportions of SARI cases that required ICU care were found in the three years (2009: 22%; 2008: 21% and 2007: 21%). However case-fatality rate for SARI was 14% (20 cases) in year 2009 compared to 6% in year 2008 (p 0.031). Mortality proportion was highest in year 2009 in both age groups. (Figure 4)

Twenty nine laboratory-confirmed A/H1N1 patients were admitted, five of them died.

All five ill-confirmed enrollees who died had at least one comorbidity (obesity/overweight, CHF, Diabetes, asthma, hypertension, VIH, chronic kidney disease and/or cancer).

Mortality among those laboratory-confirmed inpatient A/H1N1 cases was 17% (4/23) for adults and one out of a total of 6 for pediatric cases.

However in a manual check of the electronic medical records of the 20 enrollees who had contracted SARI and died during 2009, only 10 had been swabbed. The ten non-swabbed mortalities had clinical criteria to be swabbed; six of them were admitted before the national swab requirement for people that had not been in Mexico. Applying the MoH weekly reported percentage of A/H1N1 to our non-swabbed deceased patients, 4 of them could have been unregistered positive deceased A/H1N1 patients.

After adding confirmed and estimated unregistered positive dead A/H1N1 patients, the A/H1N1 fatality rate for severe acute respiratory ill patient was estimated as 6.2 percent. The A/H1N1 mortality rate between May 24th and July 11th among middle class Argentinean HMO members was estimated as 6 per 100000.

Geographical spread

The distribution of people that sought care due to flu like symptoms during the earlier weeks (EW 21) had spread throughout the entire Buenos Aires city. A/H1N1 cases also spread while the MoH still recommended contingency plans. (Figure 5)

Discussion

In 150000 middle class Argentinean HMO members the A/H1N1 epidemic sharply dispersed over a 6 week period. When comparing this seasonal period to previous years the impact on the health care system was primarily in ambulatory care; there was a marginal increase in admissions. The outbreak started among children preceding the adult peak by one week. The quick dispersion of this virus had let behind the health public policies adopted to contain it.

Morbidity from respiratory diseases between May 24th and July 11th 2009 was similar to the same period in the previous year. Mortality from SARI was 3 fold higher for year 2009 compared to the 2008 period and similar to 2007, a year when Influenza A also reached an epidemic threshold. However, a new pattern of SARI mortalities was observed in 2009: no cases had been registered in enrollees under 65 years old in previous years while the mortality rate for elderly was highest.

We considered this to be the first study to quantitatively estimate the four recommended indicators measuring the epidemic. The time period covered by this study was during the main epidemic wave but incompletely describes the winter

season. By August 20th no secondary wave had been documented in our HMO surveillance system.

We are not able to describe the impact in Buenos Aires city as a whole due to the dearth of low income enrollees in our HMO population.

Rate Comparisons to other national populations were not feasible. We were unable to find standardized SARI morbidity and mortality rates for this period of time. However in Mexico during four weeks time period (from March 24th to April 29th, 2009) they found 5% case fatality rate for severe pneumonia while we found 14% during six weeks (from May 24th to July 11th, 2009) for severe acute respiratory diseases. The age specific mortality rate for Mexican population for younger than 65 was 4.9% and for older 28% while ours were 6.2% and 23% respectively. These differences may be due to different seasonal pathogens and case definition.[23]

The epidemic seems to have started among children and then spread to adults. Probably schools and other locations where children are involved in social activities are places where the initial strategies should be implemented.

The number of people that received oseltamivir was very low when compared to other developed countries.[24] Viral resistance might be delayed by this policy but some cases might have been more severe because of this restriction.

The rates of consultations surpassed epidemic values the week 23 while there was a policy of containment with restricted swab indication to people who had been in contact with other confirmed case. The few nasopharyngeal swabs obtained from suspected cases visiting our hospital during the first weeks reflected a high h1n1 viral circulation. A high predictive positive value of the swab indication also showed high incidence of the disease and a low indication to make the test.

Pandemic activity appears to be decreasing; however it is uncertain if additional waves will occur. We believe that our surveillance system was not fully prepared to provide us with prompt alerts on a daily basis. For this reason our HMO did not initiate a policy to swab severe acute respiratory patients in the very beginning. It is important during this post peak period to maintain surveillance in order to have early warning feedback and a more rapid clinical response. Informatics alerts are being improved to immediately advise us in the event that daily case rates start to climb.

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Competing interest statement:

All authors declare that the answer to the questions on the competing interest form are all No and therefore have nothing to declare.

Authorship statement:

All authors included on a paper fulfil the criteria of authorship. In addition we want assurance that there is no one else who fulfils the criteria but has not been included as an author.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Ethics approval Every patient signs consent for using his/her medical data for research purpose and without personal identification when entering the HMO. The institutional Ethics Committee (*Comite de Etica del Hospital Italiano de Buenos Aires*) gave favorable ethical approval for the Spanish version of the protocol (internal number 1450).

This study was founding by the Hospital Italiano de Buenos Aires, no special study sponsor or funder can be identified. There is independence of researchers from funders.

Data sharing: technical appendix, statistical code, and dataset available from the corresponding author at <email silvana.figar@hospitalitaliano.org.ar

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Figure 1 Number of Influenza Like Illness visits to the Hospital Italiano's HMO from year 2007 to the epidemiological week number 28 of year 2009.

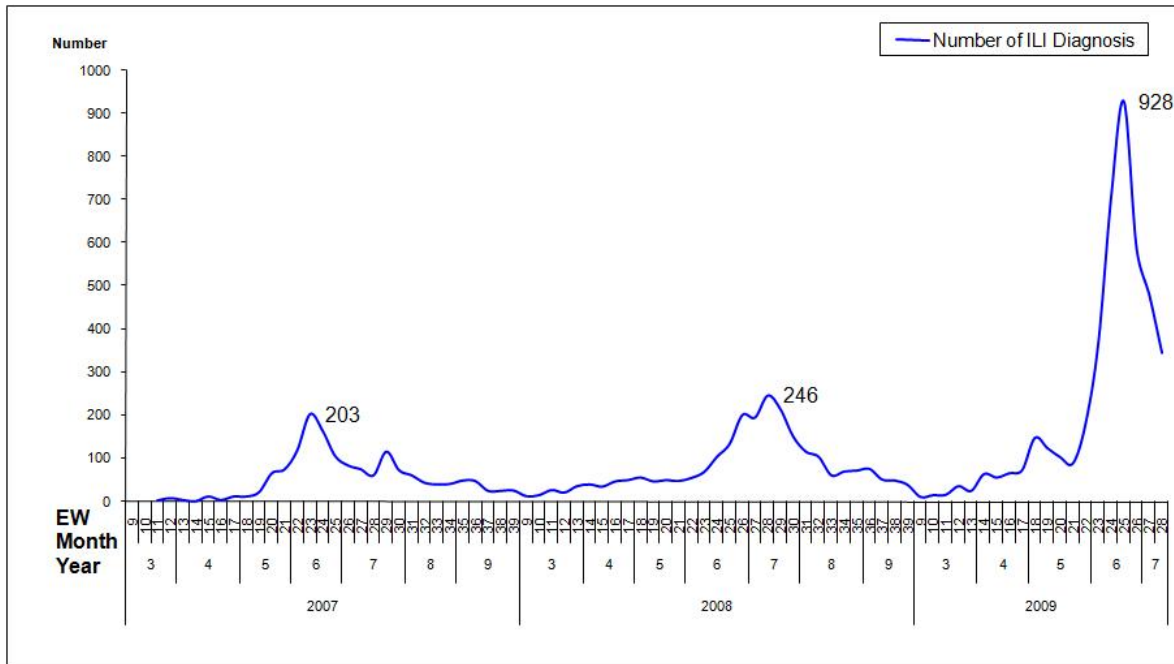


Figure 2 Daily number ARI (ILI and Pneumonia) visits to the Hospital Italiano's HMO for older and younger than 15 years from May 24th 2009 to July 11th 2009.

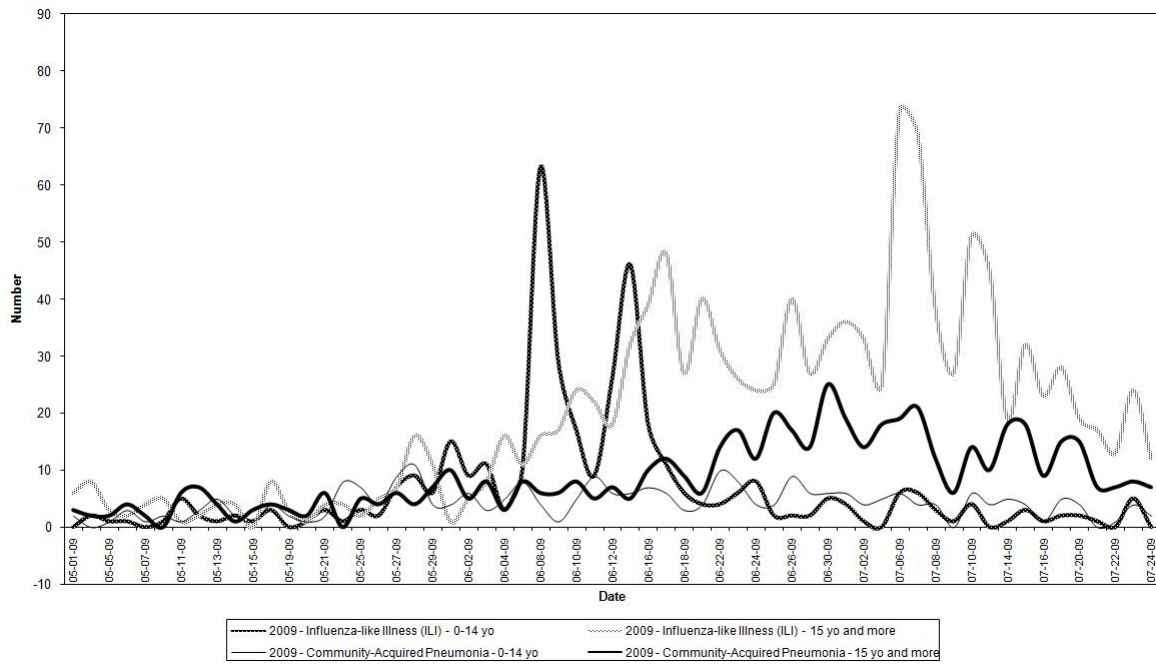


Figure 3 Weekly ARI (Influenza-like illness + Pneumonia) rate and number of suspected cases reported to the Ministry of Health, from May 24th 2009 to July 11th 2009.

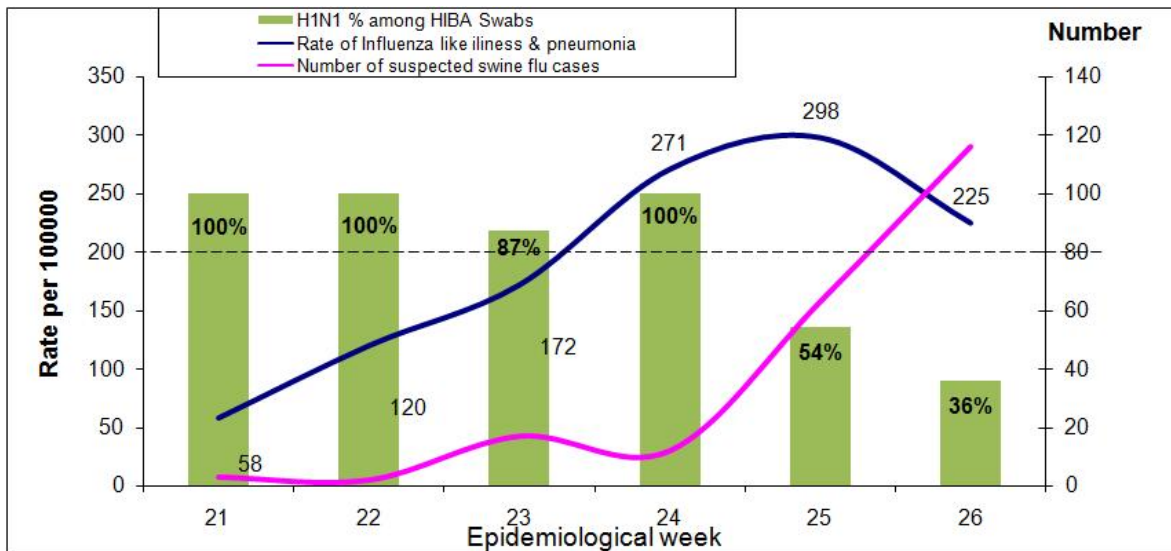


Figure 4 Age specific SARI mortality rates (younger and older than 65) for years 2007 to 2009 at the Hospital Italiano's HMO.

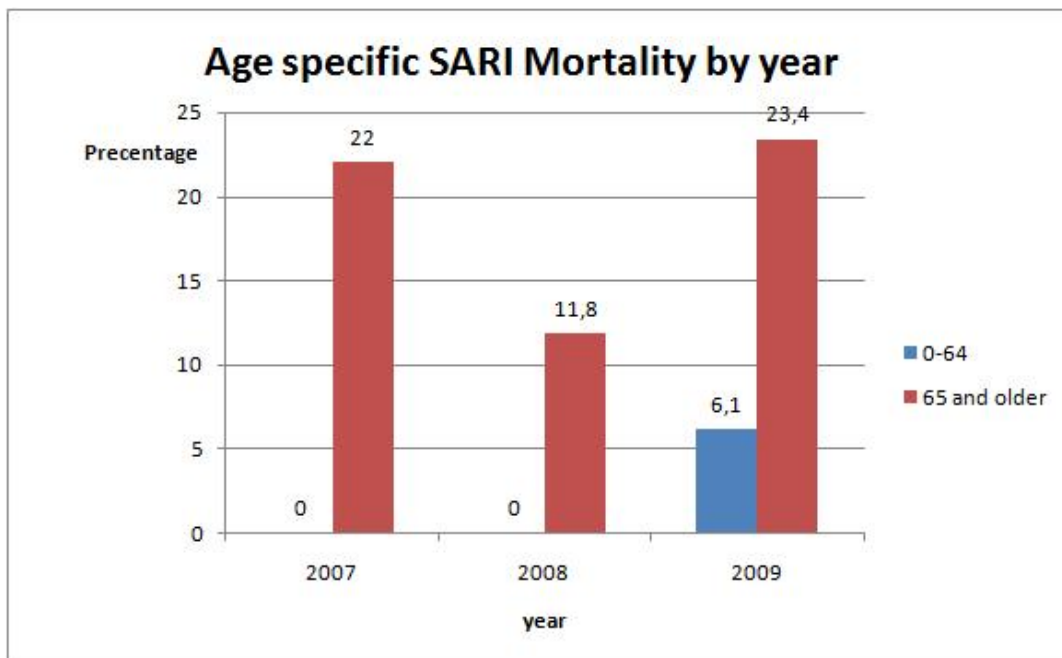
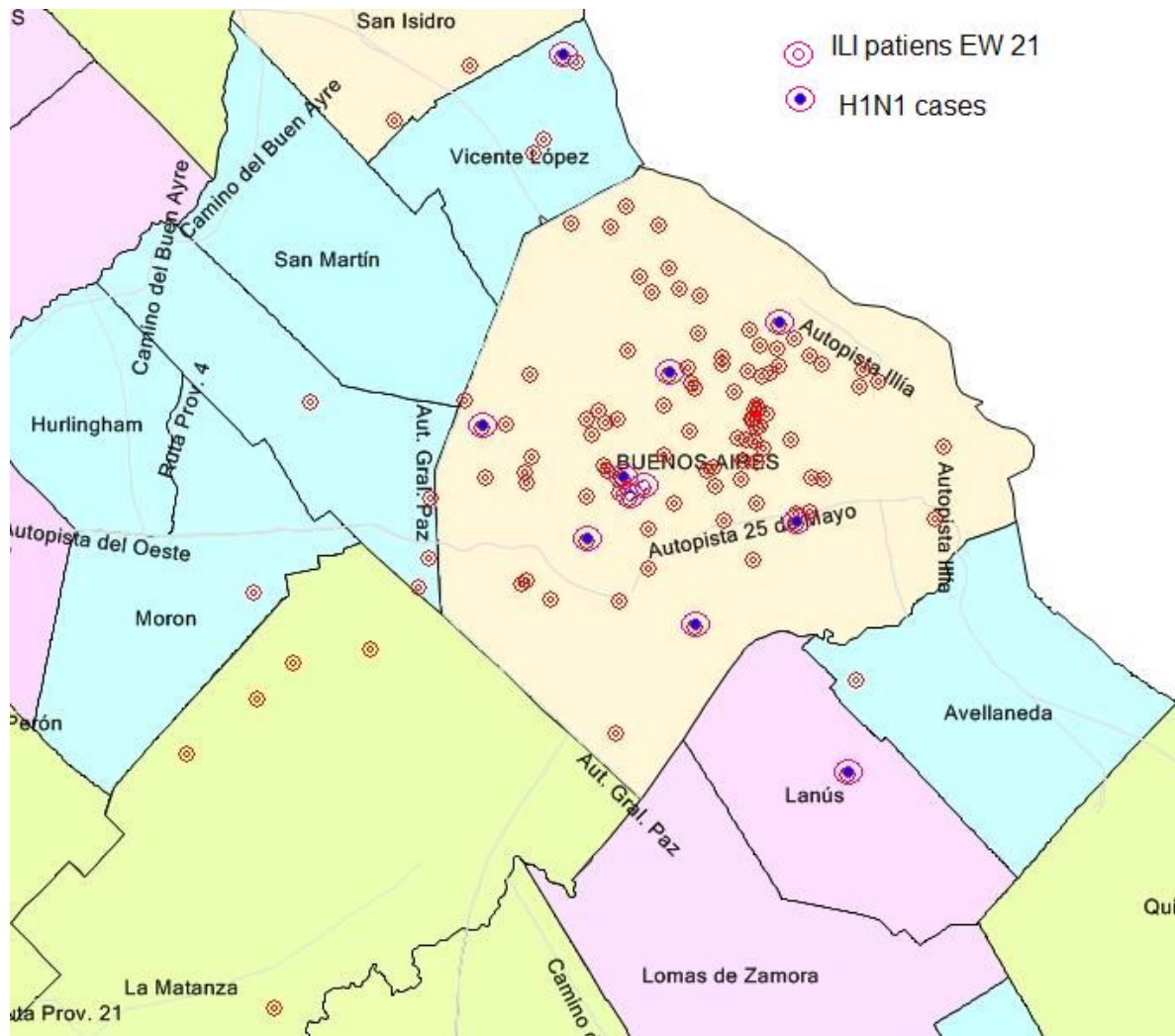


Figure 5 Georeferency of ILI patients from May 24th to June 6th and the first ten confirmed H1N1 cases from the Hospital Italiano's HMO.



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