

THE INFLUENCE OF COVID-19 PANDEMIC ON THE VACCINATION OF THE POPULATION WITH THE INFLUENZA VACCINE IN THE REPUBLIC OF NORTH MACEDONIA

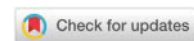
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Abstract: The implemented actions to minimize the spread of the COVID-19 pandemic had a powerful effect on the transmission of other respiratory viruses, particularly influenza viruses. Influenza is a disease of viral aetiology that causes epidemics and occasionally pandemics during the wintertime almost every year. Generally, it is a mild and self-limiting disease, but it can represent high morbidity and even mortality when affecting the elderly population or people with latent chronic diseases. The existing circumstances of a persistent and ongoing epidemic caused by the SARS-CoV-2 virus, increase the probability of having active coincidence with the anticipated annual epidemic of influenza. Thus, the key is a logistic strategy for clinical and viral diagnosis of the SARS-CoV-2 virus that will determine the importance of understanding the role of influenza vaccines in virus-induced COVID-19 disease. This paper aims to compare the potential impact of the COVID-19 pandemic on the vaccination coverage of the population with the influenza vaccine. The official data for seasonal influenza vaccination were used, obtained from the weekly reports on the influenza situation in the Republic of North Macedonia from the Institute of Public Health as well as the data from the national system "MojTermin" for total vaccinated individuals with influenza vaccine for the season 2020/2021 and 2021/2022 including the 5th week.

The analyzed data for the season 2021/2022 show an increase of applied doses by 8.3% compared to the season 2020/2021 and an increase of 11.5% compared to the season 2019/2020. Regarding the target groups in the season 2021/2022, including the 5th week, the coverage of influenza vaccination in children aged 6 months to 5 years has a significant decrease of 87.9% compared to the season 2020/2021. There is an increase in coverage in health professionals by 24.3% compared to last season, in the chronically ill the decrease of the applied doses is by 11.4% compared to last season, and in the elderly, over 65 it is noticeable an increase in coverage by 100% compared to the 2020/2021 season. Furthermore, there is a significant decrease of 95.7% in the vaccines administered to pregnant women compared to last season. The reduced coverage of influenza vaccination is partly due to the ambiguities arising from the influenza immunization campaign, which emphasized the importance of receiving a vaccine to minimize the spread of the influenza virus as an additional threat to the presence of COVID-19. Although the influenza vaccine does not protect against COVID-19, influenza vaccination has been part of the public health strategy to flatten the disease curve caused by respiratory viruses that attack the respiratory system, to protect and preserve the health of healthcare professionals providing care to patients with COVID-19. Influenza vaccination is still the most efficient preventive measure against influenza infections at our disposal and it is recommended by the most expert bodies including CDC, WHO, ECDC, and the National Committee for Immunization of the Republic of North Macedonia.

Keywords: vaccination, influenza, COVID-19, coronavirus, SARS-CoV-2.

INTRODUCTION

The COVID-19 pandemic challenged society around the world. It has been more than two years since the pandemic first began. Policymakers worldwide have implemented stringent mitigation efforts to reduce transmission of severe acute respiratory syndrome virus 2 [SARS-CoV-2] (Groves, HE., et al., 2021). The Government of North Macedonia has been very dedicated to taking measures for handling the situation with the pandemic, so on March 18, 2020, it declared a state of emergency to fight against the spread of Covid-19. When deemed necessary, the government did not hesitate to take strong action. Having only 35 confirmed cases, the state of emergency was declared across the country on March 18, 2020. All borders and the airport were closed. To fight corona virus almost all government actions have

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been mobilized, along with the increasing emergency response mechanisms in all sectors. There has been a positive response and consent from society as well as more confidence in the government protective measures and guidelines for social distancing. Simultaneously, through social networks, television, and other media, the Ministry of Health has launched an active risk communication campaign, having substantial support from the WHO and the other international agencies. But, such restrictions resulted in many negative effects too. Namely, people could not access medical services, although available due to economic difficulties, interruptions in transportation, and the fear of leaving home or visiting a physician as a preventive measure against exposure to SARS-CoV-2. The effect on health and early death caused by the suspension of ordinary daily obligations is not known yet. Generally, the extensive research performed during the initial pandemic phase by the World Health Organization informed a serious reduction in all routine health services, having a 70% reduction in routine immunization services. Vaccination coverage estimations in 2020 indicate that 23 million children missed their regular vaccination through the scheduled immunization services, which is about 3.7 million more compared to 2019 (World Health Organization [WHO], 2020).

Seasonal flu, a highly contagious acute disease of the respiratory tract caused by influenza viruses is a serious risk to the health of the world's population. It is estimated that half a million deaths and five million cases of critical illness occur as a result of seasonal influenza worldwide each year (Schmid, P., et al., 2017).

In the northern hemisphere, including Europe, seasonal flu mainly occurs in the form of epidemics between November and April each year, while in the southern hemisphere between June and October. Many other viruses and bacteria cause similar symptoms, so much of the flu-like illness (ILI) is not caused by the flu.

Flu pandemics appear at irregular intervals. Influenza monitoring is performed worldwide.

Due to the epidemiological characteristics of influenza as a medical entity, the occurrence of an epidemic form such as damage to human health, death rate, high morbidity, and mortality, is not only a medical but also a social, economic and financial problem for any health system as well as a significant threat to the population.

The Republic of North Macedonia (MKD) is a relatively small country with a population of 2 million people, which has a long-standing tradition of immunization. Compulsory immunization, with a strong legal basis, is present since the 1960s, while influenza vaccination is optional. Until the 2018/2019 season, the people who were vaccinated participated with their financial means, and seasonal influenza vaccine coverage was low, with an average of 25,000 to 30,000 people being vaccinated per year.

There is a multi-year influenza vaccination plan or policy in MKD. Every year MOH prepares Annual Information for influenza immunization which is approved by the Government of MKD. This information specifies the (1) quantities of vaccines to be procured, (2) necessary budget, (3) the categories that will be covered by free vaccination, and (4) the implementation of the vaccination. The recommendation for influenza vaccination is given by the National Commission for communicable diseases in coordination with National Committee for Immunization, both as advisory bodies in MOH. The information on influenza immunization, influenza program, estimation of the number of vaccines to be procured, target groups, and recommendation of the type of influenza vaccines to be used is prepared by the Institute for Public Health, accepted by the National Commission for communicable diseases in coordination and National Committee for Immunization and then proposed to the Minister of Health, who gives the final decision. The type of vaccines, their formulation, and presentation is defined by National Committee for Immunization in coordination with experts from the Macedonian Agency for Medicines and Medical Devices – MALMED and following the relevant legislation and regulations.

The free of charge influenza vaccines that are procured by MOH are for specific population groups defined as (1) Elderly people (over 65 years old), (2) People with chronic diseases, (3) Healthcare workers, (4) Pregnant women, and (5) Children aged 6 months to 5 years. There is low acceptance of maternal immunization against influenza due to general reluctance to vaccinate among pregnant women, the complexity of vaccination pathways, as well as lack of understanding of the need for vaccination. The same low acceptance is present for influenza vaccination in children.

At the start of the influenza season 2021-22, all along with the still growing COVID-19 pandemic, the potential impact on complications caused by the flu should have been taken into consideration since that could further burden an already overloaded and strained health system (Patel Murthy, B., et al., 2021).

As a reaction to the coronavirus pandemic, much attention has been paid to promoting vaccination against Covid-19. Nevertheless, the effect and the power of seasonal influenza should not be overlooked, especially during the winter influenza wave.

MATERIALS AND METHODS

The data used for the seasonal influenza vaccination are obtained from the weekly reports on the flu situation in the Republic of North Macedonia, disclosed weekly on the website of the Institute of Public Health. (www.iph.mk) as well as the data obtained from the national system "MojTermin" for the season 2020/2021 and 2021/2022. The data on the total influenza vaccination for the seasons 2019/2020, 2020/2021, and 2021/2022 up to the 5th week in 2022 have been compared.

Influenza monitoring includes levels of regular reporting, organized collection, processing, analysis, and evaluation of data as well as distribution of relevant information to the institutions that propose and adopt legal solutions that should be implemented at the national level. According to the legislation, the Centers for Public Health of RNM, weekly submit (distribute) data for individuals vaccinated with influenza vaccine to the Institute of Public Health of RN Macedonia, (IPH), additionally processed by the department of epidemiology.

RESULTS

In the season 2021/2022, a total of 49.320 people were vaccinated against influenza. There is an increase of the applied doses by 8.3% compared to the season 2020/2021 when the total number of applied influenza vaccines was 45.561 and an increase of 11.5% compared to the season 2019/2020 when the number of applied vaccines was 43.639.

The analyzed data for the season 2021/2022 show that the coverage of influenza vaccination in children aged 6 months to 5 years has a significant decrease of 87.9% compared to the season 2020/2021. Taking into consideration the health professionals and compared to last season, there is a 24.3% increase in the coverage, the reduction of the applied doses in the chronically ill is by 11.4%, while in the elderly over 65 we identified an increase in coverage by 100% compared to the season 2020/2021. Furthermore, compared to last season there is an extreme drop of 95.7% in the vaccines administered to pregnant women.

Figure 1. Total number of vaccinated people for the seasons 2019/2022

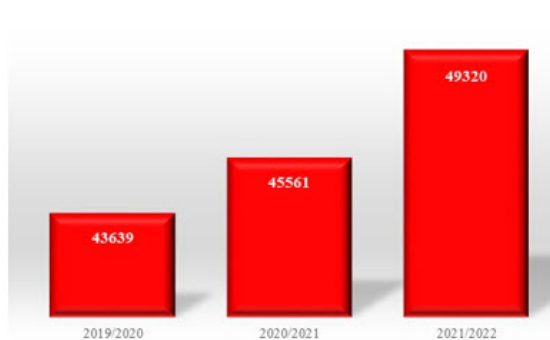
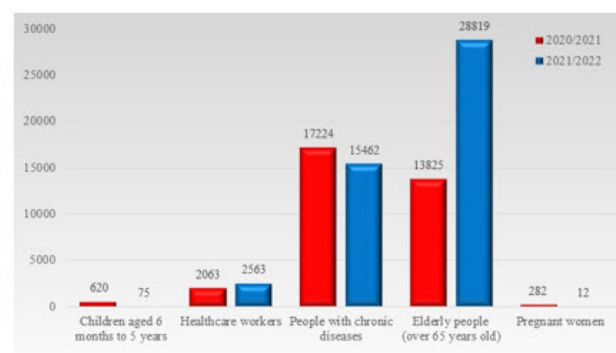


Figure 2. Vaccinated people with influence vaccine according priority groups for the period 2020/2022



DISCUSSION

The changes in influenza vaccination intention and reasons for changes were reported in recent meta-analysis and systematic review conducted on Embase, PubMed, and CNKI including twenty-seven studies with 39,193 participants, reporting rates of influenza vaccination pre-COVID-19 (19/20 season) and post-COVID-19 (20/21 season). All studies reported increased influenza vaccination intention in post-COVID-19 season (Kong, G., at al., 2022).

Our results show that the total number of applied influenza vaccines in the season 2021/2022 was higher by 8.3% compared to last season. This increase happens to be due to the 40.000 free doses of quadrivalent seasonal influenza vaccines for populations at-risk and the additional 20.000 doses of quadrivalent vaccines provided through a donation from PIVI (Partnership for Influenza Vaccine Introduction), procured by the Ministry of Health.

Although 40.000 doses of free quadrivalent influenza vaccines were procured for the season 2020/2021, the overall increase is due to the 100% increase in the applied doses of influenza vaccines in the elderly over 65 years. In contrast, the number of doses administered to children 6 months to 5 years of age, chronically ill, and pregnant women have been significantly reduced.

There is also an increase in the coverage of influenza vaccine among health professionals since the priority groups for influenza vaccination and of course a challenge given by the small coverage are healthcare workers. Their influenza vaccination is recommended, and they participate in it from their funds. Similar to these results, findings from one observational study conducted in an Italian teaching hospital located in Rome, Italy, showed an encouraging vaccination coverage rate among healthcare workers, where physicians reached the highest coverage followed by others healthcare workers and nurses (Ambrosio, FD., et al., 2021). In addition, results from survey conducted on flu and COVID-19 vaccines attitudes, distributed to employees and residents in Pisa university hospital, showed that 70.97% of healthcare workers agreed that being vaccinated against influenza would be more important than the previous years because of COVID-19 emergency (Scardina, G., 2021).

In 2019, a survey was conducted on knowledge, attitudes, and practices (KAP) related to influenza vaccination among health professionals in the Republic of North Macedonia. The results of this study were unfortunately negative, which is why an even greater challenge to increase the coverage in this target group. Through this research, it was concluded that for some health professionals the price of the vaccine is the reason why they are not vaccinated, as well as more difficult logistics because the vaccines are applied only in one Center on the territory of the city of Skopje. Therefore, the MOH made some changes to increase the availability of vaccines. In the season 2019/2020, it included the health workers in free of charge vaccination and included 3 additional vaccination points in Skopje (part of the Health Home Skopje). With these changes, in season 2019/2020, 1.252 health workers were vaccinated with free vaccines, which is an increase of 58% compared to the previous season. Also, the low consumption of vaccines in this target group is affected by the legislation. Unfortunately, it does not allow healthcare professionals (secondary and tertiary level) to be vaccinated in their health facilities by a team from the facility itself. Therefore, the possibility of finding an administrative solution to vaccinate health workers in their home institutions is being considered. Another option is for the Centers to carry out field vaccination, but this method is more difficult due to the staff capacity of the Centers.

The reduction in influenza vaccination coverage is partly due to ambiguities stemming from the influenza immunization campaign, which highlighted the importance of taking a vaccine to reduce the spread of the influenza virus as an additional threat to the presence of COVID-19. Although the influenza vaccine does not protect against COVID-19, influenza vaccination has been part of the public health strategy to mitigate the incidence of diseases caused by respiratory viruses that invade the respiratory system, to protect and preserve the health of healthcare professionals providing care to patients with COVID-19 (Patel Murthy, B., et al. 2021).

The coverage of seasonal influenza vaccination world wide and also in RNM for the season 2020/2021 was unusually low. Preventive public health measures to restrain the spread of the SARS-CoV-2 virus, such as wearing masks, following recommendations to stay at home, closing schools, and physical distance, have helped in reducing the number of flu-like illnesses by 2020 (Fogel, B., et al., 2021).

Online classes were one of the measures in R.N. Macedonia that certainly influenced parents not to vaccinate their children since homeschooling as an alternative lowered the risk of catching the flu (Fogel, B., et al., 2021).

Although there are optimal conditions for sustained vaccination and also there is still a sufficient amount of vaccines to implement the regular immunization calendar, the regular vaccination reports show that there is a reduction in regular vaccinations of children. All of this suggests that the COVID-19 pandemic indirectly led to a reduction in vaccine coverage in the routine vaccination calendar (Santoli, JM., 2020). The effect of the restrictive measures and of course, parents' fear of a potential COVID-19 infection that actually exists, led to a decline in interest and thus a significant reduction in the vaccination coverage of children in 2020 (Patel Murthy, B., et al. 2021).

CONCLUSION

This flu season 2021/2022 also coincided with the ongoing COVID-19 pandemic, so MOH should provide necessary strategic efforts, to ensure a higher vaccination coverage of the population with influenza vaccine on all age groups. The focus should be particularly placed on children aged 6 months to 5 years since there is a serious decline in the number of administered doses of influenza vaccine, as well as those

from the scheduled vaccination calendar because children at this age are not yet eligible to the COVID-19 vaccine (Grohskopf, LA., 2021). The National Immunization Committee recommends routine annual influenza vaccination for all individuals over 6 months of age, in those who have no contraindications.

The CDC, WHO, and ECDC recommend that all healthcare professionals should advise their patients and convince them to take the COVID-19 vaccine at the same time as the routine influenza vaccine (Grohskopf, LA., 2021) to emphasize the importance of influenza vaccination during the COVID-19 pandemic.

WHO and the CDC have increased influenza vaccines availability and conducted targeted communication contact with higher-risk populations, such as patients ≥ 65 years of age, young children, pregnant women, and people with specific chronic health conditions.

Influenza vaccination can reduce the spread of the virus, which will also reduce the number of potential patients with respiratory diseases in the health care system that is already overloaded with patients infected with COVID-19.

REFERENCES

- Ambrosio, FD., Pascucci, D., Nurchis, MC., Di Pumpo, M., Foti, F., Vetrugno, G., et al., 2021. Flu vaccination during COVID-19 pandemic: a lesson from an Italian teaching hospital. *European Journal of Public Health*, 31, Issue Supplement_3. <https://doi.org/10.1093/eurpub/ckab165.482>
- Fogel, B., Schaefer, EW., & Hicks, SD., (2021). Early influenza vaccination rates decline in children during the COVID-19 pandemic. *Vaccine*, 39(31), 4291-4295. <https://doi.org/10.1016/j.vaccine.2021.06.041>.
- Grohskopf, LA., Alyanak, E., Ferdinands, JM., Broder, KR., Blanton, LH., Talbot, HK., et al., 2021. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices, United States, 2021–22 influenza season. *MMWR Morbidity and Mortality Weekly Report-Recommendation and Reports* 70(51), 1–28. <https://doi.org/10.15585/mmwr.rr7005a1>.
- Groves, HE., Piché-Renaud, PP., Peci, A., Farrar, DS., Bucknell, S., Bancej, C., et al. (2021). The impact of the COVID-19 pandemic on influenza, respiratory syncytial virus, and other seasonal respiratory virus circulation in Canada: a population-based study. *The Lancet Regional Health-Americans*, 1, 100015. <https://doi.org/10.1016/j.lana.2021.100015>.
- Kong, G., Lim, NA., Chin, YH., Ng, YPM., Amin, Z., 2022. Effect of COVID-19 Pandemic on Influenza Vaccination Intention: A Meta-Analysis and Systematic Review. *Vaccines* 2022, 10(4), 606. <https://doi.org/10.3390/vaccines10040606>.
- Patel Murthy, B., Zell, E., Kirtland, K., Jones-Jack, N., Harris, L., Sprague, C., et al. (2021). Impact of the COVID-19 pandemic on the administration of selected routine childhood and adolescent vaccinations—10 US jurisdictions, March–September 2020. *MMWR Morbidity and Mortality Weekly Report*, 70(23), 840–845. <http://dx.doi.org/10.15585/mmwr.mm7023a2>.
- Santoli, JM., Lindley, MC., DeSilva, MB., Kharbanda, EO., Daley, MF., Galloway, L., Gee, J., Glover, M., Herring, B., Kang, Y., Lucas, P., Noblit, C., Tropper, J., Vogt, T., Weintraub, E., 2020. Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration—the United States, 2020. *MMWR. Morbidity and mortality weekly report*, 69(19), 591-593. <http://dx.doi.org/10.15585/mmwr.mm6919e2>.
- Scardina, G., Ceccarelli, L., Casigliani, V., Mazzilli, S., Napoletano, M., Padovan, et al., 2021 A. Evaluation of Flu Vaccination Coverage among Healthcare Workers during a 3 Years' Study Period and Attitude towards Influenza and Potential COVID-19 Vaccination in the Context of the Pandemic. *Vaccines* 2021, 9, 769. <https://doi.org/10.3390/vaccines9070769>.
- Schmid, P., Rauber, D., Betsch, C., Lidolt, G., & Denker, M. L. (2017). Barriers of influenza vaccination intention and behaviour—a systematic review of influenza vaccine hesitancy, 2005–2016. *PloS one*, 12(1), e0170550. <https://doi.org/10.1371/journal.pone.0170550>.
- World Health Organization (2021, July). *UNICEF immunization coverage estimates 2020 revision*. https://www.who.int/docs/default-source/immunization/immunization-coverage/wuenic_notes.pdf?sfvrsn=88ff590d_6.

