

Transition from the old to the new viral normality: Where are we?

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Summary

Background: The seasonality of respiratory diseases caused by viruses has been altered by the emergence of SARS-CoV-2. After a period of almost no bronchiolitis and influenza diagnoses, these seasonal infectious diseases are progressively recovering their pre-pandemic dynamics. We aim to describe how this process is taking place in Catalonia.

Material and method: We used primary-care syndromic diagnostic data of bronchiolitis, influenza, and COVID-19 in Catalonia (Spain), which are publicly available through the new Information System for the Surveillance of Infections in Catalonia (SIVIC). We carried out a descriptive study of their dynamics from 2014 to 2023, focusing on the changes induced by the pandemic.

Results: The results show that the old viral normality was significantly disrupted by SARS-CoV-2 and that we are experiencing a transition to a new viral normality where this novel infectious agent could play a role, but its precise dynamics remains unclear.

Conclusions: We are slowly moving towards regular influenza and bronchiolitis seasonality. The role of SARS-CoV-2 in the viral landscape in Catalonia remains uncertain, but its effects on other pathogens are relevant and warrant further investigation.

Key words:

Virus diseases. Respiratory Tract Infections. Population surveillance.

Transición de la antigua a la nueva normalidad viral: ¿dónde estamos?

Resumen

Antecedentes: La estacionalidad de las enfermedades respiratorias causadas por virus se ha visto alterada por la aparición del SARS-CoV-2. Tras un periodo de casi ausencia de diagnósticos de bronquiolitis y gripe, estas enfermedades infecciosas estacionales están recuperando progresivamente su dinámica prepandémica. Nuestro objetivo es describir cómo se está produciendo este proceso en Cataluña.

Material y método: Se utilizaron datos de diagnóstico sindrómico de bronquiolitis, gripe y COVID-19 en atención primaria en Cataluña (España), que están disponibles públicamente a través del nuevo Sistema de Información para la Vigilancia de las Infecciones en Cataluña (SIVIC). Realizamos un estudio descriptivo de su dinámica desde 2014 hasta 2023, centrándonos en los cambios inducidos por la pandemia.

Resultados: Los resultados muestran que la antigua normalidad viral fue significativamente perturbada por el SARS-CoV-2 y que estamos experimentando una transición hacia una nueva normalidad viral donde este nuevo agente infeccioso podría jugar un papel, pero cuya dinámica precisa aún no está clara.

Conclusiones: Estamos avanzando lentamente hacia una estacionalidad regular de la gripe y la bronquiolitis. El papel del SARS-CoV-2 en el panorama vírico de Cataluña todavía no está claro, pero sus efectos sobre otros patógenos son relevantes y deben estudiarse más a fondo.

Palabras clave:

Estacionalidad viral. Infecciones virales respiratorias. Vigilancia.

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Introduction

In temperate climate regions, the seasonality of respiratory viral infections (RVI) has been broadly recognised and studied. Climate factors such as temperature or humidity have been associated with the seasonal pattern of these infections¹, despite this association may be partially driven by resulting changes in human behaviour. Prior to 2020, the two most prevalent problem-causing respiratory infections in Catalonia, Spain, were influenza and bronchiolitis. After the outbreak of SARS-CoV-2 in winter 2019, COVID-19 took the lead. Before the pandemic, bronchiolitis seasons started in October and ended in March, annually. For influenza, its range was typically between November and March. Once COVID-19 arose and measures to prevent the spreading of SARS-CoV-2 were taken, the seasonality of the other RVI was lost. Influenza disappeared until February 2022, while there was a delayed epidemic of bronchiolitis in summer 2021 followed by another almost-regular epidemic starting in September 2021. The last season 2022-2023 for both diseases showed a pattern similar to the pre-pandemic ones, although slightly advanced. On the other hand, since the Omicron waves for COVID-19 in January and June 2022, its autumn epidemic peak achieved a much lower incidence and it has maintained low levels to date.

This trend has not only been the case in Catalonia and the rest of Spain, but RVI in many other countries suffered the same effects due to the pandemic. Data reports by the World Health Organization (WHO) show that little to no activity from influenza viruses was observed in both the Northern and Southern Hemispheres. While prior influenza pandemics altered the seasonality of flu at local levels, the global perturbation to disappearance caused by COVID-19 had not been reported². On the other hand, the respiratory syncytial virus (RSV), the most important cause of bronchiolitis, has been showing up in different ways in a variety of countries. In Brazil, for example, no cases were recorded during the time of a typical season of May to August 2020. In countries like Israel, Germany and France, the first observed epidemic peak during the pandemic was from May to August 2021, with lower incidence than the pre-pandemic seasons, in accordance with what was observed in Spain. Regardless, in South Africa and Australia, RSV infections were spotted during 2020, from July to October for the first one, and during November for the latter, which epidemic also exceeded previous pre-pandemic seasons incidences³.

The differences in RVI among countries during the pandemic could be explained by the variety of scenarios observed worldwide regarding governmental measures to control COVID-19². Our objective is to properly describe the epidemiological dynamics

of bronchiolitis and influenza during the pandemic in Catalonia (Spain), how they changed, and how they are evolving.

Material and methods

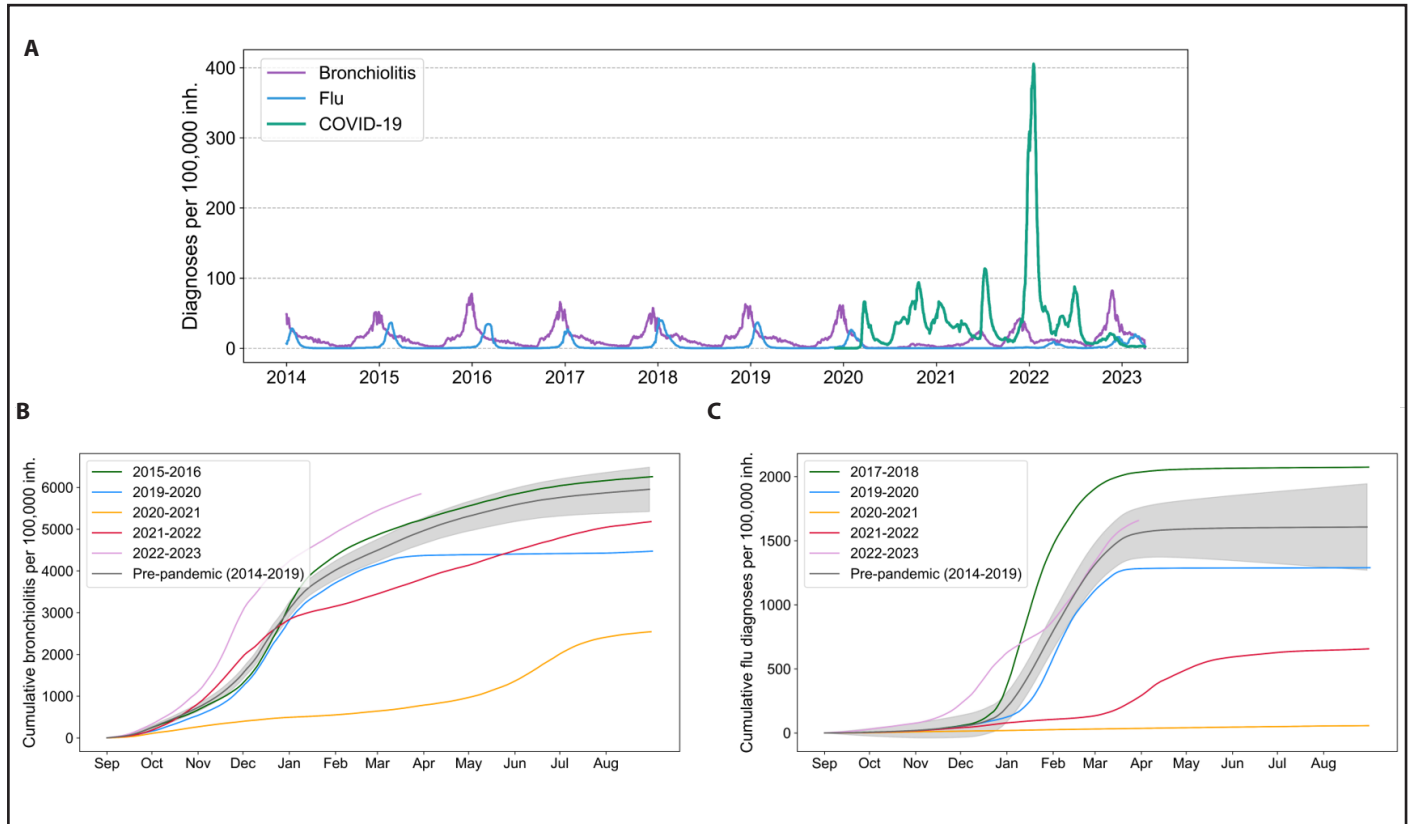
For the present analysis, we used publicly available data from the Information System for the Surveillance of Infections in Catalonia (SIVIC)⁴. This database contains clinical diagnoses of bronchiolitis, influenza, and COVID-19 in public healthcare centres from 2012 to 2023. We limited our study period to September 2014 to March 2023. An epidemic season comprises September one year to the end of August the following year. Pre-pandemic seasons correspond to season 2014-2015 until season 2018-2019.

For each of the series, we compute its 7-day moving mean average and incidence as diagnoses per 10⁵ population. The population considered for bronchiolitis is infants under 5 years old, while for influenza and COVID-19, the general population in Catalonia is considered. For comparative purposes, we also compute the daily mean number of diagnostics of bronchiolitis and influenza across pre-pandemic seasons, as well as their 95% confidence intervals. Moreover, we resampled daily incidence to weekly and provide the boxplot of seasonal weekly incidences both for influenza and bronchiolitis, although only taking into account months from September to March so that previous seasons are comparable with the current one. This way we can measure the differences between maximum and minimum values, together with the median and interquartile range (IQR). The code is accessible in "SARS-CoV-2 and other respiratory viruses in childhood: modelling approaches to understand and predict their epidemiological evolution"⁵.

Results

Figure 1A shows the historical data on bronchiolitis, influenza, and COVID-19 diagnoses. This figure shows the clear seasonal pattern before the appearance of COVID-19. We observe that the maximum pre-pandemic peaks were achieved in 2015-2016 and 2017-2018 for bronchiolitis and influenza, respectively. Once SARS-CoV-2 started spreading, the seasonality was altered. Subsequent smaller bronchiolitis peaks are noticeable, as well as the abovementioned out-of-season wave that appeared in spring 2021. We can also see that the last bronchiolitis peak achieved a similar incidence as in the 2015-2016 season. Figure 1B depicts the cumulative incidence of bronchiolitis in seasons 2015-2016 (maximum pre-pandemic) and 2019-2020 to 2022-2023 (pandemic) in comparison to the average dynamics of pre-pandemic ones. This plot highlights that pandemic seasons behaved differently both

Figure 1. Incidence of the most prevalent respiratory infections in Catalonia. (A) Historical diagnoses per 10⁵ population of influenza in blue, bronchiolitis in purple and COVID-19 in green. For (B) and (C), cumulative diagnoses per 10⁵ population during different seasons and the pre-pandemic mean for bronchiolitis (<5 years) and influenza (all population) diagnoses, respectively.



in time and incidence. In particular, the current season shows 5-week anticipation while the cumulative incidence achieved would be in the range of those in 2015-2016. Besides, there is a sudden stop in the increase of cases once the pandemic started, in March 2020, followed by a season with a global lower incidence of bronchiolitis (2020-2021) and a third one when the final cumulative incidence was close to pre-pandemic values but achieved in a more progressive way.

As for influenza, the cumulative incidence depicted in Figure 1C shows the same sudden stop in March 2020 but is followed by an almost complete disappearance of the disease during the 2020-2021 season and a late and low-incidence season in 2021-2022. Regarding the current wave, we observe a two-phase growth corresponding to two consecutive waves; the first one showed a 6-week anticipation, while the second one would have brought the curve back to expected pre-pandemic dynamics.

With Figures 2 and 3, the aforementioned can be ascertained. In Figure 2A the daily incidence of bronchiolitis diagnoses is presented. We observe how the latter season has outbroken

before pre-pandemic seasons but follows the same scheme as the season 2021-2022. Besides, its peak has been the greatest historically, although it is not significantly different from that of season 2015-2016, also displayed in the figure. The weekly incidences distribution (Figure 2B) has also been noticeably greater than in previous seasons, with the highest maximum incidence and median. This indicates that the latter bronchiolitis epidemic has also been the steepest one. In addition, we discern from the plot that from September 2020 to March 2021, when the COVID-19 pandemic was utterly present, the incidence of bronchiolitis decayed broadly although the disease did not disappear.

Regarding influenza, as depicted in Figure 3A, the daily incidence of the latter season has not reached its historical maximum. However, it has been the broadest one, with a double peak caused by the two main variants of influenza virus in Catalonia, A and B, which respectively caused the first and second waves of the 2022-2023 influenza season. We also observe that the influenza epidemic in 2022-2023 was anticipated with respect to what would be expectable due to pre-pandemic seasons, as

Figure 2. (A) Daily incidence of bronchiolitis (diagnoses per 10⁵ population <5 years) during different seasons and the pre-pandemic mean for bronchiolitis diagnoses. (B) Boxplot of the weekly incidences of bronchiolitis (MM7) per season (September to March) of study.

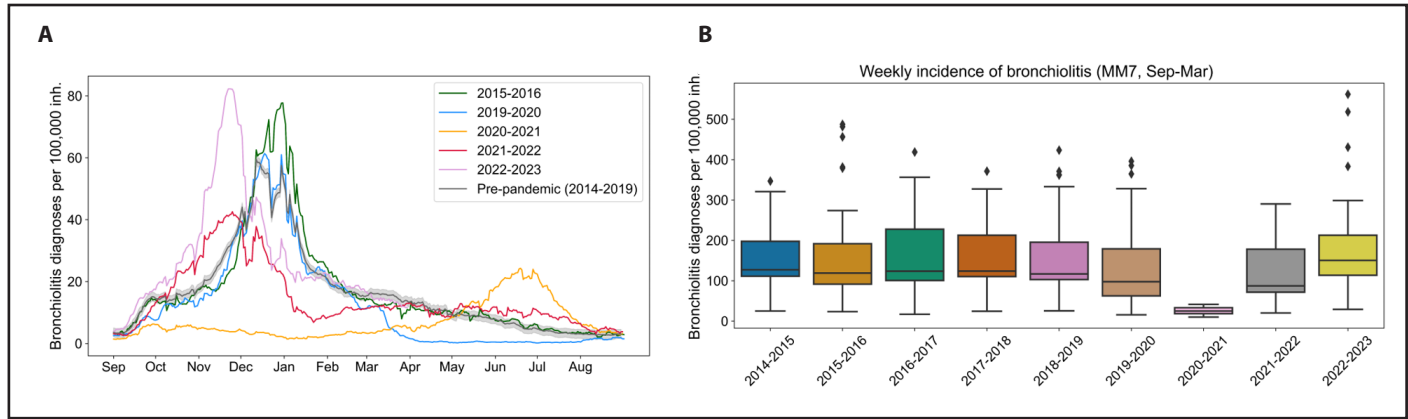
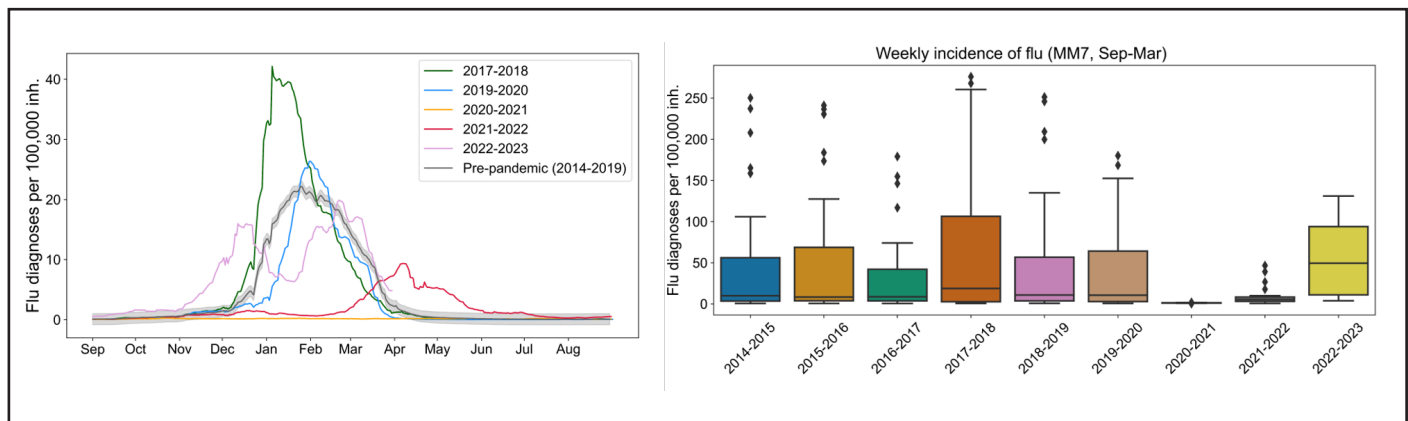


Figure 3. (A) Daily incidence of influenza (diagnoses per 10⁵ population, general population) during different seasons and the pre-pandemic mean for influenza diagnoses. (B) Boxplot of the weekly incidences of influenza (MM7) per season (September to March) of study.



previously described. With Figure 3B, one cannot only ascertain that the latter influenza epidemic was not the greatest one in terms of incidence but also see the contrast between influenza and bronchiolitis, since we see that the former disappeared during 2020-2021 and had minor importance in season 2021-2022.

Discussion

The analysis of the syndromic diagnoses provides a straightforward picture of the changes in viral dynamics driven by the appearance of SARS-CoV-2: from a pre-pandemic viral normality with two consecutive RVI waves each season to a three-year period when the dynamics of the old viruses have broken their strong pattern. At the moment, Catalonia (and most of the countries) are still transitioning towards a new viral normality where the

third RVI that came into play three years ago may play (or not) a role. The current season seems to be progressively recovering the typical dynamics and magnitude of autumn-winter consecutive waves, thus pointing to a closer new viral normality. Other studies corroborate the observations that we performed, finding similar dynamics in other regions^{6,7}.

In the new normality, we can expect a return to the typical seasonality of respiratory viral infections, although the exact dynamics may change due to the presence of SARS-CoV-2. The role of this virus in the overall landscape of respiratory infections remains uncertain, but its effects on other pathogens will expect to be relevant. It is possible that SARS-CoV-2 may become another seasonal virus like the influenza or the RSV, with the potential for occasional outbreaks depending on various factors like immunity levels and the emergence of new variants, but there are also

other plausible scenarios⁸. The new normality may also involve ongoing adaptation of public health measures, such as continued monitoring, surveillance, and vaccination efforts, as well as the potential need to address other infectious agents that have been impacted by the pandemic. Nevertheless, neither the duration of the transition period nor the final seasonal dynamics can be precisely anticipated, despite some modelling efforts are being made in this direction. As an example, the modelling approach published by Ali S., Lau Y. *et al.*⁹ pointed to a higher burden for post-pandemic influenza seasons which, to this moment, has not been observed in Catalonia.

One thing that should be considered and is a limiting factor for this analysis is that the unspecific bronchiolitis syndromic diagnosis, even though in the vast majority of cases it is caused by the Respiratory Syncytial Virus (RSV), it can also be a clinical manifestation of SARS-CoV-2. Perhaps, some diagnoses without microbiological confirmation performed during the pandemic actually correspond to COVID-19. Nonetheless, this is improbable because during the pandemic further testing was being done, and other studies proved that SARS-CoV-2 was unlikely to cause bronchiolitis to children <2 years¹⁰. Besides, it would not affect the conclusions made. However, we have to consider that access to diagnostic tools and protocols of diagnosis have changed throughout the pandemic and this can affect our results, particularly in periods with a high incidence of these viral infections.

All things considered, even though the new respiratory viral seasonality is of great importance, we should widen the focus to address other infectious agents whose typical dynamics have also been altered by the pandemic, either by SARS-CoV-2 itself or by non-pharmaceutical interventions, such as some enteroviruses or streptococcus. In addition, the severity patterns of all these agents should be explored as well in order to detect potential changes, as reported in¹¹. In summary, this study underscores the need to continue researching and monitoring the dynamics of respiratory viruses and other infectious agents in the post-pandemic context to better understand their patterns and adequately address any emerging public health challenges.

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