# *Comparative analysis of the evolution of influenza, ARI, SARI and COVID-19 for the 2019/2020 - 2020/2021 seasons in the Republic of Moldova*

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**Annotation**. In the Republic of Moldova, influenza and acute viral respiratory infections are registered every year, the number of cases varying from one year to another, but generally representing 2/3 of the total number of infectious diseases registered during the year. However, the flu season 2020/2021 is special compared to the other seasons, not only in the country. For these reasons, this study aimed to highlight the differences between the 2020/2021 season and the 2019/2020 season on the evolution of influenza, ARI and SARI, including the evolution of COVID-19 during these seasons.

**Key-words**: ILI, ARI, SARI, COVID-19

## Introduction

Influenza, acute respiratory infections (ARI) and severe acute respiratory infections (SARI) are infectious diseases that require increased attention due to the level of morbidity and mortality that cause it, producing a negative impact on the health of the population, the health system and directly on the national economy. [1]–[5].

Diseases caused by influenza viruses can develop into epidemics lasting 4-6 years or even pandemics lasting decades, inducing a high number of cases from mild to severe severity or even death. The need for hospitalization and deaths occur more frequently in people in at-risk groups, such as: children, adults over 65, people with chronic diseases, etc. [1], [3], [5], [6].

Globally, influenza epidemics are estimated to cause approximately 3 to 5 million severe illnesses and 290,000 to 650,000 deaths. As a result, epidemics lead to high levels of job losses, increased absenteeism and declining productivity. [3], [5].

In the Republic of Moldova, influenza, acute respiratory infections and severe acute respiratory infections are registered every year, the number of cases of diseases varying from year to year, but generally representing 2/3 of the total number of infectious diseases registered during the year.[3], [6], [7], [8]. In the Republic of Moldova there is the routine epidemiological surveillance system of influenza, ARI and SARI (36 administrative territories) and the sentinel surveillance system (9 sentinel points) represented in figure 1 from which the data are collected

weekly, and during the weeks 40-20 samples are collected weekly for investigation of the presence of influenza viruses from the 9 sentinel points.

The appearance of the new type of coronavirus (SARS-CoV-2) in 2019, in China, disturbed everyone. Thus, on March 11, 2020, the WHO stated that due to the rapid spread of this virus we can characterize it as a pandemic. [9]. In the European region the first cases caused by SARS-CoV-2 were registered in France, Germany, Italy and Spain [10], [11]. In the Republic of Moldova, the first case was registered on March 7, 2020, a case of import from Italy [12].

In the flu season 2019/2020 the circulation of both type A and B virus was observed in the European region, namely subtypes A(H1N1)pdm09, A (H3N2), B/Victoria [13]. According to published data from 2182 laboratory-confirmed cases in the intensive care unit, 64% were of type A, and 36% of type B. In the report of week 15/2021, in the European region it is observed that the flu activity that is at the interseasonal level [14]. During the 2020/2021 season, out of 682,485 investigated samples, 791 were confirmed, of which 396 were type A and 395 type B [14].

The interaction between the SARS-CoV-2 virus and the influenza virus is not clear yet, but it is certain that they played an important role in morbidity, mortality and the capacity of medical services. [15]. There is evidence that there is a pathogenetic competition between these 2 viruses, this may be due to short-term immune-mediated interference in the host, which has the ability to decrease the activity of another virus in its peak activity, otherwise this is a known phenomenon several decades [16]. Another study showed that seasonal flu vaccination may increase the risk of developing other viruses, this phenomenon is called viral interference [17].

Both COVID-19 and influenza remain a public health threat, although anti-epidemic measures can prevent them from spreading. [18].

**Materials and methods**

Epidemiological data were collected through the national system of surveillance and monitoring of influenza, ARI and SARI from all administrative territories of the Republic of Moldova.

Virus detection in samples of nasopharyngeal exudates from individuals with influenza, ARI or SARI was performed by molecular biology (rRT-PCR) techniques.

A descriptive incidence study was planned with the evaluation of the following data: Cases of influenza, ARI and SARI submitted weekly (week40-week20) to the section for surveillance and control of influenza and viral respiratory infections in the seasons 2019/2021 (2331 completed annexes from 37 administrative territories); Accompanying bulletins for pathological products for laboratory diagnosis of human influenza virus infection in the seasons

2019-2021 (1601 accompanying bulletins for pathological products); The results of laboratory investigations on the presence of influenza virus in patients with a presumptive diagnosis of influenza, ARI and SARI in the seasons 2019-2021 (285 positive results); Reports of deaths with the presence of influenza virus confirmed by the laboratory submitted to the National Agency for Public Health in the seasons 2019-2021 (10 reports).

The volume of research and interpretation of the study results is based on traditional statistical methods, ensuring the degree of representativeness of the data accepted for medical studies. The obtained data are processed with the help of Epi Info ™ 7 programs and Microsoft Excel 2019.

**Results and discussions**

The flu season 2020/2021 is totally different from the flu season 2019/2020 both at national and international level. Referring only to influenza, then in the 2020/2021 season no cases of influenza were registered compared to the 2019/2020 season when 3258 cases of influenza were registered.

In the 2019/2020 season, the first 2 cases of influenza were registered in week 48/2019, following week 51/2019, a sudden increase up to 21 cases, maintaining up to 35 cases in week 02/2020. Subsequently, influenza cases increased exponentially until the week 06/2020 to 372 cases (13.9 cases per 100,000 population) following a small decrease after which in the week 09/2020 there was a peak of 442 cases of influenza (16.5 cases per 100,000 population). The last case of influenza in the 2019/2020 season was registered in week 16/2020 (figure 1).

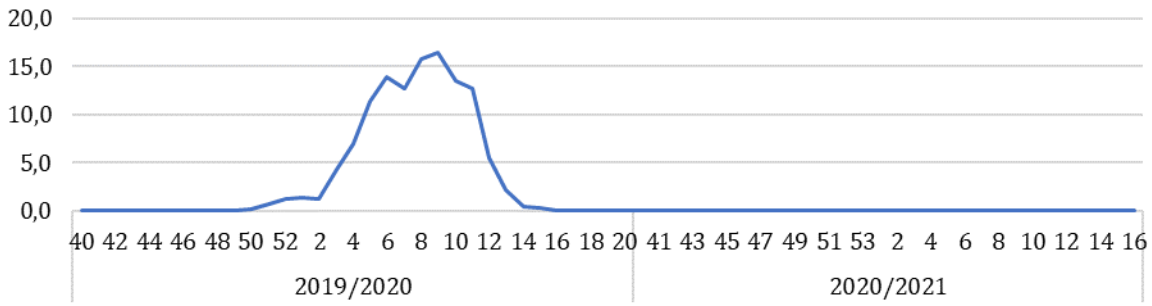


*Figure 1 Evolution of influenza morbidity per 100,000 population, 2019/2020-2020/2021 seasons*

The cases of acute respiratory infections also had a different evolution in these 2 seasons. Thus, during the weeks 40/2019 - 16/2020, 243045 cases of ARI were registered compared to 128883 cases of ARI during the weeks 40/2020 - 16/2021, in other words in the 2020/2021 season there were registered by almost 2 times fewer cases.

For the 2019/2020 season, the epidemic threshold of 308.32 cases per 100,000 population was established, of medium intensity - 463.45, of high intensity 626.14 and of very high intensity 715.19. Respectively, this season the epidemic threshold was exceeded in week 04/2020 (370.96 cases per 100,000), the average intensity threshold was exceeded in week 05/2020 (511.09 cases per 100,000) and the high intensity threshold of was exceeded in the week 09/2020 when the peak of this season of 17518 ARI cases was registered (653.24 per 100.00 population) following a decrease of up to under a thousand cases in the weeks 18/2020 - 20/2020, being few in compared to previous seasons, probably due to the start of COVID-19 cases in the country (Figure 2).

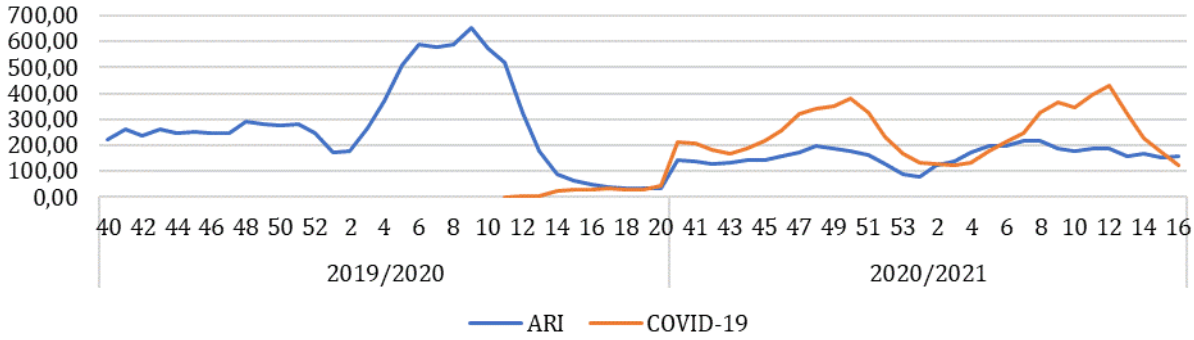


*Figure 2 Evolution of morbidity through ARI and COVID-19 per 100,000 population, 2019/2020-2020/2021 seasons*

For the flu season 2020/2021, the epidemic threshold of 283.63 cases per 100,000 population was established, of medium intensity - 399.20, of high intensity 535.01 and of very high intensity 608.93. During this season, the number of IACRS cases did not exceed the epidemic threshold, having a evolution without pronounced peaks, registering between 2058 cases (76.74 cases per 100,000 population) and 5856 cases of ARI (218.37 cases per 100,000 population). However, two increases in the intensity of ARI cases were registered in the same period when there were the 2 peaks of increase in the intensity of COVID-19 cases.

In the compartment of severe acute respiratory infections, a difference is observed between the analyzed seasons. Thus, if we refer to the total number registered, then in the period 40/2019 - 16/2020 9408 SARI cases were reported compared to the period 40/2020 - 16/2021 when 17568 SARI cases were registered, being almost 2 times more.

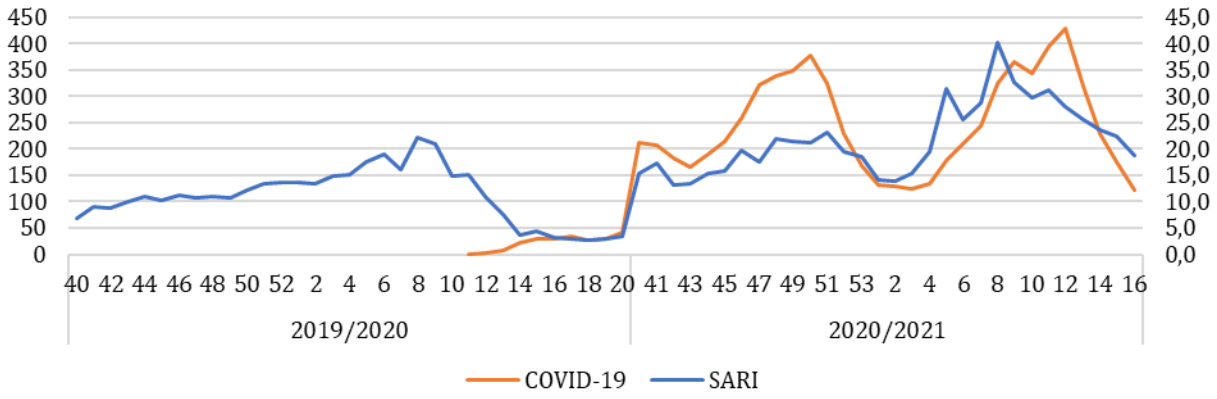


*Figure 3 Evolution of morbidity through SARI and COVID-19 per 100,000 population, 2019/2020-2020/2021 seasons*

Thus, in the 2019/2020 season there was a slow increase in the number of SARI cases until week 08/2020 when 592 cases were registered (22.1 per 100,000 population) following a decrease until week 14/2020 following a plateau until the end of the season of up to 100 SARI cases per week (figure 3).

The 2020/2021 season started with an increased number of SARI cases (15.4 per 100,000) gradually increasing after which two peaks were recorded, one in week 05/2021 with 843 cases (31.4 per 100,000) and the second in the week 08/2021 - 1079 (40.2 per 100,000). It is curious that the evolution of SARI cases coincides with the evolution of COVID-19 cases which denotes that the COVID-19 pandemic had an influence on both the registration of ARI and SARI cases.

As the flu was registered only in the 2020/2021 season, we can see that the highest share was among children up to 14 years with 59%, namely in the age group 5-14 years with 38%. The lowest percentage of all influenza cases was recorded in people over 65 years of age (3%).

Of the total number of ARI cases registered in the 2019/2020 season, most were among children aged 0-14 years with a share of 67% compared to the 2020/2021 season where 48% were registered in this age group. An inverse situation is observed in the age category over 30 years, registering 20% of the total number of cases in the 2019/2020 season and 36% of the total number of cases in the 2020/2021 season, at the same time we observe that most cases of COVID-19 were registered in this age group.

Among severe acute respiratory infections, there is a major discrepancy in the recordings of these cases in different age groups. Thus, if in the 2019/2020 season most cases of SARI were registered in the age group 0-14 years - 64%, followed by the age groups 30-64 years with 16% and the group 65+ with 15%, then in 2020/2021 season the least cases of SARI were registered in the age group 0-14 years - 12%, and the age group 30-64 has 51% and the age group 65+ has 33%. Percentage of COVID-19 cases registered in the age category 30+ is practically similar to

the percentage of SARI cases registered in the same category. This again demonstrates the influence of the COVID-19 pandemic on the influenza epidemiological surveillance system, ARI and SARI.

During the weeks 40/2019 - 16/2020 in the virological laboratory of NAPH were investigated 955 samples collected in the sentinel and non-sentinel points. Of these, 29% were positive for the presence of influenza viruses (14% - influenza A(H1N1)pdm09 virus, 7% - influenza A(H3N2) virus and 8% - influenza B virus).

During the weeks 40/2020 - 16/2021 in the virological laboratory of NAPH were investigated 638 samples collected in the sentinel and non-sentinel points, being 33% fewer samples than in the same period of previous season. However, no influenza viruses were identified in any sample but it should be noted that all samples were investigated including for SARS-CoV-2 virus. Thus, in 31% of the samples, the virus that causes COVID-19 infection was identified.

The detection of the presence of influenza viruses in the 2019/2020 season per week is represented in figure 4. Thus, the first influenza virus was identified in week 48/2019 being A(H3N2) and the last 2 were recorded in week 14/2020 being A(H1N1)pdm09. During the season, all 3 types of influenza virus A(H1N1)pdm09, A(H3N2) and type B virus were recorded.

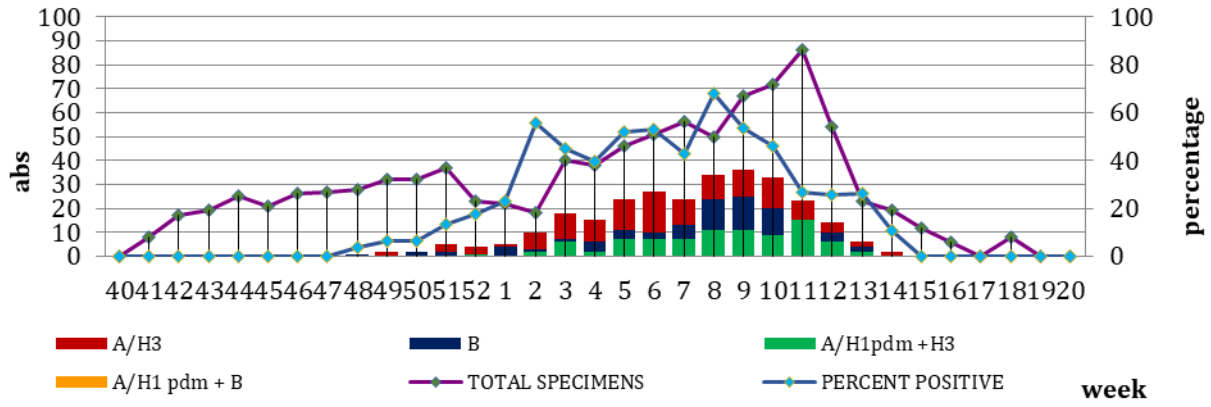


*Figure 4 The evolution of the investigated samples and the laboratory results, 2019/2020 season*

In the flu season 2020/2021 the number of samples investigated per week varied between 12-31 samples, without an increased number during the weeks 09-12 as in the previous season when it reached 86 samples per week.

Even if the number of samples per week remained almost constant, SARS-CoV-2 virus has come to detect less, from 50% to 60% of the samples investigated in the first part of the flu season to 5% -12% of the investigated samples towards the end of the season (figure 5).

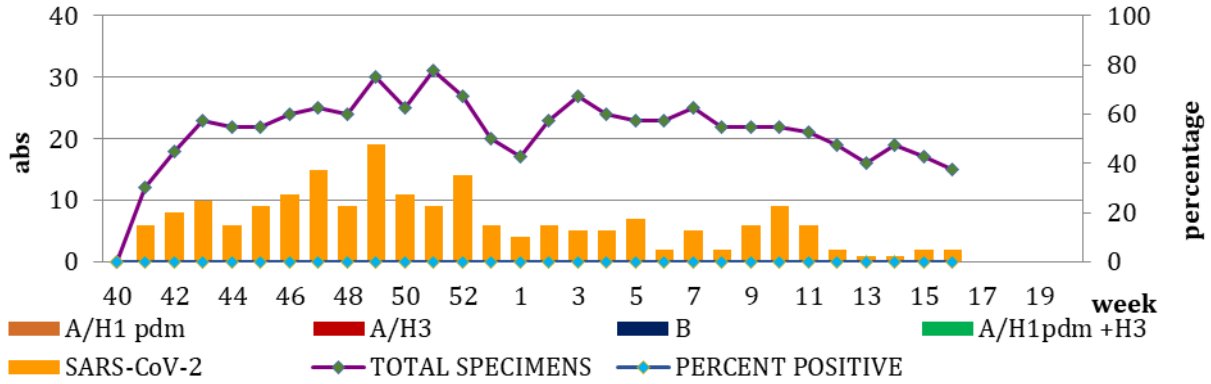


*Figure 5 The evolution of the investigated samples and the laboratory results, 2020/2021 season*

The percentage of samples examined in these 2 seasons by age group and gender shows that most samples in the 2019/2020 season were collected from children up to 9 years (37.6% CI [34.4-40.7]) and predominantly male (21.0%). In the flu season 2020/2021 also, most samples were collected from children in the age group 0-9 years but with a lower% with 10 (27.5% CI [24.1-31.0]) however, there was an increase in the percentage of samples collected in adults, namely in the age groups 50-59 years and 60-69 years, mainly in females.

Analyzing the percentage of samples collected depending on the presumptive diagnosis established, it was found that most samples were collected from people with a presumptive diagnosis of ARI, however a higher percentage was recorded in the flu season 2020/2021 of 63.0% CI [59.2-66.6].

At 9.2% CI [7.1-11.6] of the samples were collected in the 2020/2021 season from people with a presumptive diagnosis of ILI but who have not been confirmed by the laboratory. Also in the current season, the percentage of people analyzed with the diagnosis of SARI increased by about 10% more compared to the previous season.

With regard to influenza deaths, in the influenza season 2019/2020 there were 10 deaths, and in the 2020/2021 season, taking into account that there were no cases of influenza, there were no cases of death due to influenza infection. So, we deduce that all deaths in the 2019/2020 season were recorded during the 50/2019 - 12/2020 weeks, most being found in the 08/2020 week - 4 cases of death.

Analyzing the reports of deaths, it was found that people also had concomitant diseases as follows: in 10% of cases - cardiovascular disease, in 10% of cases - obesity and in 20% of cases - diabetes.

**Conclusions**

The 2020/2021 flu season is totally different from the 2019/2020 flu season due to the COVID-19 pandemic. Thus, in the 2020/2021 season no case of influenza was registered, ARI

cases had a constant evolution without exceeding the epidemic threshold being 2 times less than in the previous season, and SARI cases were reported by 2 or more cases compared to the previous season and had an evolution practically similar to the evolution of COVID-19 cases.

The cases of ARI in the 2019/2020 season were mainly registered in the age group 0-14 years and in the 2020/2021 season mainly in people over 30 years. SARI cases in the 2019/2020 season were also registered mainly in the age group 0-14 years, while in the 2020/2021 season in this group were registered 6 times less SARI cases, being the most in the group 30+, a situation similar to the share of COVID-19 cases.

Despite the fact that the sentinel surveillance system operated without deviations, with the weekly collection of samples and their investigation for the presence of influenza viruses, however, laboratory-confirmed cases of influenza were not recorded.

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