ORIGINAL

Lower COVID-19 incidence in Bulgaria in 2022 can be attributed to the Delta variant's belated intense spread

La menor incidencia de COVID-19 en Bulgaria en 2022 puede atribuirse a la intensa propagación tardía de la variante Delta

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Abstract

Objectives: The first COVID-19 wave caused case fatality rates (CFRs) of above 7% globally. In 2021 and 2022 the values of the same indicator went down to 2%. Differences between countries are still observed. The present study aimed to assess the CFRs dynamics in Bulgaria in relation to the specificity of the epidemic process in the country.

Methods: Descriptive analysis of cumulative incidence, mortality rates, and hospital admissions during the Delta and Omicron waves in Bulgaria and in the EU was performed. Differences in stringency index and testing capacities were analyzed to provide reasoning behind the findings. Indicator values were compared temporally and quantitatively.

Results: Data was reviewed for 27 EU countries. Opposing trends in Bulgaria and in the EU were reported. During the Delta wave incidence in Bulgaria was 25% higher than in the EU and increased by 67% during the Omicron period. In the EU, the increase during the Omicron wave was five-fold. Mortality in Bulgaria decreased by 38% between the two waves but it continued to be above the median mortality rate in the EU. Hospital admissions followed similar trends. Out of 16 countries only 5 experienced a drop in the number of new hospital patients. In Bulgaria, admissions shrank by 45% during the Omicron predominance.

Conclusions: Higher incidence during the Delta wave resulted in the accumulation of a population with recently obtained natural immunity. Given the evidence from countries with good vaccination coverage, it is reasonable to conclude that some of the mortality in Bulgaria could have been averted. Due to the observed positive association between acceptance of vaccines and other antiepidemic measures, we recommend that future risk communication efforts highlight the importance of personal decision-making and social behaviour.

Keywords: COVID-19, Delta variant, Omicron variant, incidence, Bulgaria.

Resumen

Objetivos: La primera ola de COVID-19 provocó tasas de letalidad (CFR) superiores al 7% a nivel mundial. En 2021 y 2022 los valores del mismo indicador bajaron al 2%. Aún se observan diferencias entre países. El presente estudio tuvo como objetivo evaluar la dinámica de los CFR en Bulgaria en relación con la especificidad del proceso epidémico en el país.

Métodos: Se realizó un análisis descriptivo de la incidencia acumulada, las tasas de mortalidad y los ingresos hospitalarios durante las ondas Delta y Omicron en Bulgaria y en la UE. Se analizaron las diferencias en el índice de rigurosidad y las capacidades de prueba para proporcionar un razonamiento detrás de los hallazgos. Los valores de los indicadores se compararon temporal y cuantitativamente.

Resultados: Se revisaron los datos de 27 países de la UE. Encontramos tendencias opuestas en Bulgaria y en la UE. Durante la onda Delta, la incidencia en Bulgaria fue un 25 % más alta que en la UE, pero aumentó un 67 % durante el período Omicron. En la UE, el aumento fue del 576%. La mortalidad en Bulgaria disminuyó un 38 %, mientras que en la UE aumentó un 56 %. Los ingresos hospitalarios siguieron tendencias similares. De 16 países, solo 5 experimentaron una caída en el número de nuevos pacientes hospitalizados. En Bulgaria, las admisiones se redujeron en un 45% durante el predominio de Omicron.

Conclusiones: La mayor incidencia durante la onda Delta resultó en la acumulación de población con inmunidad natural recién obtenida. Dada la evidencia de países con buena cobertura de vacunación, es razonable concluir que parte de la mortalidad en Bulgaria podría haberse evitado. Debido a la asociación positiva observada entre la aceptación de las vacunas y otras medidas antiepidémicas, recomendamos que los futuros esfuerzos de comunicación de riesgos destaquen la importancia de la toma de decisiones personales y el comportamiento social.

Palabras clave: COVID-19, variante Delta, variante Omicron, incidencia, Bulgaria.

Introduction

In 2021 the COVID-19 case fatality rate (CFR) decreased substantially. While in 2020, the first wave caused CFR of above 7% globally, in 2021 and 2022 the values of the same indicator went down to 2%¹. However, differences between countries are still observed.

The main factors that drive CFR down refer to changes in the SIR (Susceptible, Infected, Removed (or Resistant)) structure of the population². Therefore, the immune response of the infected and the healthcare sector's capacity are related to the severity of the epidemiologic situation³. For instance, several studies confirm that some demographic determinants of the immune reaction related to patients' sex and age affect CFRs dynamics⁴⁻⁸. The natural course of the pandemic leading to accumulation of recovered population together with the social efforts for mass vaccination have also contributed to minimizing fatality outcomes.

Although CFR as a measurement implies some biases due to differences in testing strategies and case and death definitions adopted in different countries, we consider it important to provide an explanation for opposing trends in the dynamics of the indicator. Despite its values being highly dependent on testing rates (both of vaccinated and non-vaccinated populations)⁸⁻¹⁰, one of the reviewed studies concludes that testing percentage is not a driving factor for the different outcomes between the first and second wave of COVID-19 in Canada¹¹. The authors explain the decrease in CFRs with the higher incidence among the younger age groups after the first wave.

Nevertheless, with the introduction of the EU Digital Green Certificate in October 2021 in Bulgaria and the subsequent increase of performed tests for SARS-CoV-2, CFRs are believed to be less inaccurate as asymptomatic and mild infections were more likely to be registered.

The aim of the present study is to highlight the determining factors for the increasing fatality rates in Bulgaria in the period after July 2021 when the Delta variant became predominant, and the Omicron wave up to 1 May 2022.

Materials and methods

We chose for the subject of our analysis the epidemiologic situation in Bulgaria where CFRs are higher than the values from the region in the study period. A descriptive comparative analysis of cumulative incidence and mortality rates per 1 million for the conditional period of the Delta and Omicron waves in Bulgaria and in the EU was performed. The study compares the dynamics of biweekly incidence and total vaccine coverage temporally and quantitatively to explain changes in the share of immune population. Hospital admissions per million

To compare outcomes between the two waves periods of conditional variant predominance were analyzed. For the onset of the Delta wave 1 July was accepted as incidence in the EU started to grow approximately at that time¹. Co-circulation of Delta and Omicron makes the differentiation between the two waves a particular challenge. Given the ECDC's information that first local transmission within Europe has been registered on 2 December 2021¹² and the report on Omicron prevalence from the period between 20 December 2021 and 9 January 2022¹³, the onset of the Omicron wave was conditionally considered to be from 1 December 2021 for incidence rates. When analyzing mortality, we considered deaths registered from 15 July to 15 December 2021 as related to the Delta wave. This is due to time distance between symptoms onset and disease outcome. For the same reason, deaths caused by the Omicron variant are considered until 15 May 2022.

Along with the dynamics of incidence and mortality studied, we compared testing approaches as determinants of the recorded incidence. We also measured the average value of the stringency index regarding application of antiepidemic measures for the period of Delta and Omicron per country to analyze whether incidence dynamics could be affected by the different measures imposed.

Publicly available sources were used for the analysis – the site "Our world in data" from where we have generated some of the graphs.

Ethical considerations

The study received an ethical exemption as it met one of the criteria for exemption (research that does not collect identifiable data).

Results

While most of the countries presented higher CFR in 2020 that decreased in time, in Bulgaria the indicator remained with no significant change. At the beginning of the pandemic, its values were drastically lower than the ones from the EU. The maximum cumulative value recorded in Bulgaria is from June 2020 - 6.05%, while in the EU during May 2020 the CFR surpassed 11%. While in the following few months CFRs decreased and met at slightly above 2%, after the fall of 2020 values in Bulgaria were gradually growing. The tendency was not observed in the region. For the second year of the pandemic, CFR in Bulgaria remained around 4% while the average value for the EU went down to 2%. Values of the indicator in Bulgaria went up with the peak of the Delta wave in November 2021.

Biweekly incidence dynamics show that the Delta wave started earlier in the EU but after the swell there was a long-lasting plateau (1500-2000 cases per 1M biweekly). A second increase was recorded in the region, starting mid-October, which merged with the Omicron wave. Biweekly incidence until the end of November in the EU was with the highest value of 7719 cases per million.

In Bulgaria, the cases started growing later with a steep increase from the beginning of October 2021. The peak was registered in the beginning of November when the new cases per million surpassed 9300 per 1M on a twoweek basis. Therefore, during the Delta wave (1 July – 30 November 2021) the cumulative number of infections per million in Bulgaria (39974.63 cases per 1M) was substantially higher than in the EU (30067.68) (**Table I**). Total cumulative incidence in Bulgaria was higher by 25% compared to the EU.

Just as with Delta, there was a significant delay of the Omicron wave in Bulgaria. When Omicron gained ground, the number of new cases went several times up in the EU – from 7700 new cases per million on a biweekly basis in the end of November to 38000 during the Omicron predominance. In Bulgaria the raise was not so striking. The new cases per million during the Omicron wave there reached a peak of 17500 biweekly. Regarding cumulative values of incidence from the wave period starting 1 December 2021 to the end of the study period 30 April 2022, during the Omicron wave in Bulgaria there were recorded 66740.61 infections per million in comparison with 203283.74 in the EU (**Table I**).

Total cumulative incidence in Bulgaria was lower by 67% compared to the EU.

Cumulative mortality per million in the EU during both waves was substantially lower than in Bulgaria. The more severe Delta variant led to 1696.81 deaths per million in Bulgaria and 298.38 in the EU. Deaths during the Omicron wave increased with 56.48% in the EU (466.9 per 1M) and decreased with 38.4% in Bulgaria (1045.77 per 1M) but were still consistently higher than in the EU (**Table II**). With higher incidence and reduction in the number of deaths, CFR in Bulgaria went down from 4.14% on 15 December 2021 to 3.19% on 15 May 2022.

Hospitalizations in Bulgaria during both waves as well as during previous waves occurred much more often than elsewhere in the EU. Hospital admissions per million during the Omicron wave in Bulgaria decreased by almost half in comparison with the Delta period while in most EU countries with few exceptions they went up (Figure 1, Table III).

Regarding testing efforts, the total number of tests performed per 1000 in different countries varied between 237.412 and 9348.24 during the Delta wave (1 July – 30 November 2021) and between 445.042 and 8126.62 during the Omicron wave (1 December 2021 – 30 April 2022). In the first period of the study Bulgaria was placed in the second quarter (491.406 tests per 1000) compared with the other EU countries, while during the second period the country presented with the second lowest result (475.623 tests per 1000) (**Figure 2**).

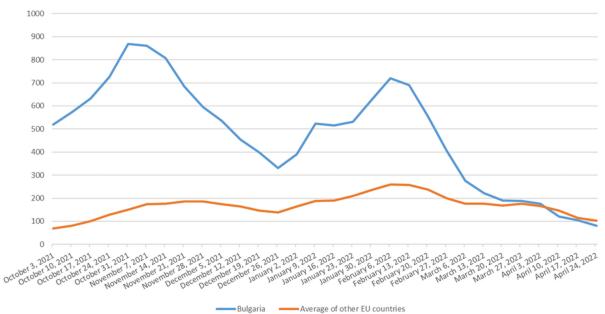
Table I: Dynamics of COVID-19 cumulative incidence across the EU on dates marking conditional wave period¹.

Country	7/1/2021	12/1/2021	4/30/2022	Delta INC	Omicron INC	Waves Ratio		
Romania	55918.44	92133.51	149720.21	36215.06	57586.70	1.59		
Poland	75180.92	93170.16	156535.37	17989.24	63365.21	3.52		
Bulgaria	61270.71	101245.33	167985.94	39974.63	66740.61	1.67		
Hungary	83231.49	114756.39	195783.62	31524.90	81027.22	2.57		
Malta	58143.55	75045.37	174164.88	16901.82	99119.50	5.86		
Sweden	104188.68	115361.31	238931.29	11172.63	123569.98	11.06		
Croatia	88660.85	151205.32	276458.54	62544.47	125253.22	2.00		
Spain	80470.66	108971.45	250514.21	28500.79	141542.76	4.97		
Finland	17378.10	34287.80	184793.08	16909.71	150505.28	8.90		
Czechia	158640.92	206653.57	371534.00	48012.65	164880.43	3.43		
Ireland	54704.22	115091.15	304242.27	60386.93	189151.12	3.13		
taly	71923.77	85138.28	277905.27	13214.51	192766.99	14.59		
Belgium	93518.71	153852.33	349349.86	60333.62	195497.54	3.24		
EU	73926.80	103994.48	307278.22	30067.68	203283.74	6.76		
Germany	44708.04	70784.10	297448.93	26076.06	226664.83	8.69		
Greece	40514.14	90479.84	318219.80	49965.70	227739.96	4.56		
Lithuania	100186.21	170690.91	412679.23	70504.70	241988.32	3.43		
Slovakia	142276.02	217078.57	464095.34	74802.55	247016.77	3.30		
Estonia	98656.51	167961.79	430640.90	69305.28	262679.11	3.79		
Slovenia	121429.08	199660.28	476575.09	78231.21	276914.80	3.54		
Portugal	85714.01	111944.36	391413.38	26230.35	279469.02	10.65		
atvia	73375.64	135913.03	438659.84	62537.39	302746.81	4.84		
Netherlands	96526.87	153660.94	460456.18	57134.06	306795.24	5.37		
rance	86328.66	115242.70	425667.69	28914.03	310425.00	10.74		
Austria	72409.33	129568.64	467911.41	57159.31	338342.78	5.92		
Cyprus	86346.42	150629.40	535955.63	64282.98	385326.23	5.99		
Denmark	50245.98	84130.65	532375.68	33884.67	448245.03	13.23		

Table II: Dynamics of COVID-19 cumulative mortality across the EU on dates marking conditional wave period¹.

Country	7/1/2021	12/1/2021	4/30/2022	Delta MORT	Omicron MORT	Waves Ratio		
Romania	1771.73	2997.38	3394.56	1225.65	397.18	0.32		
Poland	1962.82	2341.93	3033.51	379.11	691.58	1.82		
Bulgaria	2637.72	4334.53	5380.30	1696.81	1045.77	0.62		
Hungary	3091.01	3834.48	4772.81	743.48	938.33	1.26		
Malta	797.35	894.17	1353.59	353.59 96.82 459.42		4.75		
Sweden	1398.96	1454.18	1805.37	55.22	351.20	6.36		
Croatia	2027.77	2901.14	3923.52	873.37	1022.38	1.17		
Spain	1707.50	1866.18	2220.48	158.68	354.31	2.23		
Finland	179.01	284.86	773.85	105.85	488.98	4.62		
Czechia	2886.09	3312.13	3829.03	426.04	516.90	1.21		
Ireland	1006.31	1170.15	1444.49	163.84	274.34	1.67		
Italy	2157.99	2281.86	2789.38	123.87	507.53	4.10		
Belgium	2170.97	2388.08	2722.58	217.11	334.50	1.54		
EU	1662.20	1960.58	2427.48	298.38	466.90	1.56		
Germany	1094.84	1279.01	1648.50	184.17	369.49	2.01		
Greece	1227.24	1871.93	2828.72	644.69	956.79	1.48		
Lithuania	1580.39	2530.64	3277.05	950.24	746.42	0.79		
Slovakia	2298.99	2867.49	3678.85	568.51	811.36	1.43		
Estonia	956.57	1406.64	1923.68	450.06	517.05	1.15		
Slovenia	2087.85	2568.64	3124.45	480.79	555.82	1.16		
Portugal	1670.25	1817.09	2194.63	146.84	377.55	2.57		
Latvia	1356.52	2352.29	3094.05	995.78	741.76	0.74		
Netherlands	1017.44	1161.60	1278.73	144.16	117.13	0.81		
France	1653.17	1795.33	2185.40	142.16	390.07	2.74		
Austria	1468.94	1831.64	2222.24	362.70	390.60	1.08		
Cyprus	428.57	685.26	1172.98	256.70	487.72	1.90		
Denmark	433.87	519.11	1073.92	85.24	554.81	6.51		

Figure 1: Weekly hospital admissions within countries providing data for the selected indicator, measured in the end of the week - between 3 October 2021 and 24 April 2022. Starting period is selected according to the availability of data for Bulgaria^{1,16}.

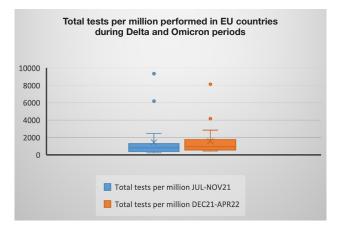


Hospital admissions per Million

Table III: Average number of weekly hospital admissions for the periods 3 October 2021– 28 November 2021 (Delta wave) and 5 December 2021 – 24 April 2022 (Omicron wave). 1,15 Highlighted in red are values greater than the ones recorded in the country for the earlier period. Starting period is selected according to the availability of data for Bulgaria gathered through recordings from the COVID-19 Informational Portal.

PERIOD	Belgium	Bulgaria (croatia	Czechia	Denmark	Estonia	France	Germany	Greece	Ireland	Italy	Latvia	Malta	Netherlands	Slovenia	Spain
OCT-NOV21	97.40	696.57	293.17	202.55	54.59	236.25	32.16	73.87	200.63	79.61	31.32	448.03	8.18	56.76	237.66	32.34
DEC21-APR22	131.92	382.77	242.78	237.15	249.81	227.92	169.88	107.11	250.79	153.21	109.16	341.04	100.11	71.54	171.04	143.86
RATIO OMICRON TO DELTA	1.35	0.55	0.83	1.17	4.58	0.96	5.28	1.45	1.25	1.92	3.49	0.76	12.24	1.26	0.72	4.45

Figure 2: Distribution of total tests performed in EU countries during the two 5-month periods – 1 July 2021 – 30 November 2021 (Delta) and 1 December 2021 – 30 April 2022 (Omicron). Values are obtained by subtracting measurements on respectively 1 July 2021 from the measurement on 30 November 2021 (total tests per 1 M during Delta) and on 30 November 2021 from the measurement on 1 May 2022 (total tests per 1M during Omicron)¹



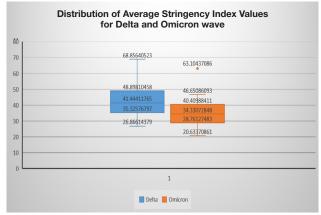
In terms of imposed restrictions, we measured the average value of the stringency index calculated by Our World in Data for the two studied periods. Country scores during the Delta and Omicron periods ranged respectively as follows (26.87-68.86) and (20.63-63.10) (**Figure 3**). Results show that during both waves Bulgaria had similar averages of the indicator (39.85 during Delta and 36.95 during the Omicron wave) and ranked around the middle in both studied periods. The greatest release of measures was observed in Portugal where the indicator's value dropped by 23.11 units. Only two countries show higher average for the Omicron period – Estonia (stringency index increase with 8.98 units) and Slovakia (1.76 units).

Discussion

Differences in the incidence during the Delta wave could be related to differences in established immunity among populations. Although antibody effectiveness decreases with the emergence of new variants, vaccination remains the best means for prevention of infection^{16,17}. With a vaccinated population of less than 30%18 and assumable other 40% recovered from previous infection in Bulgaria¹⁹, in October 2021 there were supposedly 30% who remained susceptible. In contrast the average vaccination coverage in the EU at this time reached and surpassed 70% (Table III). Even if vaccination effectiveness against infection declines over time to around 22%²⁰, evidence suggest that COVID-19 incidence in Europe, which nevertheless increased, was suppressed by the obtained vaccination immunity. In contrast, low vaccination rates in Bulgaria did not allow the peak of new infections to be averted.

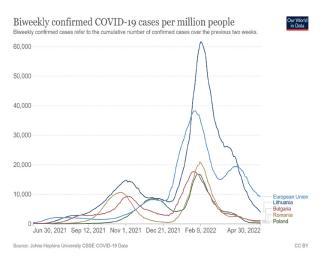
Interesting is the fact that the Omicron wave in Bulgaria presented with much lower infection rates than most of

Figure 3: Distribution of Average Stringency Index for the two studied wave periods'



EU countries with the exception of Romania and Poland. A reason for this observation we find in the virtual delay of the Delta wave in the three countries and its intensive spread at a later stage demonstrated through large swells on the graph (**Figure 4**). However, intensive spread of Delta in Lithuania at approximately the same stage of the pandemic as Bulgaria, Romania and Poland did not suppressed the incidence growth levels in 2022.

Figure 4: Dynamics of COVID-19 incidence in EU, Bulgaria, Romania, Lithuania, and Poland'

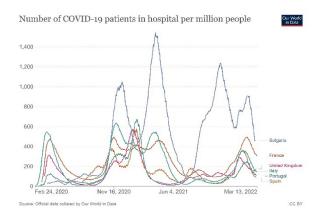


The more intensive spread of Delta and the short time window between the two waves in Romania, Poland and Bulgaria at the end of 2021 allowed for the accumulation of naturally immune population. In fact, the belated Delta wave in Poland reached its peak after the conditional onset of the Omicron wave that this study assumes²¹. Furthermore, we argue that the longer co-circulation of Delta and Omicron was an important determinant of the epidemiological situation in 2022. In our interpretation, we link the lower incidence rate during the Omicron predominance to the proximity between the fourth and

the fifth wave. While reports prove the latest variant's capacity to escape neutralizing antibodies especially time after infection or vaccination²², the Bulgarians, Romanians and Polish who recently recovered from Delta were relatively protected from contracting the new variant. In contrast, the rest of Europe may have experienced wane in immunity levels among recovered and vaccinated without a booster. The observed exception in Lithuania could be related to the considerably lower average stringency index (23.51).

A possible explanation for the observed higher values of COVID-19 mortality in Bulgaria in comparison with the rest of Europe in the second half of 2021 and the beginning of 2022 could be found again in mismatches in COVID-19 vaccine coverage. In general, a decrease in hospitalizations and deaths once vaccination was extended to cover the whole population was observed in the countries with good vaccination coverage²³⁻²⁷. In comparison, hospitalization rates in Bulgaria have not changed after the introduction of COVID-19 vaccines (**Figure 5**).

Figure 5: Number of COVID-19 patients in hospital per 1 M people¹.



Given the higher incidence observed everywhere during the Omicron predominance, values of hospital admissions and mortality across Europe were bound to increase compared to the previous period. Reduction was only observed in Bulgaria, Croatia, Estonia, Latvia and Slovenia. Despite the steep swell in the incidence, with the increase in the numerator (number of cases), CFRs did not grow either in the rest of Europe.

The higher CFRs in Bulgaria could be explained with the low number of tests performed per 1000 as many of the infections may have gone unnoticed by the health system. However, values of weekly hospital admissions and cumulative deaths per 1M for both of the periods studied appear substantially higher in comparison with the rest of Europe. High numbers of hospital patients and fatal outcomes indicate an epidemic situation with greater severity. That is why despite biases, the CFRs are a useful indicator for intervention necessity in the case. Observations regarding both incidence and mortality were made in an environment of varying social behaviors. Although most of the countries introduced almost identical anti-epidemic norms to control the virus, surveys show that deviations from mask wearing and social distance practice appeared at a different level around the EU²⁸. According to the collected data in the Covid Behaviors website, Bulgaria had one of the lowest degrees of population compliance. Provided the fact that vaccine acceptance correlates positively with anti-COVID measures compliance²⁹, it is difficult to ascertain whether the rapid spike in incidence in Bulgaria during the Delta wave was only due to low vaccination rates. However, since vaccine confidence and responsible social behavior are both determined by acceptance of measures, a recommendation of interventions consolidating COVID-19 social awareness and vaccination acceptance seem equally valid.

Another well-known factor that has a direct impact on COVID-19 is the resilience of the health system. Bulgaria is ranked first for mortality of cardiovascular diseases -cardiovascular death rate measures 424.688 (EU range 86.06–424.688)¹. Patients with such conditions have been reported of higher risk for severe COVID-19 disease³⁰. Therefore, the bad general health of the Bulgarian population is an exacerbating factor and affects negatively CFR values causing them to soar. Existing pre-morbidity determines higher COVID-19 severity and therefore, results in higher hospitalization rates. During the pandemic bad general health dwindles the effect of interventions that were successful in countries with healthier population. Measuring the association between different health systems' performances and CFRs dynamics would be a subject of a prospective analysis.

Conclusion

In conclusion, we would like to highlight that the introduction of mass vaccination coincides with the reduction of hospitalizations and deaths in the countries with high vaccination coverage. Higher incidence during the Delta wave resulted in accumulation of population with recently obtained natural immunity. It is related to lower intensity of consequent Omicron wave in Bulgaria. However, reasons for the observed higher mortality in the country are complex and it is difficult to differentiate to what extent the exuberant number of deaths is related solely to low vaccination rates. Other factors such are health system resilience and population's general health are key confounders worth to study in prospective works. As limitations of our analysis we point out it does not consider other confounding factors that may be additionally pushing death rates up.

Given the evidence from countries with good vaccination coverage, it is reasonable to conclude that some of the

mortality in Bulgaria could have been averted if higher immunity was achieved through vaccines. Due to the observed positive association between acceptance of vaccines and other anti-epidemic measures, we recommend that future risk communication efforts highlight the importance of personal decision-making and social behavior. Persuasive communication should underline the benefits of collective responsibility. Increasing confidence in all measures will reduce pandemic burden related to incidence and mortality.

Conflicts of interest

None.

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