Patterns of Hospitalizations, Mortality, Incidence and Prevalence of Respiratory Diseases in Brazil Before the Advent of Covid-19: Systematic Review

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Abstract:

Background*: In the setting of lung disorders, ASMA, COPD, and SARS stand out worldwide for the number of deaths; therefore, they were included in the list of diseases with the highest risk of worsening and death from covid 19.*

Materials and Methods*:It is a systematic review of the literature based on ecological and individualized studies that sought to identify the epidemiological behavior (of morbidity and mortality) of the central respiratory diseases (asthma, COPD, and SARS) before the emergence of COVID-19 in Brazil to verify whether the emergence of a new respiratory disease modified patterns of morbidity and mortality (hospitalizations) of asthma, COPD and SARS; as well as mortality, incidence/prevalence of asthma, COPD and SARS. This study followed the criteria of preferred reporting items for systematic reviews and meta-analyses (PRISMA), except for items that deal exclusively with meta-analyses. The studies were searched using the electronic databases Medical Literature Analysis and Retrieval Sistem Online (Medline/Pubmed) and the Latin American and Caribbean Literature in Health Sciences (LILACS). Studies not selected by the electronic search strategy were also considered but identified in the references of the included articles or in the references used in this review. Data were collected from December 2021 to March 2022.*

Results*: Of the 15 articles selected, 04 (26.6%) described asthma and COPD morbidity, 07 (46.6%) mortality, 02 (13.3%) incidence, and 04 (26.6%) prevalence. No studies were found to assess hospitalizations for SARS. Asthma was the third leading cause of hospitalizations, showing a reduction in the period studied. The analysis of pre-COVID-19 mortality showed that asthma and COPD decreased the absolute number of deaths; it was not performed for the SRS, as there are no studies. COPD death rates tended to decline before the pandemic and have remained in decline or stability. Regarding SARS, there was an increase in incidence due to its relationship with SARS-CoV-2*

Conclusion: *The articles bring data on asthma, COPD, and SARS before the pandemic, revealing a decrease in hospitalizations and deaths in Brazil, confirmed in other scientific productions in the same period. However, we still cannot understand whether this trend continues after the COVID-19 pandemic, as few studies have been conducted.*

Key Word*: SARS-CoV-2, epidemiology, morbidity and mortality, respiratory diseases, epidemiological research*

I. Introduction

Pulmonary involvement, evidenced by airway and/or alveolar abnormalities associated with persistent respiratory symptoms, are prevalent characteristics of respiratory disorders such as ASTHMA, COPD, and SARS. In this context of respiratory diseases with persistent symptoms, COVID-19 appeared in 2020, characterized by significant respiratory repercussions, and which quickly directed global health care to lung diseases.[1,2]

In the scenario of pulmonary disorders, ASTHMA, COPD, and SARS stand out worldwide for the impacting numbers of deaths and deaths; therefore, they were included in the list of diseases with a higher risk of worsening and death by covid 19. Thus, to treat patients with chronic diseases affected by the new coronavirus, the health services adjusted to provide care to these people. [1,2,3]

Considering that the disease caused by SARS-Cov-2 presents symptoms similar to other respiratory diseases, it seems essential to understand the epidemiological behavior of asthma and COPD before the COVID-

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19 pandemic and whether the onset of the disease modified variables such as mortality and hospitalization. Knowing this information will help design actions capable of preventing injury.

Furthermore, this study aimed to systematically review the literature on the epidemiological behavior of asthma, COPD, and SARS in the face of COVID-19 in Brazil to verify whether the emergence of a new respiratory disease modified the patterns of morbidity and mortality (hospitalizations) of asthma, COPD and SARS; as well as mortality, incidence/prevalence of asthma, COPD and SARS. ³. (10)

II. Material And Methods

It is a systematic review of the literature based on ecological and individualized studies that sought to identify the epidemiological behavior (of morbidity and mortality) of the central respiratory diseases (asthma, COPD, and SARS) before the emergence of COVID-19 in Brazil to verify whether the emergence of a new respiratory disease modified patterns of morbidity and mortality (hospitalizations) of asthma, COPD and SARS; as well as mortality, incidence/prevalence of asthma, COPD and SARS.

This study followed the criteria of preferred reporting items for systematic reviews and meta-analyses (PRISMA)4, except for items that deal exclusively with meta-analyses.

The studies were searched using the electronic databases Medical Literature Analysis and Retrieval Sistem Online (Medline/Pubmed) and the Latin American and Caribbean Literature in Health Sciences (LILACS). Studies not selected by the electronic search strategy were also considered but identified in the references of the included articles or in the references used in this review. Data were collected from December 2021 to March 2022.

The search descriptors were defined after consultation with the DeCS (Descriptors in Health Sciences) and MeSH (Medical Subject Headings), which were Asthma, Chronic Obstructive Pulmonary Disease/COPD (Pulmonary Disease, Chronic Obstructive, COPD), Severe Acute Respiratory Syndrome (SARS), mortality (mortality), morbidity, hospitalization, epidemiology (epidemiology). The Boolean operators "AND" and "OR" crossed these terms according to language and other associations. Articles in English and Portuguese published ten years before the COVID-19 pandemic (2009 - 2019) were considered since, in this period, there was a reduction in deaths and hospitalizations of these diseases in Brazil. The search strategy is detailed in Table 1.

Table 1 - Search strategy, descriptors and keywords.

PUBMED			
Search	**Filters**	**Query**	**Results**
#1	Full Text	Search: Asthma[Title]	65,587
#2	Full Text	Search: Chronic obstructive pulmonary disease[Title] OR COPD[Title]	37,198
#3	Full Text	Search: Severe Acute Respiratory Syndrome[Title] OR SARS[Title]	45,434
#4	Full Text	Search: #1 OR #2 OR #3	146,004
#5	Full Text	Search: epidemiology[Title/Abstract] OR mortality[Title/Abstract] OR morbidity[Title/Abstract] OR hospitalization[Title/Abstract]	1,160,288
#6	Full Text	Search: #4 AND #5	18,968
#7	Full Text	Search: comment[Publication Type] OR review[Publication Type] OR editorial[Publication Type] OR letter[Publication Type] OR clinical trial[Publication Type]	4,906,248
#8	Full Text	Search: #6 NOT #7	13,516
#9	Full text, From 2009/1/1 to 2019/12/31, Humans, English, Portuguese, Adult: 19+ years.	Search: #6 NOT #7	3,050
LILACS			
Search	**Filters**	**Query**	**Results**
#1	Title Words	search : Asma [Palavras do título] and Epidemiologia OR Mortalidade [Palavras] and Hospitalização OR Morbidade [Palavras]	351
#2	Title Words	Doença Pulmonar Obstrutiva Crônica OR DPOC [Palavras do título] and Epidemiologia OR Mortalidade [Palavras] and Hospitalização OR Morbidade [Palavras]	33
#3	Title Words	search : Síndrome Respiratória Aguda Grave OR SRAG [Palavras do título] and Epidemiologia OR Mortalidade [Palavras] and Hospitalização OR Morbidade [Palavras]	04

To determine the eligibility of the studies, the titles and abstracts of all research results were selected in two stages by two reviewers (A1 and A2) using the predefined inclusion and exclusion criteria described below:

(1) Inclusion Criteria: original scientific articles, with full text available, in Portuguese language and English, whose participants were adult individuals with asthma, COPD, and/or Severe Acute Respiratory Syndrome, both sexes, who present information on the behavior of these diseases before the emergence of COVID-19 in Brazil.

(2) Exclusion criteria: duplicates, reviews, case reports, protocols, letters, editorials, monographs, and theses; individuals with another associated chronic lung disease; publications without clarity of searches or descriptions of information regarding epidemiological behavior.

Selection of studies: Step 1 of selecting articles for the result involved reading and reviewing all titles and abstracts to determine whether they should be included or excluded. Step 2 involved examining the full text of the articles identified in Step 1 to determine their eligibility for data extraction. Additional studies were identified by searching for reference lists of primary studies and review articles. The reviewers (A1 and A2) also evaluated the quality of the studies using the STROBE5 checklist for observational studies and an adaptation of the STROBE checklist for ecological studies, taking into account the adequacy of models, magnitude, and significance of the association.

The articles selected for complete reading were submitted to data extraction, considering the following variables: study characteristics (authors, year and place of publication, period of data collection, analysis method, level of spatial aggregation of data, and indicators used in the analysis); significant outcomes concerning primary and secondary outcomes. Primary and secondary outcomes were defined as (i) Primary Outcome: morbidity and mortality (hospitalizations) of asthma, COPD, and SARS; (ii) Secondary outcomes: mortality, incidence/prevalence of asthma, COPD, and SARS.

III. Result

Based on the criteria established for the review, 15 articles were selected for analysis (Figure 1), ten referring to the ecological level and 05 to the individual level.
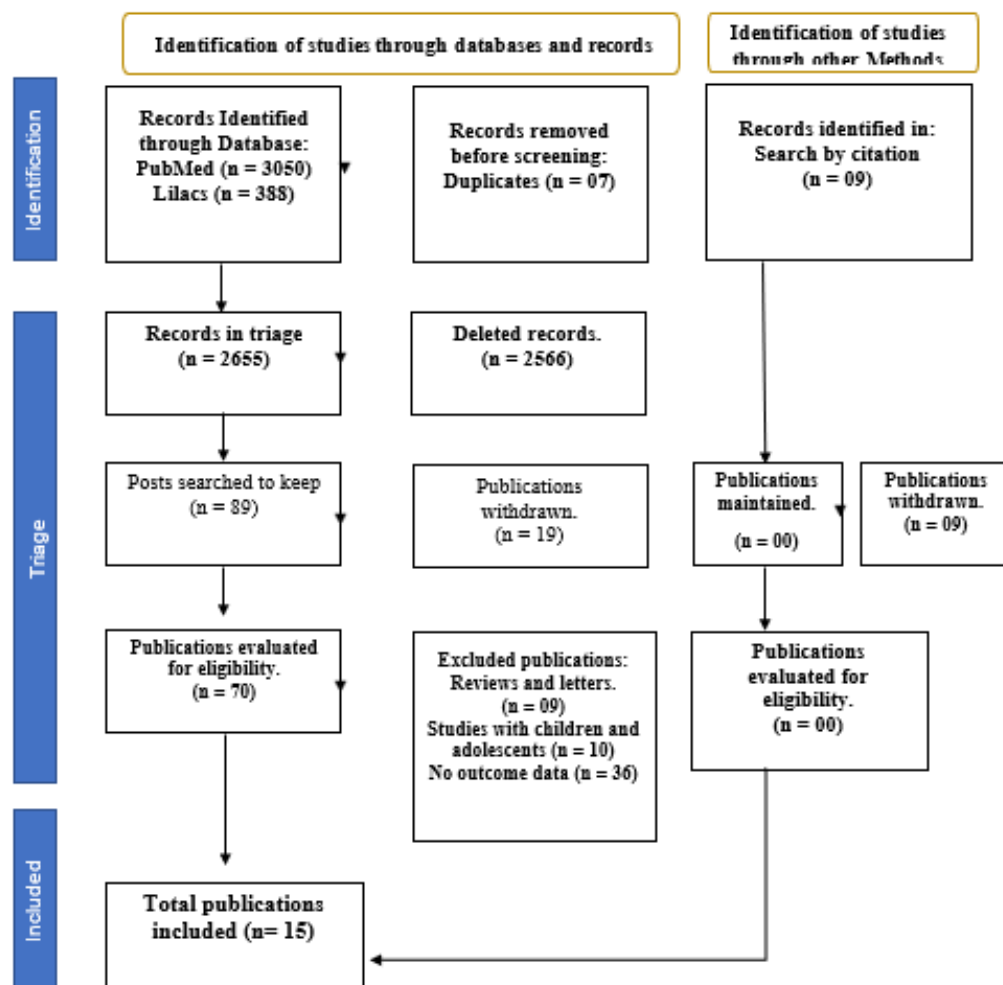

Figure 1. PRISMA flowchart of studies included and excluded

According to the estimated primary outcomes, among the 15 selected articles, 04 (26.6%) described the morbidity of asthma and COPD, 07 (46.6%) addressed mortality, 02 (13.3%) incidence, and 04 (26.6%) investigated prevalence.

The trend of hospitalizations due to conditions sensitive to primary care was described between 1998 and 2009 in Brazil. Among the results, it is possible to observe that asthma was the third leading cause of hospitalizations, behind only infectious gastroenteritis and hospitalizations for heart failure, with a substantial reduction in hospitalizations for these causes during the period studied in all Brazilian regions.
The data were categorized by outcome and results by category, presented in Table 01.

Table 1. Description of studies considering hospitalization, mortality, incidence, and prevalence of asthma, COPD, and SARS.

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Author/ Ano	Type of Study	Disease Respiratory	Outcomes	Results
Antunes cols., 2012	Time series	Asthma COPD	Hospitalization	Asthma and COPD: higher hospitalization rates in this period, representing 49% and 18%, respectively.
Boing cols., 2012	Ecological time series	Asthma	Hospitalization	Asthma was the third leading cause of hospitalizations; rates were slightly higher than 22.0 per 10,000 men and 24.0 per 10,000 women in the first years and just over 10.0 per 10,000 in the last in both sexes.
Cardoso Cols., 2017	Descriptiveecological	Asthma	Hospitalization / Mortality	2,047 people died of asthma in Brazil (5 deaths/day), with more than 120,000 hospitalizations for asthma in 2013. During the study period, the absolute number of deaths and hospitalizations due to asthma decreased by 10% and 36%, respectively. However, the hospital mortality rate increased by approximately 25%.
Gonçalves-Macedo cols., 2019	Exploratory ecological analytical	COPD	Hospitalization/ Mortality	COPD was the fourth leading cause of death from 2000 to 2006, the fifth leading cause of death from 2007 to 2014, and again the fourth leading cause of death from 2015 to 2016. During the study period, COPD mortality rates tended to decrease in Brazil.
Silva, Silva, 2013	Ecological study	Asthma	Mortality	There were 512,082 deaths, of which 1,090 in 1,090, asthma was classified as the underlying cause. Proportional mortality due to asthma, considering multiple causes in the period, was 0.35%, the male/female ratio was, on average, 1:2.3, and most deaths (61%) occurred among individuals aged 60 years and over.
José and Cols, 2017	Ecological study	DPOC	Mortality	In Brazil, in 1990, the mortality rate due to COPD for both sexes was 64.5/100,000 inhabitants (II 95% 66.3 to 62.4) and, in 2015, 44.5/100,000 inhabitants (II 95% 47.0 to 42.3), a drop of about 31%.
Silva, Maia, Souza, 2020	Ecological study	SARS	Incidence	Before the pandemic, there were 5,617 cases of SARS, 187 cases/month, and 23.8 cases/100,000 inhabitants and, in the pandemic, 15,100 cases, 2,516 cases/month, and 320.3 cases/100,000 inhabitants, an increase in monthly detection by 13 times.
Monteiro, Dezanet, França, 2016	Descriptive study	SARS	Incidence	The increase in hospitalizations for SARS varied according to the region of the country, climate, and seasonality,
Fornasa Junior cols, 2008	Cross-sectional study	Asthma	Prevalence	The national prevalence is around 20% and the prevalence in the city of 17.8%.
Santos Cols., 2018	Cross-sectional study	Asthma	Prevalence	The prevalence of asthma diagnosis was 3.6% (2003), 3.7% (2008) and 4.5% (2013), with a trend of significant increase.
Sousa cols., 2011	Cross-sectional study	COPD	Prevalence	The prevalence of chronic obstructive pulmonary disease is high and is associated with tobacco use and age above 60 years.
Menezes cols., 2015	Cross-sectional study	Asthma	Prevalence	There was a reduction or stability of the diagnosis of asthma in Brazil and several factors may be responsible for this behavior.
Graudenz, Gazetoto, 2014	specific mortality	COPD	Mortality	Overall mortality rates due to COPD in Brazil showed a trend of increase from 1998 to 2004 and then a decrease.
Graudenz, Carneiro, Vieira, 2017	Ecological study of time series	Asthma	Mortality	Asthma showed a consistent linear reduction in individuals aged ≤ 34 years; the rate of decline was higher in the age group from 0 to 4 years. The age group from 5 to 34 years also showed a linear reduction in mortality, and this reduction became more pronounced after 2004
Brito cols., 2018	Analysis of mortality rates	Asthma	Mortality	Asthma mortality rates are slightly decreasing in Brazil, being more marked in the 2002-2012 decade

Source: own authorship.

IV. Discussion

This study systematically reviewed the literature on the epidemiological behavior of asthma, COPD, and SARS before COVID-19 in Brazil, seeking to relate the pandemic with the modification of morbidity and mortality patterns, mortality, incidence, and prevalence of these post-pandemic diseases. Some limitations of the results are the lack of more ecological studies at a national level of the time trends of these diseases, especially SARS.

The results that evaluated hospitalizations (before COVID-19) for respiratory diseases showed, in several places in Brazil, records of reduction in hospitalization rates for asthma and no alteration or even decrease in hospitalizations for COPD. No studies were found to evaluate hospitalizations for SARS.[5]

The results obtained show that, although some states presented behaviors of increase or decrease in rates, it is observed that the number of hospitalizations for asthma decreased from 2008 to 2013, with a reduction of 36% in the absolute number of hospitalizations, with an average hospitalization time of about three days. [6,7,8,9].

In this sense, the analysis can be made considering the behavior of respiratory diseases in regions such as the north, northeast, and southeast, where it was possible to notice a decrease in hospitalization rates. However, the absolute numbers still remained high. When the analysis was expanded to the socioeconomic approach, this result represented increased direct and indirect costs for Brazilian society.[6,7,8]

Regarding the analysis of mortality from respiratory diseases in Brazil before the emergence of COVID-19, asthma and COPD appear as conditions whose absolute numbers of deaths have reduced; the same analysis was not made for SARS because no studies were found to evaluate their mortality rates.

Studies published between 2008 and 2013 estimated a 10% reduction in asthma deaths in Brazil. However, there was an increase of about 25% in the mortality rate in that period. The southeast region had the most deaths in people hospitalized for asthma.[6,9]

Research by authors has shown a tendency for decline in asthma-related mortality rates as an underlying and multiple cause, with a reduction among men and stability among women.[9,10,11,12]

Regarding mortality rates due to COPD, some authors obtained results of decline in the period preceding the pandemic by COVID-19, between 2000 and 2016, mainly in the South, Southeast, and Midwest regions. Ral behavior was standardized in all Brazilian regions with sharp falls throughout the period researched in this review.[13,14].

In the context of the emergence of COVID-19, the circulation of respiratory viruses in Brazil was studied in individuals hospitalized between 2011 and 2013 with notification of SARS. It was found that half of the isolated viruses were influenza A, especially subtypes A(H1N1) pdm09 in people aged 20 to 59 years and A(H3N2) in those aged 60 years or older.[15,16]

Children under five years of age had a higher frequency of respiratory sinticial virus infections, followed by influenza A virus. The seasonality analysis of some studies showed that the influenza virus circulated in all seasons of the year, and its periods of higher incidence alternated with those with higher respiratory sinticial virus activity. So, the evaluation of deaths showed that most of the people who died were infected with the influenza virus.[15,16]

The prevalence of COPD before the onset of SARS-Cov-2 was estimated by studies that associated the disease, in most individuals, with tobacco use and advanced age.[17] However, asthma was more prevalent than COPD in most Brazilian regions.[18,19]

The similarity of some pulmonary manifestations between COVID-19 and respiratory diseases in this study is undeniable. However, since the beginning of studies on COVID-19, data from the literature agree that cardiovascular diseases and diabetes are important risk factors for the morbidity and mortality of COVID-19, but differ on the role of respiratory diseases. [9,20]

Due to a lack of better evidence, the already known relationship between viral diseases and chronic respiratory diseases is considered since viral infections are important causes of worsening and exacerbation, impacting the development and progression of these. In addition, respiratory virus infections, including respiratory sinticial viruses and rhinoviruses, lead to significant physiological changes, especially through immune responses, inducing negative impacts on the respiratory tract of individuals.[13,12]

Although it is known that SARS-CoV-2 infects healthy people with respiratory diseases similarly, the latter present more severe symptoms and are more likely to be admitted to intensive care units, in addition to a higher mortality rate compared to individuals without other comorbidities[21]. Thus, investigating the trends of hospitalizations and mortality of respiratory diseases before and after the emergence of COVID-19 seems to be an essential debate for the scientific community to explore and elucidate clinical issues and guide decision-making in public health.

The articles analyzed in this review bring data related to asthma, COPD, and SARS before the COVID-19 pandemic, revealing a tendency to decrease in hospitalizations and deaths from these diseases in Brazil. These data are affirmed in other scientific productions of the literature on the same period[22,23,24]. We cannot yet

understand whether this trend continues after the COVID-19 pandemic since few studies have been conducted in this scenario.

The review and meta-analysis study 25 aimed to investigate the prevalence of asthma among patients with COVID-19 and to compare the results among patients with and without asthma. After analyzing 131 studies that resulted in about 410,382 individuals, a significant variability in the prevalence of asthma among patients with COVID-19 in different countries or regions was found, ranging from 1.1% to 16.9%.

The study was not able to find a significant difference in the prevalence of asthma among hospitalized and non-hospitalized patients (risk ratio [RR], 1,15; CI 95%, 0.92-1.43) and between deaths and survivors (RR, 0.90; CI 95%, 0.73-1.11). It suggests that asthma is not associated with a higher severity of COVID-19 or a worse prognosis and that people with asthma have a lower risk of death compared to people without asthma or other comorbidities. 21.

Another systematic review sought to summarize the prevalence of COPD in people with COVID-19, including 15 studies conducted mainly in China, involving about 2,473 individuals. A prevalence of 2% (95% CI 1–3) was reported. This low prevalence may be related to the treatment of COPD to function as protection or even to the underdiagnosis of the disease that could contribute to these findings. Still, none of the hypotheses were entirely proven26.

Concerning SARS, there was an increase in the number of notifications due to its relationship with the new SARS-CoV-2 virus.15,16 However, the study demonstrated that seasonal influenza and respiratory sinticial virus epidemics seem to have changed dramatically during the pandemic. In countries such as Australia and New Zealand, there was a significant decrease in both, and initial data from Europe showed similar trends.27.

Despite worldwide research efforts to understand the pathophysiology of COVID-19 and thus provide evidence for the development of effective interventions, treatments, and vaccines for public health, much still needs to be studied about the impacts of the pandemic around the globe. Especially about respiratory diseases, many findings were unexpected or counterintuitive to the already existing knowledge about these diseases. It is suggested that more epidemiological studies be conducted on the impact of COVID-19 on chronic and acute respiratory diseases to provide subsidies to health systems to effectively cope with and maintain adequate care for these diseases, especially in low- to middle-income countries such as Brazil.

This study presents limitations, such as the limitation of publications that assess epidemiological compartation of the main respiratory diseases in the period preceding COVID-19. Another limitation was the absence of homogeneity of the analyses in the identified studies, considering that this is a systematic review of the literature without meta-analysis. The authors record the originality of the research and that the limitations described above do not interfere with the results of this study. Further research is fundamental for the study of the epidemiologic behavior of chronic respiratory diseases with the advent of a new respiratory virus and that it is possible to contribute to the implementation of public health policies through health interventions related to the reduction of morbidity and mortality rates due to ASTHMA, COPD, SARS in Brazil and other countries of the world.

The authors state that there was no financial support for this study and declare that there are no conflicts of interest.

V. Conclusion

Before the pandemic by COVID-19, chronic respiratory diseases such as asthma and COPD were among the studies, in a decreasing curve of hospitalizations and mortality. In contrast, the behavior of acute diseases such as SARS, before 2020, was less studied and gained more prominence because of the similarity between their symptoms and those presented by SARS-COv-2.

By 2020, it was possible to notice that hospitalizations and the asthma mortality rate were in decline and that the behavior of COPD was reduced and/or stable when morbidity and mortality variables were evaluated. No studies were found regarding SARS, whose assessment of hospitalization and mortality portrayed the period before the pandemic was found.

The advent of a new respiratory virus impacted the prevalence of asthma among patients with COVID-19 in different regions of the country in the same way that it was not possible to find a significant difference in the prevalence of asthma among hospitalized and non-hospitalized individuals and between deaths and survivors.

With the emergence of COVID-19, there was a survey of people at higher risk of hospitalization and death; among them were chronic respiratory diseases. However, the behavior observed in this study may suggest that asthma and COPD are not associated with a higher severity of COVID-19 or a worse prognosis.

Concerning SARS, although there were few studies on its morbidity and mortality before the pandemic by COVID-19, there was an increase in the number of notifications in the years 2020 and 2021 when compared to previous years, possibly because it has a similar relationship between its symptoms with the new SARS-CoV-2 virus.

Relevant records should be made about the behavior of seasonal influenza epidemics and respiratory sincicial viruses, which seem to have changed dramatically during the pandemic. In countries such as Australia and New Zealand, there was a significant decrease in both, and initial data from Europe showed similar trends.

It is recommended that respiratory diseases continue to be treated to achieve their control or remission, and it is beneficial that affected individuals follow basic infection control measures, including social distancing, hand washing, and wearing a mask or facial coverage. Individuals should be protected with appropriate vaccines and seek to maintain their treatment of pharmacological treatment.

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