Ref: Ro J Infect Dis. 2024;27(1)
DOI: 10.37897/RJID.2024.1.9

Seasonal syndromic surveillance by sentinel system of ILI, ARI, SARI and pneumonia in Romania – season 2023/2024

Viorel Alexandrescu[1], Bogdan-Ioan Coculescu[2,3], Mihaela Lazar[2], Marina Pana[2], Odette Popovici[4], Rodica Popescu[4]

[1]Academy of Medical Sciences, Bucharest, Romania
[2]"Cantacuzino" National Institute for Military Medical Research and Development, Bucharest, Romania
[3]Faculty of Midwifery and Nursing, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[4]National Institute of Public Health & National Center for Surveillance and Control of Communicable Diseases, Bucharest, Romania

ABSTRACT

Syndromic surveillance was initially developed for early detection compared to traditional methods of an epidemiological event with an impact on public health, but as it was applied by more countries it was observed that it can provide information on the size, dynamics of the spread with an emphasis on the potential for national, regional and global evolution, the severity and the most affected population groups, but also to the development of a quick, specific response. Globalization, which involves the intensification of the movement of people (including sick or incubating infectious diseases), live animals, or products of animal origin in and from any part of the planet, but also climate change and pollution, amplifies the danger of the spread of communicable infectious diseases from areas so-called "specific" diseases in new areas, unknown to populations and healthcare systems. In this context, the One Health initiative needs efficient surveillance methods to help promote the health of people, animals, the environment, and ultimately the planet Earth. Recently, there have been substantial changes in the surveillance and control of infectious diseases with an impact on public health aimed at assessing the risks of the emergence of infectious agents with epidemic and pandemic potential by identifying and analyzing favorable factors related to the infectious agent (virulence, variability, transmissibility, etc.), the host organism (immunity, physiological factors, vaccination status, associated chronic diseases, nutritional status, living conditions, etc.), demographic factors (birth rate, mortality, population agglomerations), climatic factors and insect populations vectors, rodents and wild animals (including birds) and last but not least domestic animal populations (including birds). Among these methods, syndromic surveillance stands out, which in addition has the quality of using automatic data acquisition and generating statistical alerts, monitors disease indicators in real-time or near real-time to detect disease outbreaks earlier than would be possible with conventional methods traditional public health. In this context, we will present the Romanian experience regarding the syndromic surveillance of ILI, ARI and SARI in Romania through the national sentinel system season 2023/2024.

Keywords: influenza (ILI), acute respiratory infections (ARI), severe acute respiratory infections, pneumonia, syndromic surveillance, sentinel system, early epidemic markers, markers of severity, clinical data, epidemiological data, flu vaccinations, antigenic, and genetic characterization of seasonal respiratory viruses

INTRODUCTION

The concept of respiratory syndromes and syndromic surveillance was initially proposed by Claude Hannoun of the Pasteur Institute in Paris in 1990, with further development in collaboration with Jean Claude Mannuguera in 1991, wherein a

Corresponding author:
Bogdan-Ioan Coculescu
E-mail: bogdancoculescu@yahoo.fr

Article History:
Received: 12 March 2024
Accepted: 30 March 2024

surveillance methodology was established within a sentinel system, incorporating these novel concepts. This methodology was subsequently adopted by GROG (Groupes Régionaux d'Observation de la Influenza) in France in 1992, and later by EISS (European Influenza Surveillance Scheme) in 1996, which encompassed 25 European states, including Romania. Since its inception in 1996, EISS has evolved into EISN (European Influenza Surveillance Network), currently coordinated by the European Centre for Disease Prevention and Control (ECDC) [1,2]. The Cantacuzino Institute's National Influenza Center, a member of the WHO influenza surveillance network since 1969, established a sentinel-type surveillance system in Bucharest in 1995, based on syndromic surveillance principles, which was subsequently expanded nationwide, incorporating 22 sentinel units by 2000, each corresponding to an administrative unit. Romania's admission to the EISS during the 2000 meeting marked its integration into this surveillance network, with the Cantacuzino Institute's National Influenza Center serving as the country's representative, thus becoming the seventh member of this system.

It is noteworthy that in 1997, the Cantacuzino Institute's National Influenza Center commenced participation in the WHO-FLUNET system, contributing data on the detection and characterization of influenza viruses during epidemic seasons. Until 2010, the National Influenza Center coordinated influenza and acute respiratory infection surveillance in Romania. However, with the establishment of the National Center for Surveillance and Control of Communicable Diseases in 2010, along with three Regional Surveillance Centers as units of the National Institute of Public Health, a restructuring occurred wherein the former was tasked with microbiological surveillance, while the latter entities assumed responsibility for clinical and epidemiological surveillance. Integration and communication of surveillance results to ECDC were designated to be the responsibility of the National Center for Surveillance and Control of Communicable Diseases, whereas microbiological surveillance data continued to be communicated to FLUNET - WHO by the Cantacuzino Institute.

Syndromic surveillance entails monitoring both specific and non-specific indicators of epidemiological events impacting public health, providing early signals regarding onset (often 7-10 days in advance), magnitude, duration, and associated medical, demographic, and economic effects, thereby informing prevention and control measures. While initially employed in seasonal influenza epidemics, syndromic surveillance has broader applications in monitoring other infections with epidemic potential [3-5].

In syndromic surveillance, indicators of epidemic respiratory infectious agent activity, termed respiratory syndromes, are tracked, with increasing trends serving as potential signals of impending epidemiological events [6,7].

Among these indicators, non-specific indicators include school and preschool absenteeism, the consumption of common drugs for acute respiratory infections, and short-term medical leaves. Specific indicators encompass the detection and genetic and antigenic characterization, as well as antiviral sensitivity testing in the case of viruses [8,9].

Other indicators monitored in syndromic surveillance include early indicators such as test positivity rates, number of consultations and home visits, as well as markers of severity such as deaths, ambulance requests, emergency room visits, and hospital admissions including intensive care unit (ICU) admissions [1-13].

Illustrating the value of trends in the evolution of certain non-specific indicators of flu activity and acute respiratory infections:

Consumption of medicines: Prior to the onset of epidemic activity, pathogen circulation is relatively low, resulting in mild illnesses and reliance on over-the-counter symptomatic medication rather than medical visits. As pathogen activity intensifies, there is an increase in medical consultations (including prescription drugs). Additionally, the evolution of respiratory infections may include complicated forms requiring antibiotics (with associated drug reimbursements), increased demand for emergency services (ambulance, emergency room), and hospital admissions (pediatrics, infectious diseases, pulmonology) [14-16].

School and preschool absenteeism: This indicator holds particular significance in the surveillance and control of acute respiratory infections, as children (especially those of school and preschool age) exhibit the highest disease rates in the general population and play a pivotal role in the transmission of acute respiratory infections within communities and households. It is important to note that while most cases of illness in children are relatively mild, they can transmit infections to high-risk groups such as young children, pregnant women, the elderly, and individuals with chronic diseases, who are more susceptible to complications and mortality [17-19].

The effectiveness of syndromic surveillance at the national level hinges on a network of functional sentinel units corresponding to administrative units (counties), comprising selected family doctors who undergo periodic training, clinics specializing in infectious diseases, pediatric hospitals, pulmonology/internal medicine clinics, accredited microbiology laboratories subject to regular quality control checks, central ambulance stations, and central intensive care units [20-22].

Presently, Romania boasts a network of 15 sentinel units involving 400 family doctors serving approximately 350.000 individuals, in addition to the

aforementioned facilities. Among these units, seven are affiliated with hospitals overseeing Severe Acute Respiratory Infections (SARI) [23-26].

Accurate data collection and calculation are paramount, involving the enumeration of assisted individuals, hospitalizations, and tests conducted.

MATERIAL AND METHODS

Data collection and processing concerning the number of outpatient cases (including home visits and consultations), emergency room presentations, hospital admissions, and deaths related to influenza, Severe Acute Respiratory Infections (SARI), and pneumonia in both sentinel and non-sentinel units were conducted by the National Center for Surveillance and Control of Communicable Diseases.

Molecular detection of influenza, other respiratory viruses, and bacterial agents with respiratory tropism was carried out by laboratories within sentinel and SARI units, as well as by non-sentinel laboratories and the National Influenza Center of the Cantacuzino Institute.

For the analysis of indicator trends, calculations were performed by examining data from the previous five non-epidemic seasons to establish the baseline level. Additionally, for determining the epidemic threshold, average, high, and very high levels, averages of values recorded in these same preceding seasons were computed.

The calculations yielded the following results:

For Influenza (ILI) rate per 100.000: Baseline level <12, epidemic threshold = 12.1, average level = 14.92, high level = 30.05, very high level = 52.88.

For Acute Respiratory Infections (ARI) rate per 100.000: Baseline level <800, epidemic threshold = 870, average level = 1.089.6, high level = 1.560, very high level >1,841.

For influenza (ILI) + acute respiratory infections (ARI): Baseline level <600, epidemic threshold = 800, medium level > medium, high level > 1.500, very high level >2.000 [27].

Characterization of a week or an epidemic period

Non-epidemic week: ILI + ARI rates above the epidemic threshold, <10% positive tests.

Epidemic week: ILI + ARI rates above the epidemic threshold and >10% positive tests.

Epidemic period: A sequence of three epidemic weeks [27].

Indicators of Influenza activity (ECDC)

Intensity of influenza activity:

- Low: No activity or activity at baseline.
- Medium: Usual levels of activity.

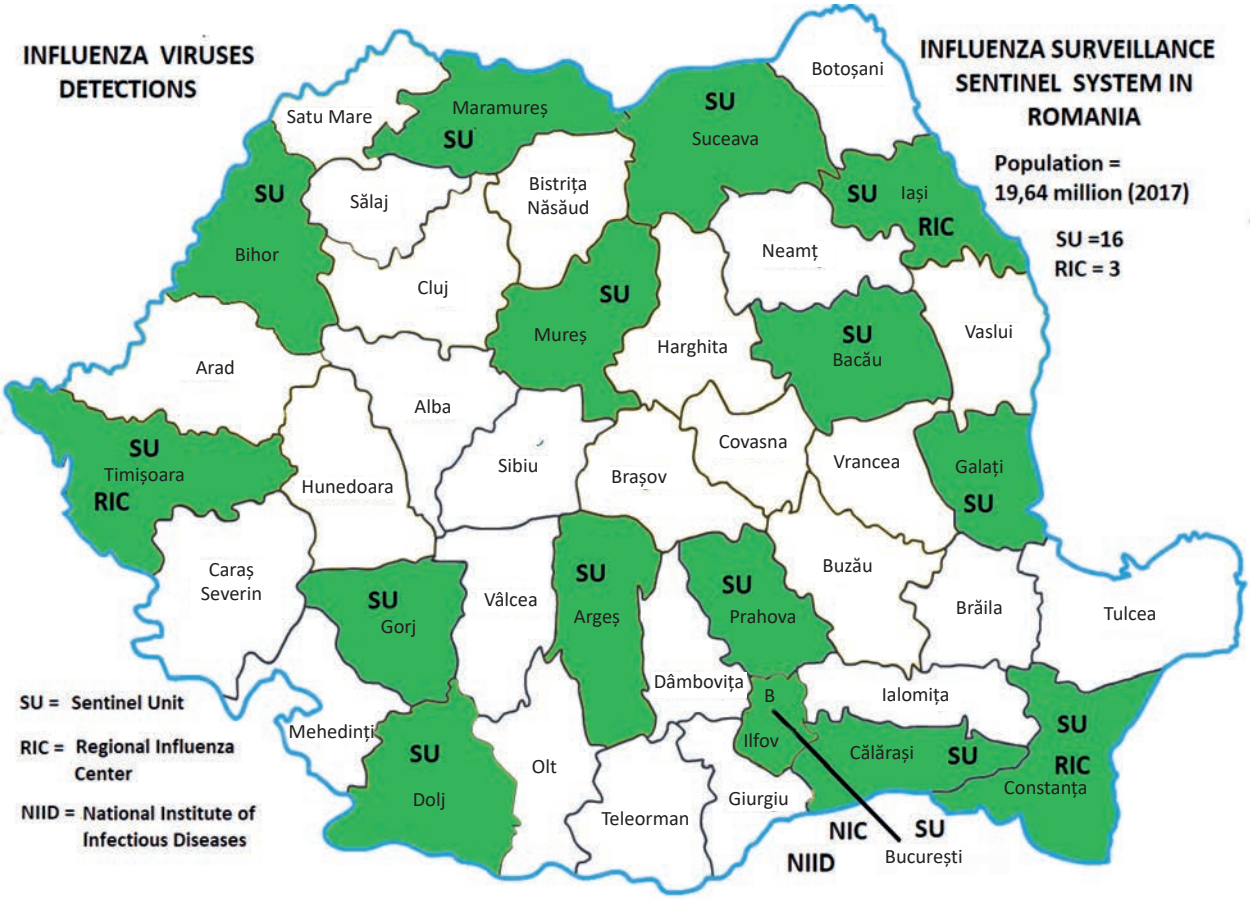

FIGURE 1. Romania - map of sentinel units

- High: Levels of activity higher than usual.
- Very high: Exceptionally high levels of activity.

Influenza trend:
- Increasing.
- Stable.
- Decreasing.

Geographical spread of influenza:
- No activity: No detection of influenza viruses.
- Sporadic: Isolated detection of influenza virus.
- Localized: Multiple detection of influenza viruses in one administrative unit or school, hospital, or enterprise.
- Regional: Detection of influenza viruses in multiple but under 50% of the administrative units of the country.
- Widespread: Laboratory-confirmed influenza infection appearing in 50% or more of the administrative units of the country.

The dominance of viruses in circulation:
- Dominant virus: >50% of a subtype.
- Codominance: 50-50% or 45%-55% [28].

Evolution of Influenza vaccine coverage:

According to WHO and ECDC recommendations, [29], influenza vaccine coverage must be a minimum of 15% (2,850,000), of which:
- 75% for persons >65 years old.
- 100% for institutionalized persons.
- 100% for pregnant women.
- 100% for small children (6 months - 2 years).
- 50% for people with chronic diseases (children and adults).

RESULTS

We will present two weeks of surveillance from the 2023-2004 season in graphical format based on the weekly bulletins of the Cantacuzino Institute (weeks 7 and 8), which are provided below.

TABLE 1. The values of the influenza epidemic in the 7th week in Romania

Geographical spread	Widespread
Intensity	Medium
Trend	Decreasing
Virus detected	141:19 A/H1, 31 A/H3, 84 A, 6 B, 1 A/H1+A/H3
Dominant virus	A/H3
Sample positivity rate	39%
Antigenic characterization (HAI)	-
Genetic characterization	-
Sensitivity to antivirals	-
Impact on medical services	Moderate
Deaths; M = male; W = women UV = Unvaccinated; V = Vaccinated; CM = Comorbidities; P = pregnancy; CI = coinfections (Flu+COVID+/- other)	8 (UV = 8; CM = 8; M = 3, W = 5; 5 A/H_1, 2A/H_3,1A; 60-79 ys. = 3 , > 80 ys.= 5

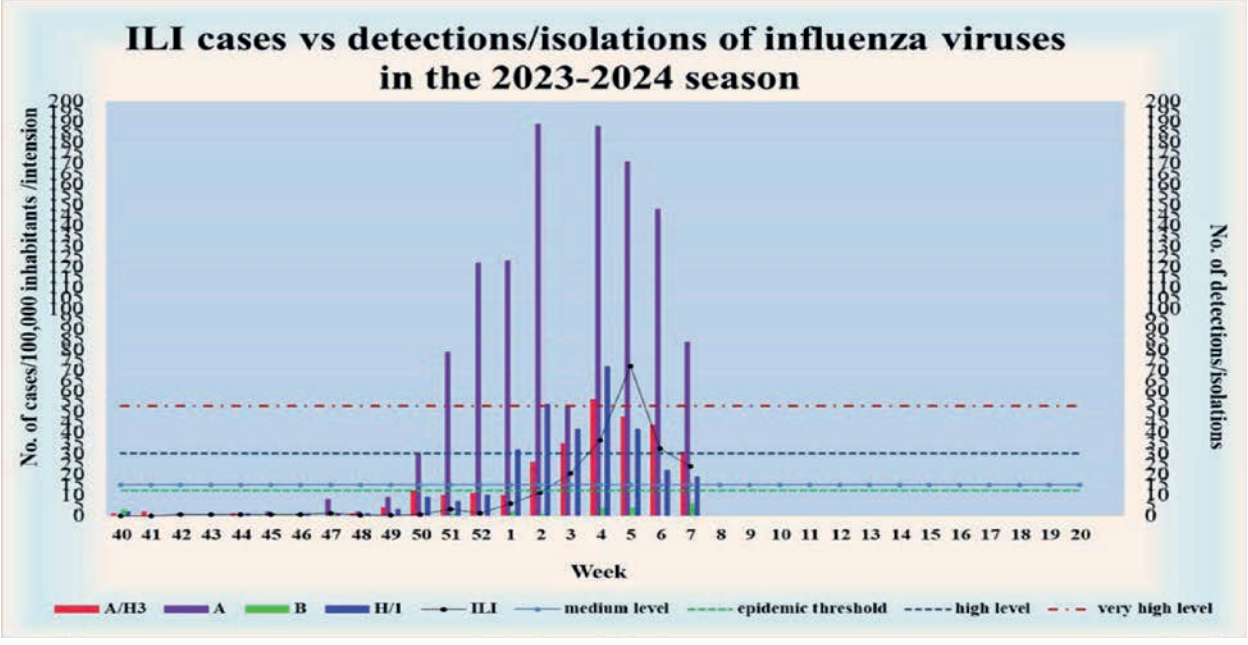

FIGURE 2. ILI cases vs. detections/isolations of influenza viruses in the 2023-2024 season (week 7)

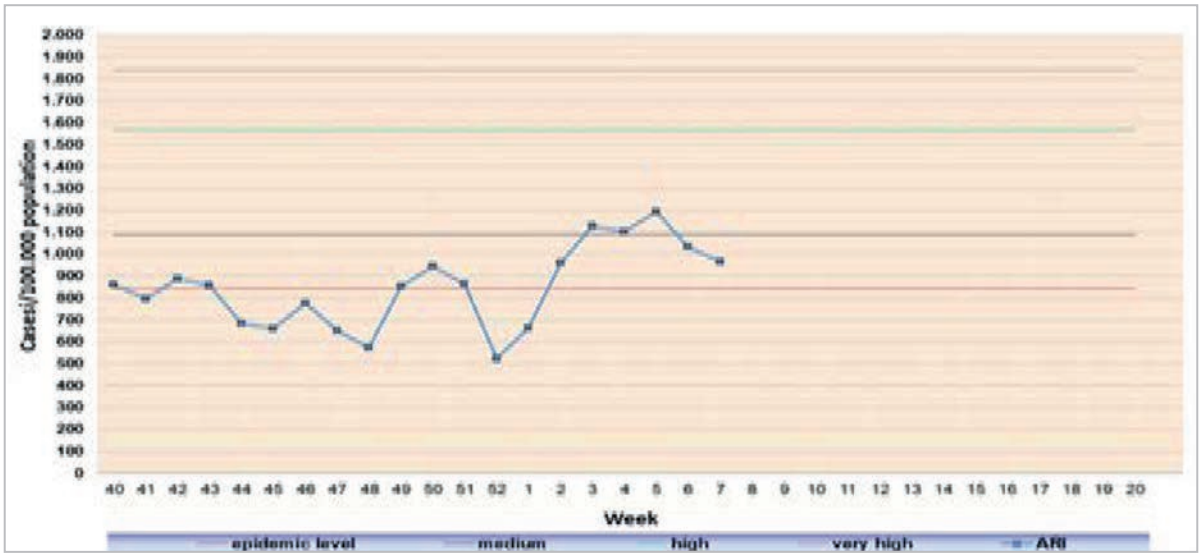

FIGURE 3. ARI cases with epidemic threshold in the 2023-2024 season (week 7)

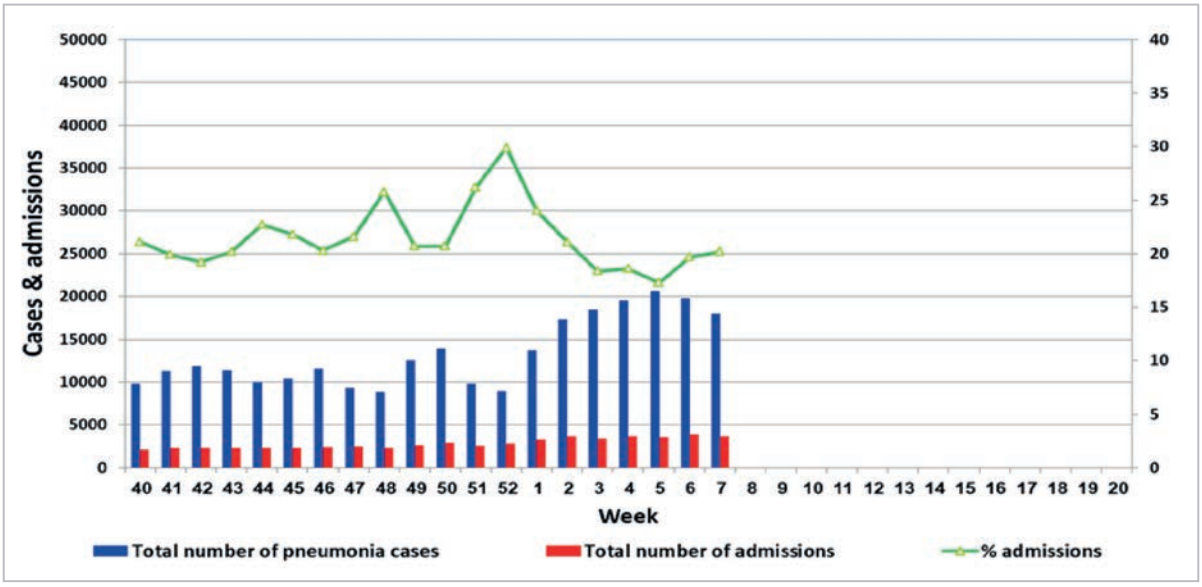

FIGURE 4. Pneumonia in the 2023/2024 season vs. admissions (%)

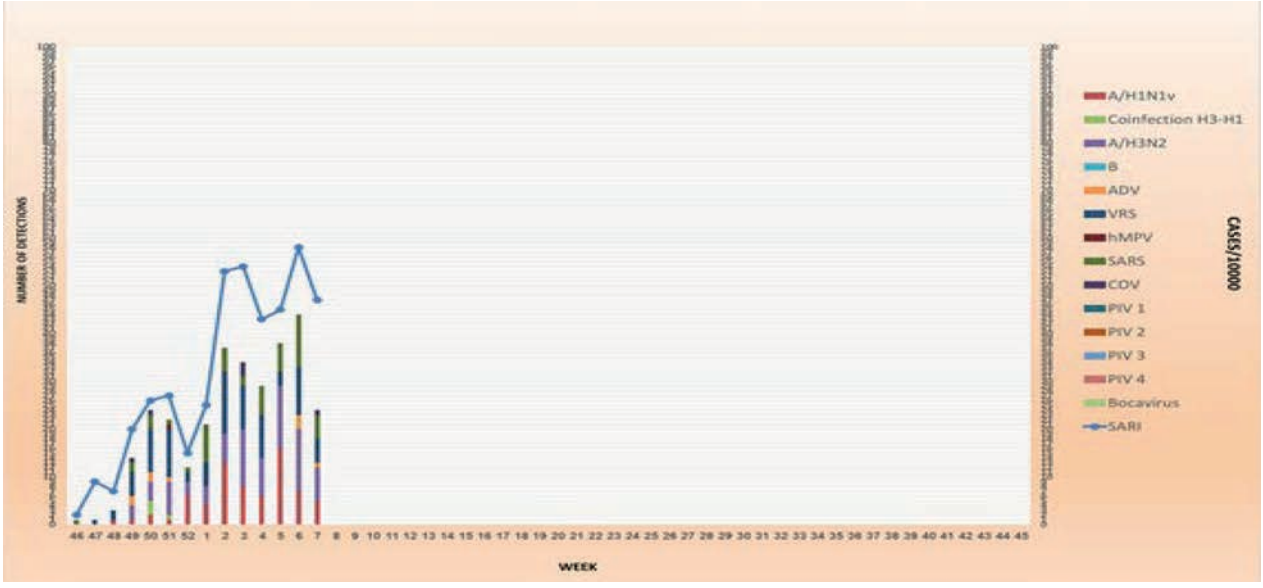

FIGURE 5. SARI cases vs. detections of respiratory viruses in the 2023/2024 season

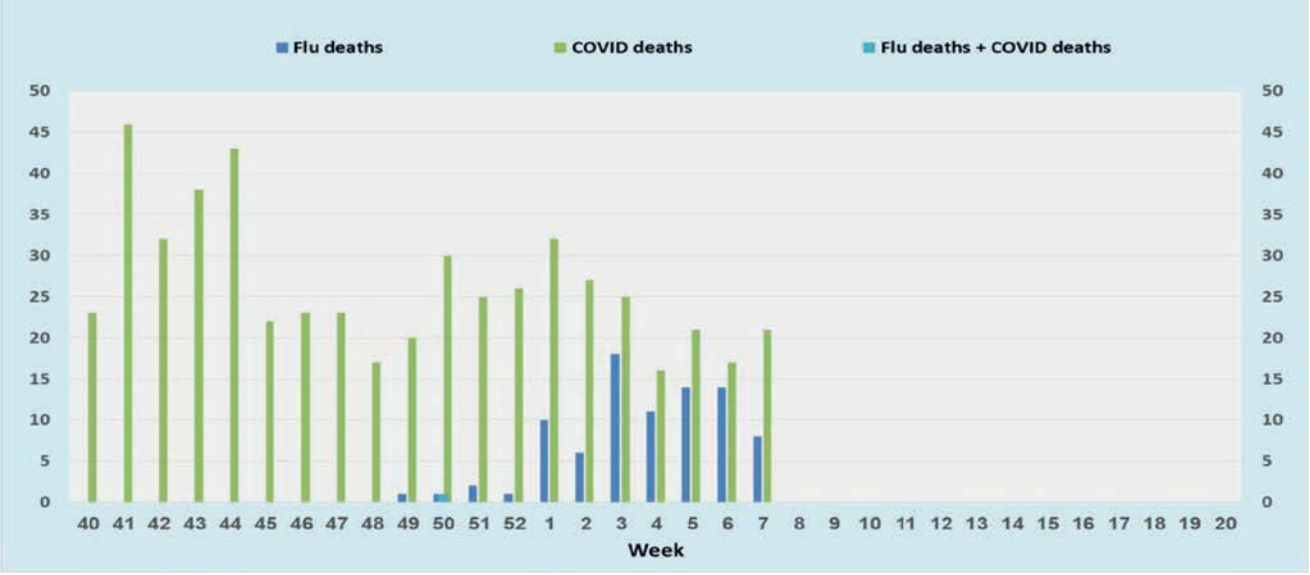

FIGURE 6. Flu deaths vs. COVID deaths in the 2023/2024 season

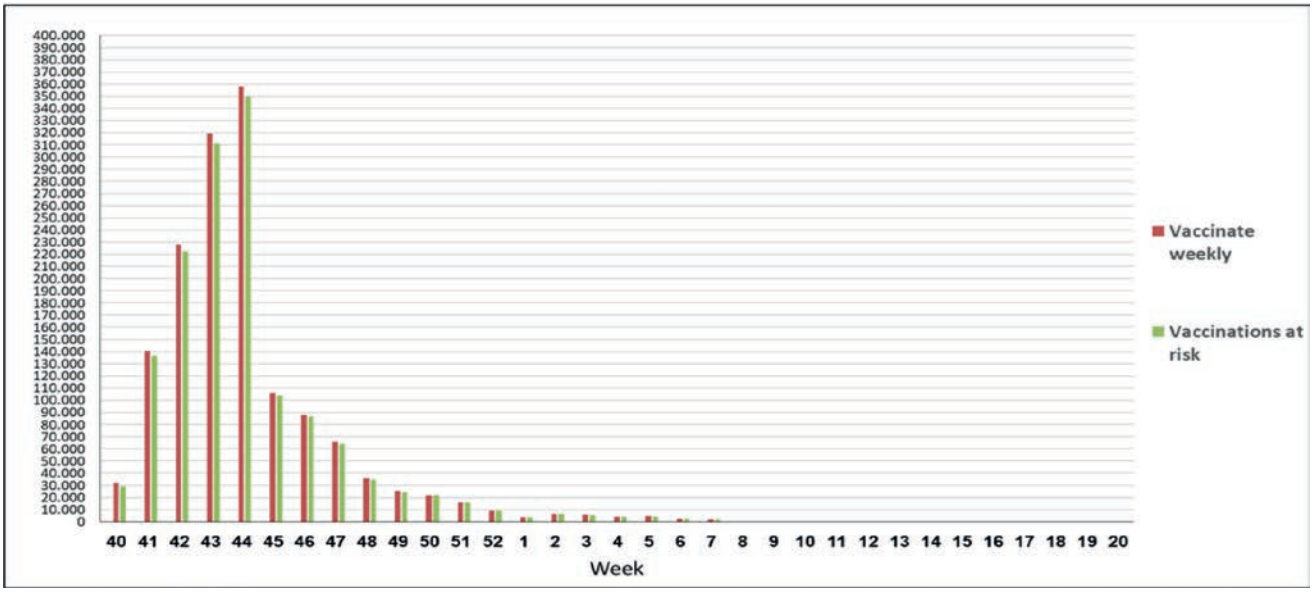

FIGURE 7. Influenza vaccinations in the 2023-2024 season

TABLE 2. The values of the influenza epidemic in the 8th week in Romania

Geographical spread	Widespread
Intensity	Medium
Trend	Stable
Virus detected	125: 7 A/H1 ,8 A/H3, 97 A, 13 B
Dominant virus	A
Sample positivity rate	38%
Antigenic characterization (HAI)	-
Genetic characterization	-
Sensitivity to antivirals	-
Impact on medical services	Moderate
Deaths; M = male; W = women UV = Unvaccinated; V = Vaccinated; CM = Comorbidities; P = pregnancy; CI = coinfections (Flu+COVID+/- other)	4(UV = 4; CM = 4; M = 1, W = 4; 1 A/H_1, 3A/H_3 0-4 ys. = 1, >80 ys.= 3

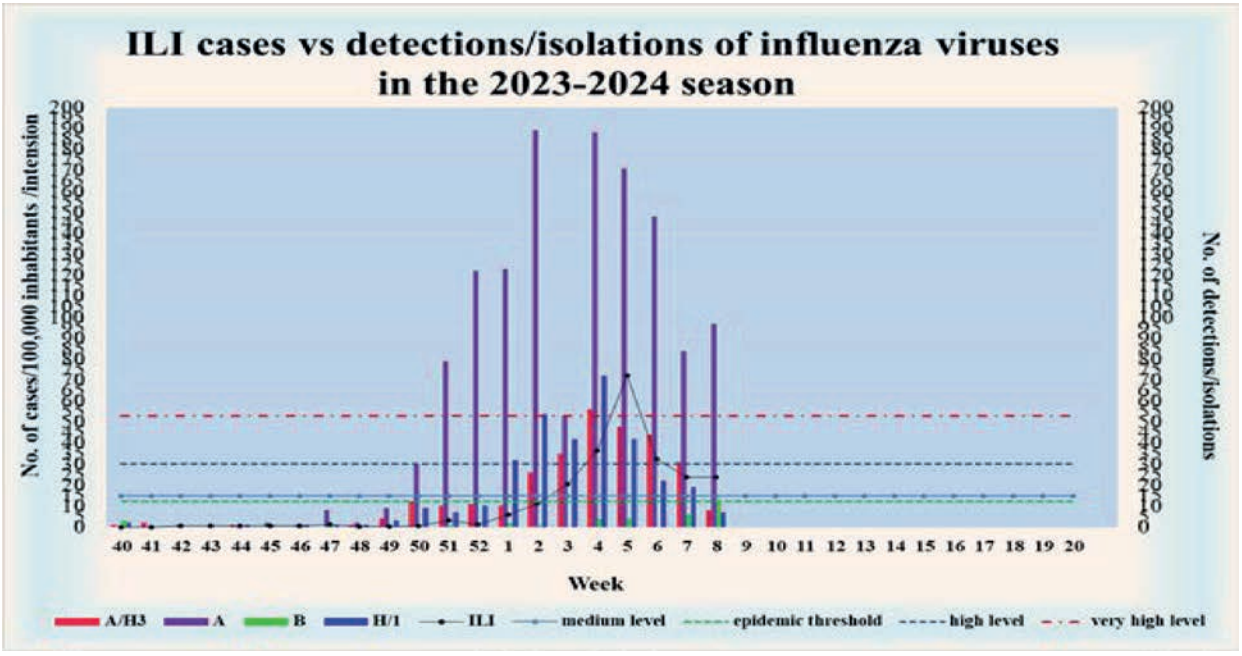

FIGURE 8. ILI cases vs. detections/isolations of influenza viruses in the 2023-2024 season (week 8)

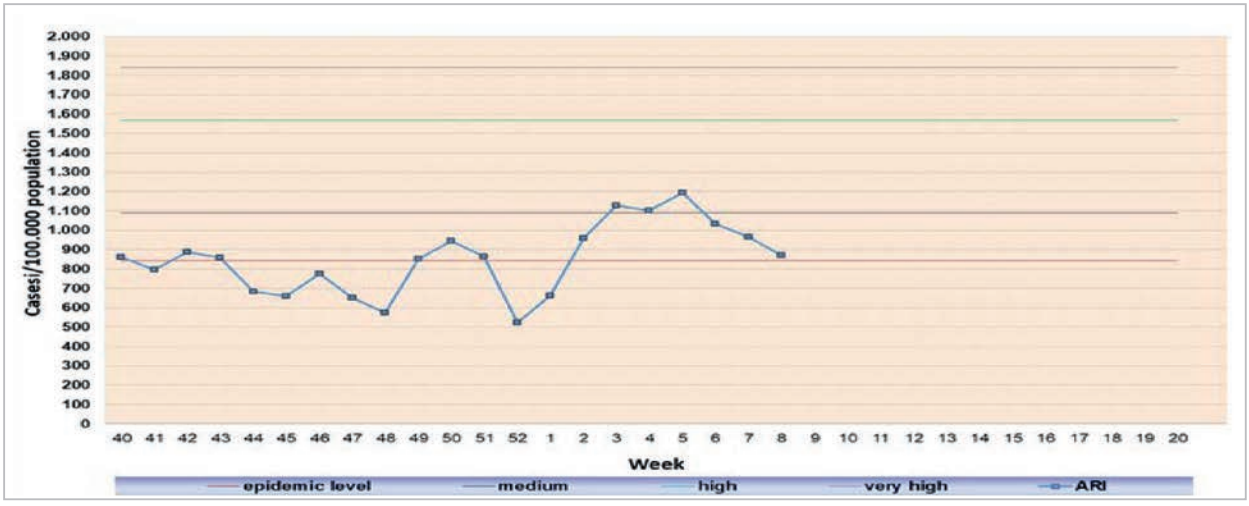

FIGURE 9. ARI cases with epidemic threshold in the 2023-2024 season (week 8)

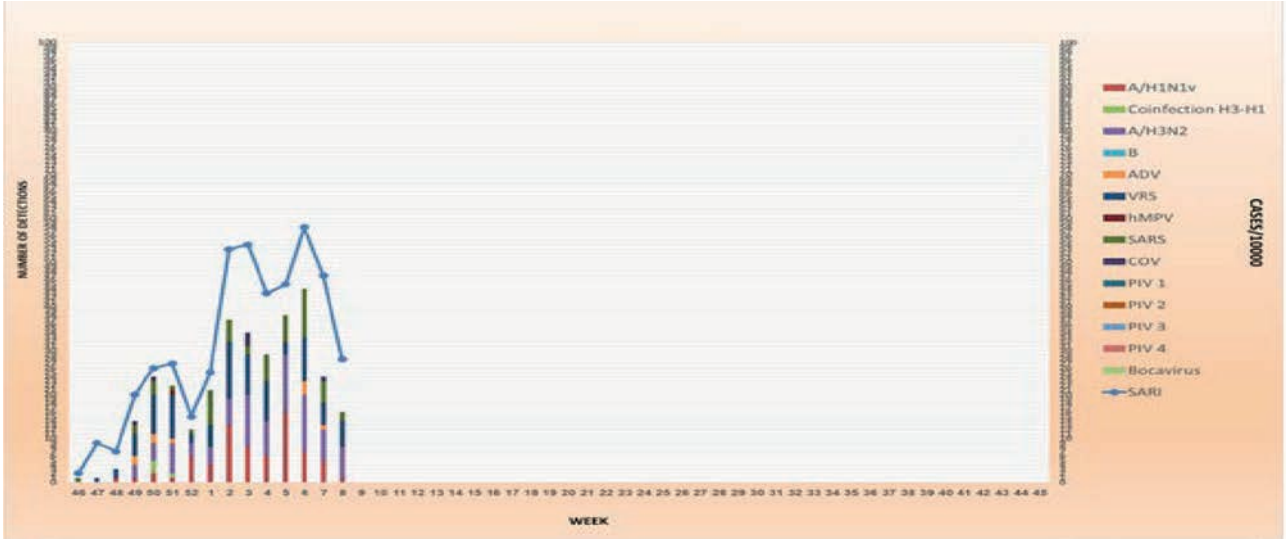

FIGURE 10. SARI cases vs. detections of respiratory viruses in the 2023/2024 season

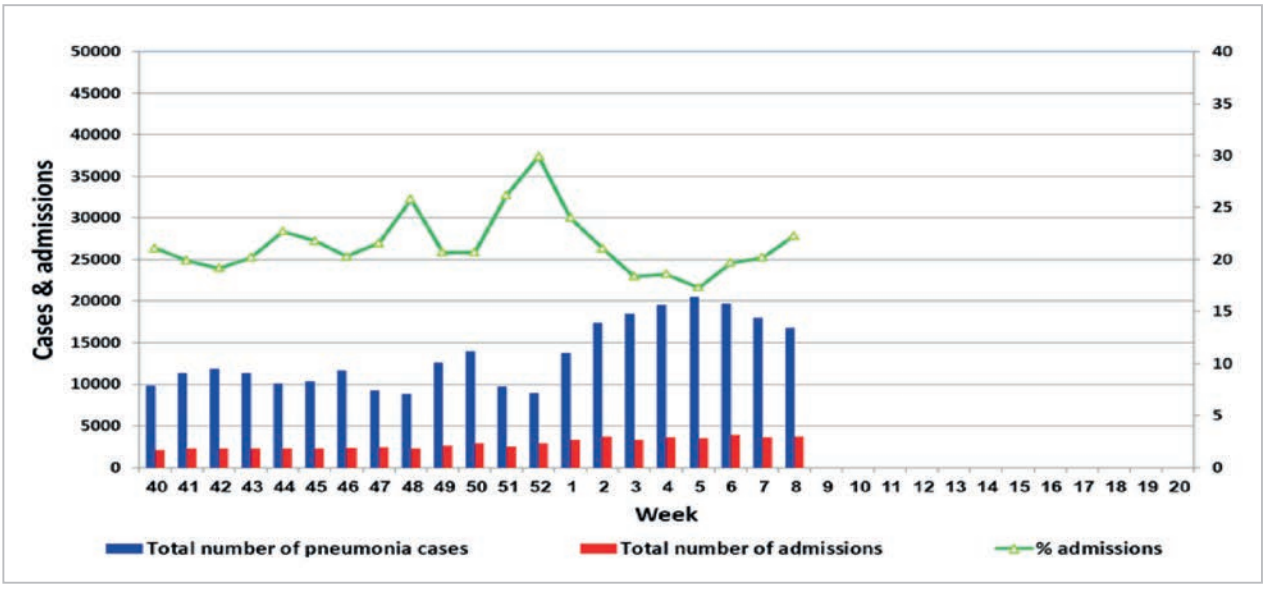

FIGURE 11. Pneumonia in the 2023/2024 season vs. admissions (%)

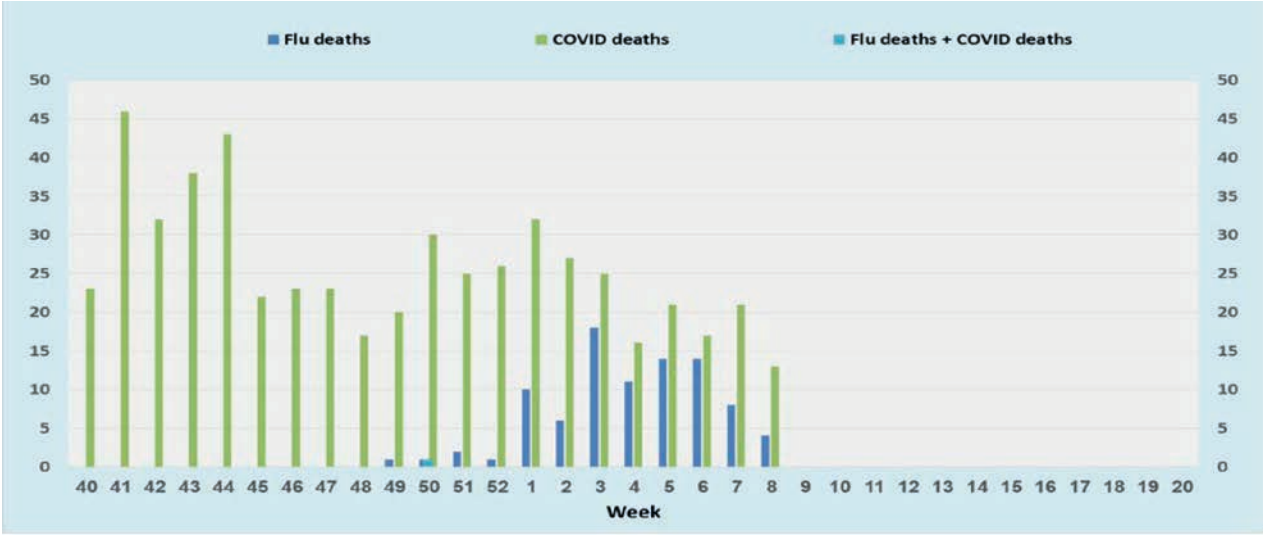

FIGURE 12. Flu deaths vs. COVID deaths in the 2023/2024 season

CONCLUSIONS

The Influenza epidemic commenced in Romania during the 1st week and peaked in the 6th week. Comparative analysis with the 2022-2023 season reveals similar recorded values. The dominant virus throughout this season has been A/H1N1; however, there were also periods where the A/H3N2 virus caused a higher number of illnesses. Towards the end of the season, an increase in detections of B viruses was observed, as expected.

Concurrent circulation of SARS-CoV-2 exerted significant pressure on medical care, particularly within infectious diseases, pneumology, and pediatrics departments, with respiratory syncytial virus (RSV) infections also contributing to the burden. Utilization of multiplex molecular diagnostics revealed a broader spectrum of viral and bacterial etiologies, as well as viral-viral and viral-bacterial co-infections, crucial for treatment and prevention strategies.

Regarding influenza-related deaths up to the 8th week, the number surpassed that of the previous season, with 91 deaths compared to 81. Notably, these fatalities occurred predominantly among the unvaccinated population, with a majority having comorbidities and being over the age of 65. In terms of influenza vaccination coverage, the current rate stands at 5.45%, significantly below the optimal minimum threshold of 15% for the Romanian population. However, as the season is ongoing, there remains an opportunity to increase vaccination coverage.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Paget WJ, Meerhoff TJ, Meijer A; EISS. Epidemiological and virological assessment of influenza activity in Europe during the 2003-2004 season. *Euro Surveill.* 2005;10(4):107-11.
2. Casalegno JS, Eibach D, Valette M, et al. Performance of influenza case definitions for influenza community surveillance: based on the French influenza surveillance network GROG, 2009-2014. *Euro Surveill.* 2017;22(14):30504. doi: 10.2807/1560-7917.ES.2017.22.14.30504
3. Berry AC. Syndromic surveillance and its utilisation for mass gatherings. *Epidemiol Infect.* 2018;147:e2. doi: 10.1017/S0950268818001735
4. Hughes HE, Edeghere O, O'Brien SJ, et al. Emergency department syndromic surveillance systems: a system-atic review. *BMC Public Health.* 2020;20(1):1891. doi: 10.1186/s12889-020-09949-y
5. Atkins N, Harikar M, Duggan K, et al. What are the characteristics of participatory surveillance systems for influenza-like-illness? *J Glob Health.* 2023;13:04130. doi: 10.7189/jogh.13.04130
6. an den Wijngaard C, van Asten L, van Pelt W, et al. Validation of syndromic surveillance for respiratory pathogen activity. *Emerg Infect Dis.* 2008;14(6):917-25. doi: 10.3201/eid1406.071467
7. Spector E, Zhang Y, Guo Y, et al. Syndromic Surveillance Systems for Mass Gatherings: A Scoping Review. *Int J Environ Res Public Health.* 2022;19(8):4673. doi: 10.3390/ijerph19084673
8. McLean HQ, Peterson SH, King JP, et al. School absenteeism among school-aged children with medically attended acute viral respiratory illness during three influenza seasons, 2012-2013 through 2014-2015. *Influenza Other Respir Viruses.* 2017;11(3):220-9.
9. Kara EO, Elliot AJ, Bagnall H, et al. Absenteeism in schools during the 2009 influenza A(H1N1) pandemic: a useful tool for early detection of influenza activity in the community? *Epidemiol Infect.* 2012;140(7):1328-36. doi: 10.1017/S0950268811002093
10. Hiller KM, Stoneking L, Min A, et al. Syndromic surveillance for influenza in the emergency department-A systematic review. *PLoS One.* 2013;8(9):e73832. doi: 10.1371/journal.pone.0073832
11. Hughes HE, Edeghere O, O'Brien SJ, et al. Emergency department syndromic surveillance systems: a sys-tematic review. *BMC Public Health.* 2020;20(1):1891. doi: 10.1186/s12889-020-09949-y
12. Feldblyum TV, Segal DM. Seasonal and pandemic influenza surveillance and disease severity. Global Virology I - Identifying and Investigating Viral Diseases. 2015:761-89. doi: 10.1007/978-1-4939-2410-3_29
13. Qualls N, Levitt A, Kanade N, Wright-Jegede N, Dopson S, Biggerstaff M, Reed C, Uzicanin A; CDC Community Mitigation Guidelines Work Group. Community mitigation guidelines to prevent pandemic influenza - United States, 2017. *MMWR Recomm Rep.* 2017;66(1):1-34. doi: 10.15585/mmwr.rr6601a1
14. Meckawy R, Stuckler D, Mehta A, Al-Ahdal T, et al. Effectiveness of early warning systems in the detec-tion of infectious diseases outbreaks: a systematic review. *BMC Public Health.* 2022;22(1):2216. doi: 10.1186/s12889-022-14625-4
15. Kamalrathne T, Amaratunga D, Haigh R, et al. Need for effective detection and early warnings for epidemic and pandemic preparedness planning in the context of multi-hazards: Lessons from the COVID-19 pandemic. *Int J Disaster Risk Reduct.* 2023;92:103724. doi: 10.1016/j.ijdrr.2023.103724
16. Fraser C, Riley S, Anderson RM, et al. Factors that make an infectious disease outbreak controllable. *Proc Natl Acad Sci U S A.* 2004;101(16):6146-51. doi: 10.1073/pnas.0307506101
17. Adema IW, Kamau E, Uchi Nyiro J, et al. Surveillance of respiratory viruses among children attending a primary school in rural coastal Kenya. *Wellcome Open Res.* 2020;5:63. doi: 10.12688/wellcomeopenres.15703.2
18. Azor-Martínez E, Gonzalez-Jimenez Y, Seijas-Vazquez ML, et al. The impact of common infections on school absenteeism during an academic year. *Am J Infect Control.* 2014;42(6):632-7. doi: 10.1016/j.ajic.2014.02.017
19. He C, Norton D, Temte JL, et al. Effect of planned school breaks on student absenteeism due to influenza-like illness in school aged children-Oregon School District, Wisconsin September 2014-June 2019. *Influenza Other Respir Viruses.* 2024;18(1):e13244. doi: 10.1111/irv.13244
20. Thomas MJ, Yoon PW, Collins JM, et al. Evaluation of Syndromic Surveillance Systems in 6 US State and Local Health Departments. *J Public Health Manag Pract.* 2018;24(3):235-240. doi: 10.1097/PHH.0000000000000679
21. Morbey R, Smith G, Oliver I, et al. Evaluating multi-purpose syndromic surveillance systems - a complex problem. *Online J Public Health Inform.* 2021;13(3):E15. doi: 10.5210/ojphi.v13i3.10818
22. Gilbert R, Cliffe SJ. Public health surveillance. *Public Health Intelligence.* 2016:91-110. doi: 10.1007/978-3-319-28326-5_5
23. Rotar Pavlič D, Miftode R, Balan A, et al. Romania. In: Kringos DS, Boerma WGW, Hutchinson A, et al., editors. Building primary care in a changing Europe: Case studies [Internet]. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2015. (Observatory Studies Series, No. 40.) 24. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459006/.
24. Meerhoff TJ, Simaku A, Ulqinaku D, et al. Surveillance for severe acute respiratory infections (SARI) in hospitals in the WHO European region - an exploratory analysis of risk factors for a severe outcome in influen-za-positive SARI cases. *BMC Infect Dis.* 2015;15:1. doi: 10.1186/s12879-014-0722-x
25. INSP &CNSCBT Evolution of acute respiratory infections, Influenza and severe acute respiratory infections (SARS) in the 2023-2024 season - Week 19.02.2024 – 25.02.2024 (S08/2024)
26. Petre I, Barna F, Gurgus D, et al. Analysis of the healthcare system in Romania: A brief review. *Healthcare (Basel).* 2023;11(14):2069. doi: 10.3390/healthcare11142069
27. Teeluck M, Samura A. Assessing the appropriateness of the Moving Epidemic Method and WHO Average Curve Method for the syndromic surveillance of acute respiratory infection in Mauritius. *PLoS One.* 2021;16(6):e0252703. doi: 10.1371/journal.pone.0252703.
28. ECDC: indicators of influenza activity (https://www.ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/facts-indicators) (accessed on 25.02.2024)
29. ECDC: seasonal Influenza (www.ecdc.eu > seasonal influenza) (accessed on 01.03.2024)