EPIDEMIOLOGICAL COMPARISON OF INFLUENZA, ARI AND COVID-19 PREVALENCE IN BULGARIA FOR THE PERIOD 2017-2022

Zh. Getsova[1], A. Minkova[1], R. Tsoneva[1], K. Petkova[1]

[1]National Center of Infectious and Parasitic Diseases

ABSTRACT

Introduction: The report presents a comparison of the incidence of respiratory infections - influenza, other acute respiratory infections and COVID-19 for the period 2017-2022. A comparative analysis of the epidemiological dynamics in different areas of the country is made and factors such as demography and vaccine coverage are also analyzed.

Materials and Methods: A comparative analysis of the prevalence of Influenza/ARI, and COVID-19 was made for the years of the studied period. Regional values were compared to the country total in order to rank regions according to the experienced disease incidence burden at a regional level. The percentile method was used to identify and filter the regions where Influenza/ARI waves appeared with the highest intensity in the country. To compare intensity of COVID-19 waves between the selected regions we used the maximal weekly incidence values per 100 000 population reached for the different periods of the pandemic. Information on the age structure of the population in the respective regions and the vaccine uptake was retrieved and compared.

Results: The regions of Blagoevgrad, Montana, Haskovo, Razgrad, Kardzhali, Sliven and Targovishte were filtered among all regions as the ones with the most intensive Influenza waves for the period 2017-2022. Blagoevgrad and Sliven were the regions with higher maximal COVID-19 incidence values before the Delta circulation and during the Omicron predominance. When the Delta variant was predominant, Blagoevgrad and Montana surpassed the incidence recorded for the country.

No data supporting the initial hypothesis that demographic structure at regional level determines intensity of spread of the two viral respiratory infections was found. However, the regions with higher COVID-19 vaccines coverage were found to have the lowest incidence levels of the infection.

Conclusion: Although COVID-19 and Influenza/ARI are both respiratory infections, they differ in their epidemiology and no specific pattern can be found. We recommend that anti-epidemic measures should be followed to limit incidence regardless of the circulating respiratory pathogen.

ADDRESS FOR CORRESPONDENCE:
Zhivka Getsova
NCIPD, Epidemiology Department
26 Yanko Sakazov Blvd, 1504, Sofia, Bulgaria
email: getsova@ncipd.org
phone: +359 2 944 6999, ext. 255

INTRODUCTION

The report presents a comparison of the incidence of respiratory infections: influenza, other acute respiratory infections (ARI) and COVID-19 for the period 2017-2022. A comparative analysis of the epidemiological dynamics in different regions in Bulgaria is made.

The study focuses on three research questions: What was the prevalence of COVID-19 in regions with higher influenza circulation in the years preceding the pandemic? (1) Can a common pattern be found in the incidence of COVID-19 and influenza and ARI at a regional level? (2) Does specific regional demography together with the vaccine coverage for the specific pathogen determine the prevalence of the two infections? (3).

MATERIALS AND METHODS

Retrospective data from the Annual analyses of the incidence of acute infectious diseases in Bulgaria and the available Information System for data collection and analysis on Influenza and ARI incidence was used for the period 2017-2022. The Annual analyses are prepared at the National Centre of Infectious and Parasitic Diseases (NCIPD) and are accessible through the website of the Centre. To access data on Influenza and ARI referring to the years before 2022 through the Information System that provides evidence from

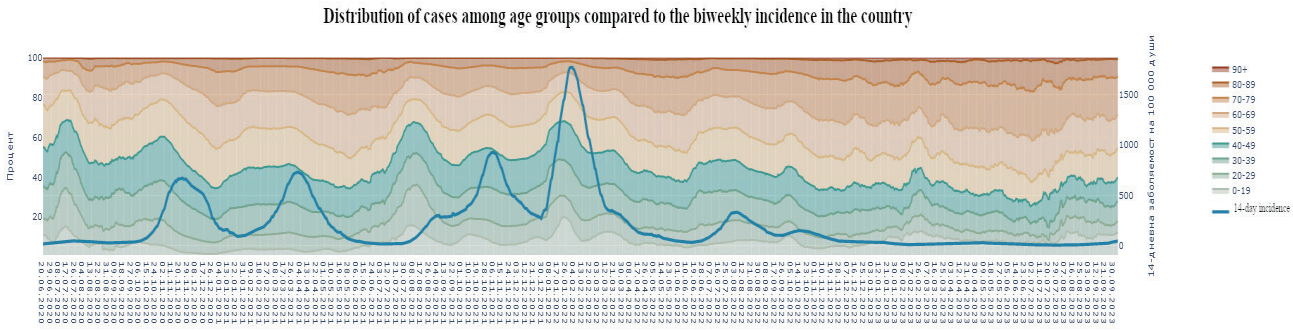

Figure 1. Distribution of cases among age groups compared to the biweekly incidence registered in Bulgaria

selected sentinel practices, a login available at the Department of Epidemiology at the NCIPD was used. For both studied infections, incidence was measured at a weekly basis. For Influenza/ARI it was counted per 10 000 population, while for COVID-19 the 100 000 population basis was used. For COVID-19, denominators have been updated with the last population enumeration data as of 31.12.2022. Sentinel data used for the Influenza/ARI surveillance is also updated with the latest population evidence on a yearly basis.

Influenza and ARI incidence were followed for the whole study period from 2017 onwards, while COVID-19 incidence was followed since the start of the local spread in the country in March 2020.

A comparative analysis of the prevalence of Influenza/ARI, and COVID-19 was made for the years of the studied period. Regional values were compared to the country total in order to rank regions according to the experienced disease incidence burden at a regional level. Incidence of the two respiratory infections was not compared in-between as their basic reproductive numbers differ significantly which naturally explains the more intensive spread observed during COVID-19 epidemic waves [1].

The percentile method was used to identify regions where Influenza/ARI waves appeared with the highest intensity in the country. The percentiles were calculated using data on Influenza/ARI spread for a 10 year period. This method was preferred as influenza epidemic intensity traditionally differs by region. For each region the threshold value of the 99th percentile marking "very high" levels of spread was identified. An additional indicator calculated through multiplication of the 99-th percentile value by 1.5 was introduced to facilitate the process of filtering the regions with the highest intensity of Influenza/ARI.

To compare intensity of COVID-19 waves between the regions we used the maximal weekly incidence values per 100 000 population reached.

To answer the third research question, the study used data on the distribution of the population within age groups for 2020. The information is used for the preparation of the Annual analyses. The shares of population in the age groups 0-14 and 30-64 years of age were compared across the regions with the highest intensity of Influenza/ARI to determine whether the different levels of prevalence of COVID-19 might be attributed to the demography of the specific region. The two age groups were selected according to available data showing that Influenza spread was more intensive in childhood population, while COVID-19 circulated more intensively among the working population (Figure 1).

During the Delta wave the tendency changed slightly and younger age groups were affected by COVID-19, as well. That is why we differentiated the periods for which the maximal COVID-19 incidence is taken according to the circulating variant in the specific period. For onset of the Delta variant we accepted 1st July 2021 when the number of infections started growing in Europe [2]. We considered infections registered until the end of November 2021 to be caused by Delta and from 1st December 2021 onwards we considered Omicron prevalence [3, 4].

Vaccination rates with the available vaccines against influenza and COVID-19 were compared at a regional level and to the country total. Data on immunizations against COVID-19 was obtained from the national COVID-19 information portal [5]. Data on immunizations against Influenza was retrieved from reports submitted by the Regional Health

Table 1. Maximal values of Influenza/ARI incidence measured per week at 10 000 within regional cities. Values higher than the 99-th percentile threshold are highlighted.

Област	Стойност 99-ти персентил 2013-2022	2017	2018	2019	2020	2021	2022
Благоевград	409.24	616.0194	507.896	410.5445	433.714	71.335	602.7077
Бургас	236.53	189.1439	226.8692	243.2285	263.275	166.0142	173.9923
Варна	199.74	159.2518	198.6914	248.887	200	194.3536	179.1976
Велико Търново	158.54	83.4188	99.2989	135.2137	223.2532	40.8401	100.6418
Видин	223.29	164.3348	290.9171	326.2348	235.816	138.8188	123.675
Враца	242.56	143.6234	351.2719	295.899	266.4821	224.9523	192.0749
Габрово	291.02	378.526	379.6296	239.2615	210.8491	253.019	291.3553
Добрич	179.09	151.7433	161.5169	265.9889	197.3685	104.4069	140.8281
Кърджали	164.84	164.8728	158.0031	486.3363	573.543	111.0608	101.9946
Кюстендил	190.14	275.4955	196.6568	206.3137	258.2391	65.1466	84.7242
Ловеч	279.05	238.1652	302.1239	115.7479	289.855	228.3511	272.8352
Монтана	340.15	658.8735	589.9021	315.6565	265.9975	122.5033	141.1452
Пазарджик	299.41	337.857	270.0027	397.2294	309.3842	174.4868	282.9913
Перник	229.17	208.5004	280.6638	277.0233	262.6181	142.5606	148.9432
Плевен	264.31	180.6322	223.3955	305.2966	309.5879	136.0544	168.9708
Пловдив	147.08	147.5549	164.4107	136.5395	183.2012	83.3212	61.8315
Разград	151.83	151.4683	319.0491	156.6997	131.2839	112.8748	144.6208
Русе	240.93	257.2369	246.3088	247.693	192.5254	181.9083	143.2792
Силистра	291.8	227.6867	297.4326	328.7415	327.3998	264.6869	277.5985
Сливен	209.75	151.2737	209.574	265.2429	316.3384	98.3213	118.7051
Смолян	207.82	209.0591	243.2046	261.0873	241.2676	155.4404	179.7754
София-град	205.86	204.1976	240.1729	276.8912	269.7993	131.58	114.529
София-област	259.31	268.6361	256.5431	259.9983	234.5416	77.2921	191.8976
Стара Загора	306.11	370.587	395.8901	310.3222	255.5136	97.1107	145.6658
Търговище	220.17	171.2423	138.6247	206.578	364.2294	122.3159	266.3768
Хасково	255.59	387.1146	199.3865	230.7259	364.6942	139.0922	332.3573
Шумен	222.39	221.3642	216.2161	326.8984	205.9202	205.9202	248.3912
Ямбол	321.62	392.9945	438.5334	377.5777	226.5466	84.2288	176.558
Общо	212.73	215.5172	230.8299	247.9181	242.6937	97.4997	126.6736

Inspectorates for the preparation of the Annual analyses of immunoprophylaxis.

RESULTS

Epidemic waves of the two infections:

Influenza/ARI thresholds in 18 of the country regions reached "very high" levels (set at the 99th percentile) and surpassed the average for the country: Blagoevgrad, Bourgas, Vidin, Vratsa, Gabrovo, Lovech, Montana, Pazardzhik, Pernik, Pleven, Russe, Silistra, Sofia-district, Stara Zagora, Targovishte, Haskovo, Shumen and Yambol. Respectively, 10 regions had a threshold scoring lower than the total for Bulgaria: Sofia-city, Smolyan, Sliven, Razgrad, Plovdiv, Kyustendil, Kardzhali, Dobrich, Veliko Tarnovo and Varna (Table 1). Considerably higher is the threshold value measured in Blagoevgrad compared to the rest of the values in the other regions in the country.

The retrospective analysis showed that in 2017 13 of the country regions registered very high incidence of Influenza/ARI. In 2018 their count was 16, for 2019 – 21, 2020 – 20, 2021 – 0 and 2022 – 5 (Table 1).

Further filtering with a new threshold set at 1.5 times the value of the 99th percentile showed that in 2017 the regions that surpassed it were Blagoevgrad (new threshold 613.86, maximum weekly incidence per 10 000 – 616.02), Montana (new threshold 510.23, max. 658.87) and Haskovo (new threshold 383.39, max. 387.11). In 2018 Montana (max. 589.9) and Razgrad (new threshold 227.75, max. 319.05) had incidence scoring above the newly introduced indicator for the respective region. In 2019 only Kardzhali (new threshold 247.26, max. 486.34) fulfilled this criterion. In 2020 there were three regions surpassing the new threshold incidence – Kardzhali (max. 573.54), Sliven (new threshold 314.63, max. 316.34) and Targovishte (new threshold 330.26, max. 364.23). In 2021 no region was affected by very high incidence of Influenza/ARI. In 2022 only the region of Blagoevgrad scored closely to the new threshold value (max. 602.71) but no region was filtered to surpass the newly introduced marker (Table 2).

After the filtering based on the Influenza prevalence,

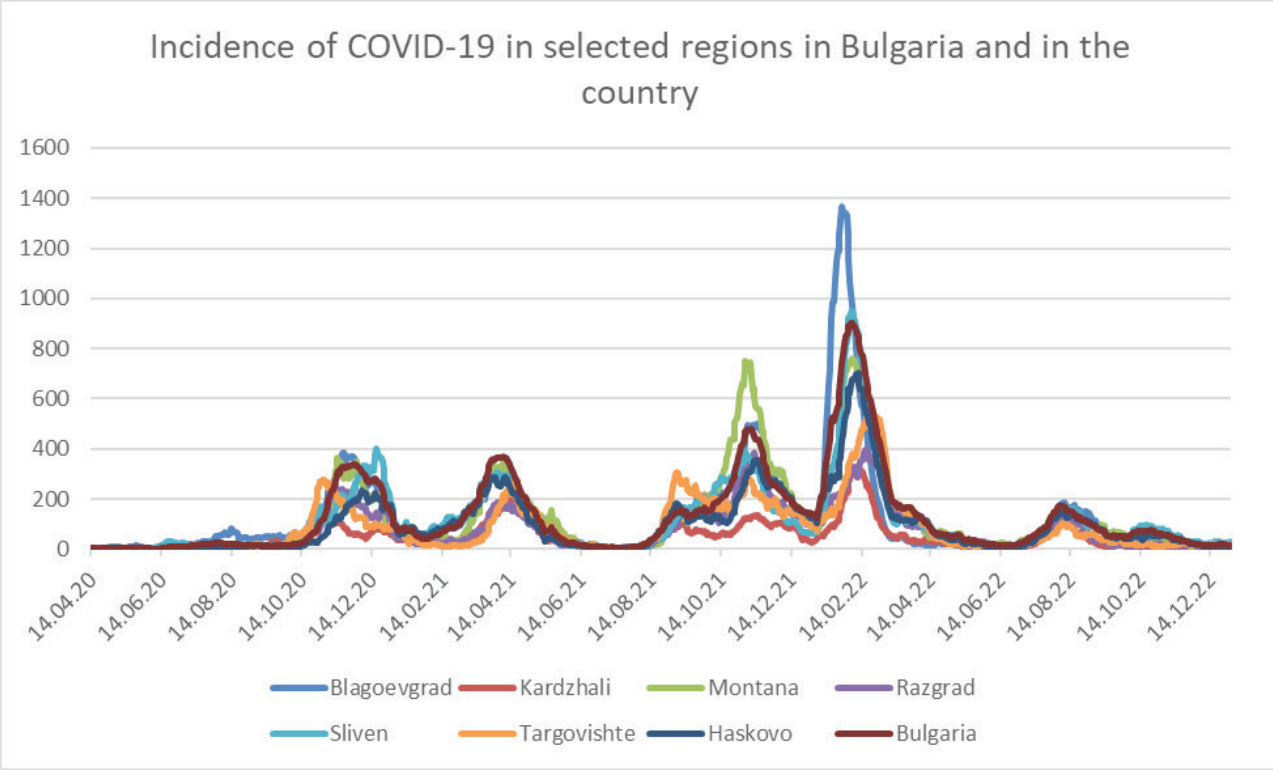

Figure 2. Incidence of COVID-19 in selected regions in Bulgaria and in the country in the period 2020-2022

the regions Blagoevgrad, Kardzhali, Montana, Razgrad, Sliven, Targovishte and Haskovo were selected for analysis of the peak values of COVID-19 incidence at a weekly level. Regarding the epidemic dynamics of COVID-19 in the selected regions, as shown in Fig. 2, no considerable deviations from the average for the country were observed in the period before the Delta variant started circulating. In Table 3 the maximal incidence values during the periods before Delta, during Delta circulation and during Omicron circulation could be seen.

The regions that registered higher maximal incidence values than the country maximum (369.49) before Delta took over were Blagoevgrad (384.22) and Sliven (402.46). During Delta circulation the national incidence value (481.62) was surpassed in the regions of Blagoevgrad (502.49) and Montana (749.60).

After the onset of the wave caused by the Omicron variant, only the regions of Blagoevgrad (1369.04) and Sliven (949.93) had higher maximal incidence values than the maximal for the country (900.35). The lowest values of the indicator were observed in Kardzhali (330.59) and Razgrad (398.05). The regions Montana, Targovishte and Haskovo can be categorized as regions with intermediate intensity of COVID-19 prevalence during the spread of Omicron according to the maximal values of the incidence there.

Demographics:

The regions Montana, Kardzhali and Razgrad presented with slightly lower share (less than 1%) of children population (0- 14 years old) as compared to the average for the country (14.44%). Sliven was the region with a considerably higher share of the 0-14 age group – 18.53%. The rest of the regions had a slightly higher share as compared to the country total – less than 0.3% difference (Table 4).

Regarding the share of actively working population (30-64 y.o.), in Blagoevgrad and Kardzhali it is higher than the country total (49.56%) and in Montana and Sliven it is lower. No deviation higher than 1% from the country total was found in the other analyzed regions.

Vaccine coverage:

Data on the vaccine coverage for COVID-19 in the selected regions is available in Table 5. All of the selected for this analysis regions but Kardzhali had lower percentage of fully immunized population as compared to the country average. Coverage with the COVID-19 vaccines was considerably higher than the uptake of the influenza vaccines in the period 2017-2022 (Table 6).

DISCUSSION

Table 2. Maximal values of Influenza/ARI incidence measured per week at 10 000 within regional cities. Values higher than 1.5 times the value of the 99-th percentile threshold are highlighted.

Област	Стойност 99-ти персентил 2013-2022	2017	2018	2019	2020	2021	2022	1.5 * прагова стойност
Благоевград	409.24	616.0194	507.896	410.5445	433.714	71.335	602.7077	613.86
Бургас	236.53	189.1439	226.8692	243.2285	263.275	166.0142	173.9923	354.795
Варна	199.74	159.2518	198.6914	248.887	200	194.3536	179.1976	299.61
Велико Търново	158.54	83.4188	99.2989	135.2137	223.2532	40.8401	100.6418	237.81
Видин	223.29	164.3348	290.9171	326.2348	235.816	138.8188	123.675	334.935
Враца	242.56	143.6234	351.2719	295.899	266.4821	224.9523	192.0749	363.84
Габрово	291.02	378.526	379.6296	239.2615	210.8491	253.019	291.3553	436.53
Добрич	179.09	151.7433	161.5169	265.9889	197.3685	104.4069	140.8281	268.635
Кърджали	164.84	164.8728	158.0031	486.3363	573.543	111.0608	101.9946	247.26
Кюстендил	190.14	275.4955	196.6568	206.3137	258.2391	65.1466	84.7242	285.21
Ловеч	279.05	238.1652	302.1239	115.7479	289.855	228.3511	272.8352	418.575
Монтана	340.15	658.8735	589.9021	315.6565	265.9975	122.5033	141.1452	510.225
Пазарджик	299.41	337.857	270.0027	397.2294	309.3842	174.4868	282.9913	449.115
Перник	229.17	208.5004	280.6638	277.0233	262.6181	142.5606	148.9432	343.755
Плевен	264.31	180.6322	223.3955	305.2966	309.5879	136.0544	168.9708	396.465
Пловдив	147.08	147.5549	164.4107	136.5395	183.2012	83.3212	61.8315	220.62
Разград	151.83	151.4683	319.0491	156.6997	131.2839	112.8748	144.6208	227.745
Русе	240.93	257.2369	246.3088	247.693	192.5254	181.9083	143.2792	361.395
Силистра	291.8	227.6867	297.4326	328.7415	327.3998	264.6869	277.5985	437.7
Сливен	209.75	151.2737	209.574	265.2429	316.3384	98.3213	118.7051	314.625
Смолян	207.82	209.0591	243.2046	261.0873	241.2676	155.4404	179.7754	311.73
София-град	205.86	204.1976	240.1729	276.8912	269.7993	131.58	114.529	308.79
София-област	259.31	268.6361	256.5431	259.9983	234.5416	77.2921	191.8976	388.965
Стара Загора	306.11	370.587	395.8901	310.3222	255.5136	97.1107	145.6658	459.165
Търговище	220.17	171.2423	138.6247	206.578	364.2294	122.3159	266.3768	330.255
Хасково	255.59	387.1146	199.3865	230.7259	364.6942	139.0922	332.3573	383.385
Шумен	222.39	221.3642	216.2161	326.8984	205.9202	205.9202	248.3912	333.585
Ямбол	321.62	392.9945	438.5334	377.5777	226.5466	84.2288	176.558	482.43
Общо	212.73	215.5172	230.8299	247.9181	242.6937	97.4997	126.6736	319.095

All 7 selected regions in the country demonstrated a much higher prevalence of Influenza and ARI in at least one of the 3 years before the pandemic than the usually observed. The maximal Influenza/ARI incidence values recorded there surpassed the threshold of 1.5 times the value of the 99th percentile.

Blagoevgrad and Sliven are the regions with higher maximal COVID-19 incidence values before Delta started circulating. This is the period when according to the evidence (Fig. 1) the actively working were the most affected by the coronavirus circulation. While it is true that Blagoevgrad has a higher share of working population as compared to the average for the country, Sliven is the region where the age group 30-64 is estimated to be less represented as compared to the average for the country.

During Delta when the number of infections among the younger population increased, the regions of Blagoevgrad and Montana surpassed the incidence recorded for the country. The region of Montana which has the lowest vaccination rate of the selected

Table 3. COVID-19 maximal weekly incidence per 100 000 recorded in selected regions in the period until Delta predominance, Delta predominance and the onset of the Omicron wave

Region	Max weekly COVID-19 incidence – before Delta	Max weekly COVID-19 incidence - Delta	Max weekly COVID-19 incidence - Omicron
Blagoevgrad	384.2164	502.4877	1369.039
Kardzhali	225.658	135.2684	330.5858
Montana	364.5641	749.6004	761.4113
Razgrad	253.6353	388.1252	398.054
Sliven	402.4571	392.1377	949.9291
Targovishte	277.6926	306.5438	544.5661
Haskovo	288.0386	354.1677	705.2286
Bulgaria	369.4895563	481.6239185	900.3547733

Table 4. Share of population within the age groups 0-14 and 30-64 years old in selected regions in 2020 presented as percentage of the respective region's population.

Region	Share of population 0-14 y.o. (%)	Share of population 30-64 y.o.(%)
Blagoevgrad	14.74	51.47
Montana	13.59	46.60
Kardzhali	14.06	52.31
Razgrad	13.57	50.08
Sliven	18.53	45.53
Targovishte	14.56	48.97
Haskovo	14.51	49.08
Bulgaria	14.44	49.56

Table 5. Percentage of population covered by primary complete vaccination against COVID-19 in the selected regions.

Region	Population covered by COVID-19 vaccine (%)
Blagoevgrad	25.55
Montana	21.44
Kardzhali	33.85
Razgrad	29.08
Sliven	26.44
Targovishte	23.70
Haskovo	24.54
Bulgaria	32.23

Table 6. Population covered by influenza vaccination in the respective years (%).

Region	2017	2018	2019	2020	2021	2022
Blagoevgrad	0.124723	0.101926	0.930312	1,89082746	2.045928	2.854654
Kardzhali	0.155513	0.114474	1.997177	2,07860382	2.664655	3.19982
Montana	0.075635	0.134992	0.173227	0,22249691	3.09464	3.219364
Razgrad	0.417715	0.271766	2.35583	1,81222111	1.791879	3.319256
Sliven	0.107731	0.099735	0.273736	0,77457806	1.602261	1.793262
Targovishte	0.054235	0.013441	0.016229	1,68504094	2.118076	2.54883
Haskovo	0.242135	0.138073	2.708628	2,64415875	3.784918	3.517661
Bulgaria	0.178808	0.145442	1.231493	1,5715354	2.107886	2.63889

regions, has the highest maximal weekly incidence (749.60) compared to the others at this specific period of the pandemic. According to the demographics of Montana, the region has lower share of both the age groups 0-14 and 30-64 y.o.

When Omicron took over, the epidemic wave was the most intensive in Blagoevgrad and Sliven regions – the same regions that were the most affected during the pre-Delta period.

The region of Kardzhali appeared to be the least affected by any of the COVID-19 waves. The Kardzhali region also differed by the considerably higher proportion of the population covered with immunizations against COVID-19.

In the region of Razgrad we observed a lower intensity of the COVID-19 waves similar to the one in the region of Kardzhali. Demographically, there are some similarities between the two regions. The shares of the children group are similar but the group of 30-64 y.o. is better represented in Kardzhali as compared to the region of Razgrad. The vaccination coverage in the Razgrad region was lower than the country average but much higher in comparison with the other regions analysed in this study.

The regions Targovishte and Haskovo were characterized by COVID-19 waves with intermediate intensity as compared to the country one, and the distribution of the population within the age groups 0-14 and 30-64 y.o. there is comparable to the one for Bulgaria as a whole.

CONCLUSION

COVID-19 prevalence in the regions with the highest Influenza/ARI incidence varied significantly. Within the 7 regions fulfilling the criteria for extremely high circulation of Influenza/ARI in the 2017-2022 period we had both Blagoevgrad and Kardzhali included. These are the regions where the COVID-19 maximal incidence at regional level was recorded (Blagoevgrad) and where the maximal COVID-19 incidence remained 3 times lower than the value for the country total (Kardzhali). Therefore, we conclude that although COVID-19 and Influenza/ARI are both respiratory infections, they differ in their epidemiology and no common pattern can be found. Our hypothesis that differences in the demographic structure of the regions might be associated with a higher prevalence of COVID-19 or Influenza/ARI, was not confirmed by the data from the 7 analyzed regions.

Differences in vaccination coverage, however, might be determining for the intensity of COVID-19 waves as the two regions that presented with the lowest maximal COVID-19 incidence during the Omicron period had also the highest vaccination rates among the 7 filtered regions.

Although we concluded that the epidemiology of the two viruses is very different, it should be recognized that their transmission paths are essentially the same. Therefore, anti-epidemic measures are strongly recommended to limit the circulation of both respiratory pathogens.

LIMITATIONS

Other factors that were not a subject of this study might also influence the incidence values. First, the analysis worked with the official numbers of registered residents. Thus, we did not account for the people who had moved and had not registered the changes in their home address.

Another limitation of this study concerns the innate differences of surveillance models used for the two infections. While data for Influenza/ARI is taken from sentinel sites and represents only regional cities, data for COVID-19 incidence represents the region as a whole.

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