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HEPATITIS B VACCINATION TRENDS AND REGIONAL DIFFERENCES IN UKRAINE DURING THE WAR

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Hepatitis B incidence remains a serious challenge for Ukraine's healthcare system during the war. Hepatitis B vaccination is an important way to prevent the disease, but the process of immunizing the population may be complicated by military operations. This study assessed national and regional trends in hepatitis B immunization in Ukraine during 2021–2025 and examined the association between vaccination and reported disease incidence. Official vaccination and epidemiological data were analyzed by age group and region. Childhood vaccination accounted for most administered doses but declined from 700,088 doses in 2021 to 565,336 in 2025, whereas adult immunization increased from 11,119 to 34,242 doses. Regional heterogeneity in vaccination volumes increased during the war, while total vaccination volumes in 2025 were lower than in 2021. Associations between regional vaccination and hepatitis B incidence were observed in several wartime years. The findings support maintaining childhood immunization while substantially expanding adult vaccination and strengthening surveillance during wartime.

Key words: hepatitis B, vaccination, immunization, disease incidence, regional variation, armed conflict, Ukraine.

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ТЕНДЕНЦІЇ ВАКЦИНАЦІЇ ПРОТИ ГЕПАТИТУ В ТА РЕГІОНАЛЬНІ ВІДМІННОСТІ В УКРАЇНІ ПІД ЧАС ВІЙНИ

Захворюваність на гепатит В залишається серйозною проблемою для системи охорони здоров'я України під час війни. Вакцинація проти гепатиту В є важливим способом профілактики захворювання, але процес імунізації населення може бути ускладнений через військові дії. У цьому дослідженні оцінено національні та регіональні тенденції імунізації проти гепатиту В в Україні протягом 2021–2025 років та досліджено зв'язок між вакцинацією та зареєстрованою захворюваністю. Офіційні дані щодо вакцинації та епідеміологічні дані були проаналізовані за віковими групами та регіонами. Вакцинація дітей становила більшість введених доз, але знизилася з 700088 доз у 2021 році до 565336 доз у 2025 році, тоді як імунізація дорослих зросла з 11119 до 34242 доз. Регіональна неоднорідність обсягів вакцинації збільшилася під час війни, тоді як загальні обсяги вакцинації у 2025 році були нижчими, ніж у 2021 році. Зв'язок між регіональною вакцинацією та захворюваністю на гепатит В спостерігався протягом кількох воєнних років. Отримані результати підтверджують необхідність збереження дитячої імунізації при одночасному суттєвому розширенні вакцинації дорослих та посиленні епідеміологічного нагляду у воєнний час.

Ключові слова: гепатит В, вакцинація, імунізація, захворюваність, регіональні відмінності, збройний конфлікт, Україна.

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Hepatitis B (HBV) remains one of the most significant vaccine-preventable infections worldwide and is a major cause of liver cirrhosis and hepatocellular carcinoma. According to World Health Organization (WHO) estimates, around 240 million people were living with chronic HBV infection in 2024, and HBV was responsible for the largest proportion of deaths related to viral hepatitis. Since effective vaccines are available, timely and complete vaccination remains the main approach to preventing HBV infection [17].

The prevention of HBV infection is particularly important in Ukraine during the ongoing full-scale war. Military actions increase the frequency of trauma and surgical procedures, potentially increasing the risk of blood exposure and, consequently, HBV transmission. Military personnel, healthcare and rescue workers, and other groups regularly involved in military operations require effective protection against HBV. At the same time, the war has disrupted the

provision of routine immunization services, verification of vaccination status, and continuity of medical follow-up [7, 8]. These challenges are particularly relevant for displaced populations, among whom incomplete vaccination histories and insufficient immunity to vaccine-preventable infections have been reported [15].

According to official data, HBV detection in Ukraine has increased. In 2024, 2,364 cases were reported, compared with 2,150 in 2023 [5]. However, this increase should also be viewed in the context of expanded testing: more than 1.1 million people were tested for HBV in 2024, with a positive screening result identified in 1.2 % of those tested [3]. On the one hand, expanded testing facilitates the detection of previously undiagnosed infections; on the other, it increases the need for confirmatory diagnostics, subsequent medical follow-up, and treatment.

Despite the complexity of the situation, the vaccination program is being actively implemented

in Ukraine. Childhood HBV immunization remains relatively high, with 83.2 % of children vaccinated against the annual target in 2024 [6]. However, serological studies indicate that anti-HBs levels may decline over time following vaccination. Among 1,322 Ukrainian children and adolescents examined in Poland, a protective anti-HBs level of ≥ 10 IU/L was detected in 64.9 %, and in less than half of adolescents aged 15–18 years [13].

The situation among adults appears to be more concerning. In a study of Ukrainian refugees in Germany, an insufficient serological response to HBV was identified in approximately 74 % of those examined [1]. The mass displacement of Ukrainians following the onset of the full-scale war has also created an additional challenge for healthcare systems in European countries. In Poland, the proportion of imported cases of chronic HBV infection and infection of undetermined stage increased from 7 % in 2023 to 9.9 % in 2024, with the majority associated with Ukrainian refugees [12].

Currently, limited data are available on trends in HBV vaccination among the Ukrainian population and on the possible impact of vaccination on HBV incidence during the war. To address these gaps, we analyzed official data from the National Health Service of Ukraine for 2021–2025 to assess trends in HBV vaccination among children and adults. We also examined regional differences in vaccination and evaluated the relationship between HBV vaccination and disease incidence during the war.

The purpose of the study was to analyze regional trends in HBV vaccination and among Ukrainian population during the war and assess relationship between HBV vaccination and disease incidence during the war.

Materials and methods. This study was conducted as a descriptive and analytical assessment of HBV immunization in Ukraine. The number of HBV vaccine doses administered to the Ukrainian population was analyzed for 2021–2025. Vaccination data were obtained from the official website of the National Health Service of Ukraine [11].

The number of HBV vaccine doses administered was assessed for Ukraine as a whole and separately by region, excluding the temporarily occupied territories of Crimea. The Kyiv region and the city of Kyiv were combined into a single administrative unit for analysis. Data for the Luhansk region were also limited due to temporally occupation, so they were used to visualize regional vaccination distribution and for estimates of overall immunization across the country, but were not taken into account in other statistical calculations. Data on HBV vaccination were available only for the civilian population; vaccination data for military personnel were not available and therefore could not be included in the analysis.

Data were analyzed separately for two population groups: children aged 0–17 years and adults aged ≥ 18 years, as well as for the entire population. The complete HBV vaccination series consists of three doses; however, because the

available official data did not allow individual vaccination courses to be identified, the analysis was based on the total number of vaccine doses administered. HBV has been included in the Ukrainian national immunization schedule since 2000 and is mandatory for children, whereas vaccination of adults is recommended for specified population groups, including military personnel, healthcare workers, and others [9].

To calculate the number of HBV vaccine doses administered per 100,000 population, regional population data were obtained from the official website of the State Statistics Service of Ukraine [14].

Descriptive statistics were calculated for the distribution of regional immunization rates for each year, including the mean, median, standard deviation (SD), interquartile range (IQR), coefficient of variation (CV), and IQR-to-median ratio.

To assess differences in the distribution of administered vaccine doses across years, the Friedman test was applied to regional raw numbers of administered doses, with regions treated as repeated observations across the five years. Pairwise Wilcoxon signed-rank tests were subsequently performed to compare each wartime year (2022–2025) with the 2021 pre-war baseline. In addition, for each region and each year from 2022 to 2025, the percentage change in the number of administered doses relative to the corresponding 2021 value was calculated. The median, first quartile (Q1), and third quartile (Q3) of these regional percentage changes were then calculated for each year.

To assess the association between HBV immunization and morbidity, regional data on the numbers of acute and chronic HBV cases were obtained from the Public Health Center of the Ministry of Health of Ukraine ([Center for Public Health of the Ministry of Health of Ukraine. Incidence of Infectious Diseases Among the Population of Ukraine.[2]. Acute and chronic HBV cases were combined to obtain the overall regional HBV incidence for each year. Spearman rank correlation analysis was performed separately for each year to assess the association between the regional number of HBV vaccine doses administered per 100,000 population and the corresponding regional HBV incidence per 100,000 population. A lagged correlation analysis was additionally performed by comparing immunization rates in year t with HBV incidence rates in the subsequent year ($t+1$).

All statistical analyses and data visualizations were performed using Microsoft Excel and the R statistical programming environment. Administrative boundary shapefiles for Ukraine were obtained from the Global Administrative Areas (GADM) database and processed for visualization of regional analytical results.

Results of the study. Our analysis focused on temporal and regional changes in hepatitis B virus (HBV) immunization in Ukraine during 2021–2025, with particular attention to differences between children and adults. We assessed the number and population-adjusted rates of administered vaccine doses, regional variability in immunization, and

changes relative to the pre-war 2021 baseline. In addition, the relationship between regional HBV immunization rates and reported HBV incidence was examined to identify potential epidemiological patterns during the wartime period. Thus, Figure 1 presents the annual number of HBV immunization doses administered in Ukraine according to age group during 2021–2025.

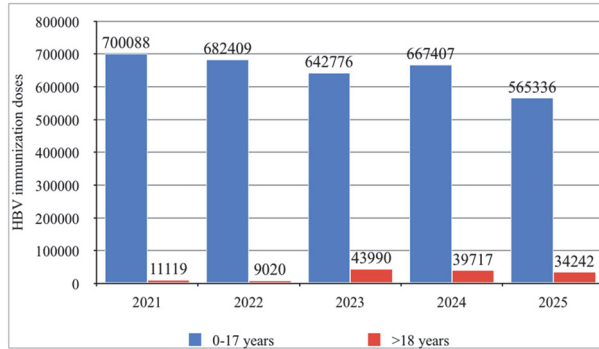


Fig. 1. Annual number of HBV immunization doses administered in Ukraine among children (0–17 years) and adults (>18 years), (absolute quantity).

Children aged 0–17 years accounted for the vast majority of administered doses throughout the study period. The number of doses in this group decreased from 700,088 in 2021 to 642,776 in 2023, increased slightly to 667,407 in 2024, and then declined to 565,336 in 2025. Thus, number of doses used for childhood immunization during wartime period was lower than the pre-war 2021 level. In contrast, immunization among persons aged >18 years increased markedly during the wartime period. Following a decrease from 11,119 doses in 2021 to 9,020 in 2022, the number increased to 43,990 in 2023 and subsequently declined to 34,242 in 2025, remaining more than three times higher than the 2021 baseline. The divergent trajectories of the two age groups indicate a substantial shift in the age distribution of HBV immunization during the wartime period, with the increase in adult immunization and the decline in childhood vaccination. Figure 2 shows the corresponding regional distribution of administered doses.

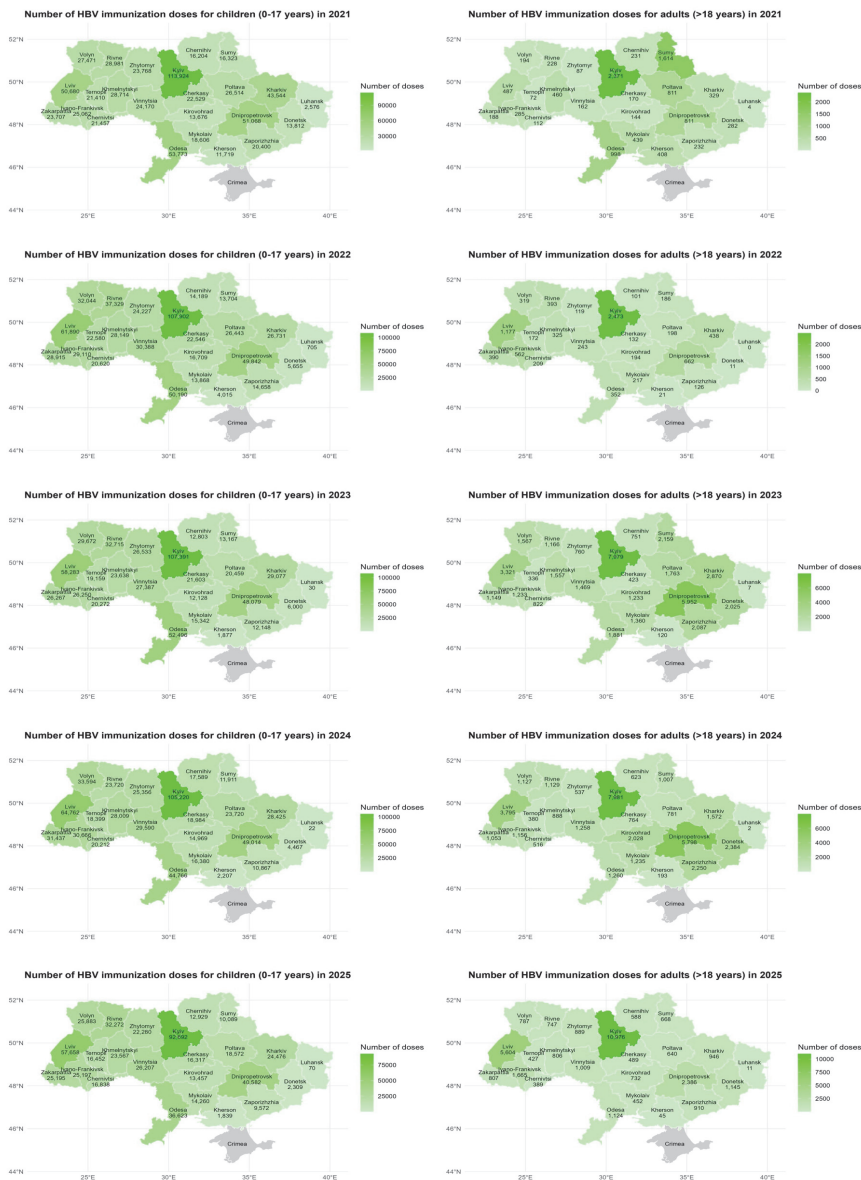


Fig. 2. Regional distribution of HBV immunization doses during 2021–2025 administrated among children (0–17 years) and adults (>18 years).

Childhood immunization demonstrated pronounced geographic heterogeneity, with the highest absolute numbers generally observed in Kyiv, Lviv, Odesa, and Dnipropetrovsk, whereas the lowest numbers occurred in Luhansk, Kherson, and Donetsk. During 2022–2025, substantial reductions in childhood doses were particularly evident in the eastern and southern regions most affected by the war. In contrast, several western regions, including Lviv, Rivne, Vinnytsia, Zakarpattia, Ivano-Frankivsk, and Volyn maintained or increased their childhood immunization volumes relative to 2021.

Adult immunization showed a different spatial pattern. In 2022, the number of administered vaccine doses decreased in some regions, mainly northern, eastern and southern regions affected by the war, but increased in western regions. During 2023–2025, the number of administered vaccine doses increased in most regions compared to 2021, with the increase occurring largely regardless of geographical location. At the same time, persistent decline patterns of adult immunization during 2023–2025 were observed in Luhansk, Kherson and Sumy.

The regional maps further demonstrate that changes in the total number of doses were driven by two contrasting processes: substantial reductions in childhood immunization in war-affected eastern and southern regions and a simultaneous expansion of adult immunization in most regions. Because childhood doses constituted the overwhelming majority of all administered doses, the national trajectory of the total population largely followed the pattern observed in children.

Following the regional and age-specific patterns in the number of administered doses, the annual distribution of HBV immunization was further evaluated after adjustment for population size (Table 1). Across Ukraine, the mean number of administered doses per 100,000 population remained relatively stable during 2021–2024, ranging from 1820.90 to 1880.17 doses, but decreased to 1604.84 doses per 100,000 in 2025. A similar pattern was observed for the median, which varied between 1914.16 and 2038.76 doses per 100,000 during 2021–2024 and declined to 1612.89 in 2025.

Table 1

Descriptive statistics of regional HBV immunization rates per 100,000 population in Ukraine, 2021–2025

Year	Mean	SD	CV, %	Median	IQR	IQR/Median ratio
2021	1880.17	518.57	27.58	1920.09	540.12	0.28
2022	1878.94	772.19	41.10	2038.76	911.75	0.45
2023	1820.90	733.30	40.27	1914.16	832.50	0.43
2024	1863.32	759.14	40.74	1915.49	686.21	0.36
2025	1604.84	705.82	43.98	1612.89	621.09	0.39

Differences in the number of HBV vaccine doses per 100,000 population between regions over the period 2021–2025 are shown in Figure 3 and Table 1. The variability among regions increased

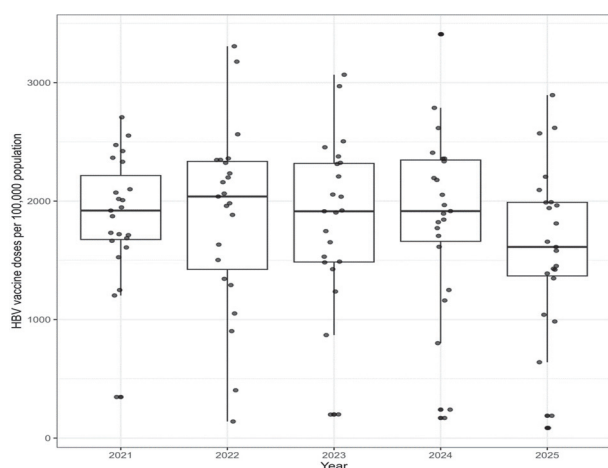


Fig. 3. Regional variability in the number of HBV vaccine doses per 100,000 population during the 2021–2025 period.

during the wartime period compared with the 2021 baseline. The coefficient of variation (CV) increased from 27.58 % in 2021 to approximately 40–44 % in 2022–2025, while the IQR-to-median ratio increased from 0.28 to 0.36–0.45. This indicates greater regional heterogeneity in immunization intensity

after the onset of the full-scale war, with the highest IQR-to-median ratio observed in 2022 and the highest coefficient of variation in 2025.

For formal comparison of annual distributions, the Friedman test was applied to the regional raw numbers of administered doses, treating regions as repeated observations across years. The test indicated a significant overall difference among the five years ($p < 0.001$). Subsequent pairwise Wilcoxon signed-rank tests comparing each wartime year with the 2021 pre-war baseline showed no significant differences for 2022 ($p=0.55$), 2023 ($p=0.39$), or 2024 ($p=0.49$). In contrast, the distribution of regional doses in 2025 differed significantly from that in 2021 ($p < 0.001$). The median decrease of doses across regions in 2025 relative to 2021 was 17.75 %, while the first and third quartiles of the regional percentage changes were -30.39 % and -0.10 %, respectively. This distribution indicates substantial heterogeneity among regions: approximately one quarter of regions experienced reductions of about 30 % or more, whereas the upper quartile showed little change relative to the 2021 baseline. Thus, HBV immunization remained broadly comparable with the pre-war level during 2022–2024, whereas a substantial and statistically significant reduction became evident in 2025.

Table 2

Regional changes in HBV immunization relative to the 2021 baseline, 2022–2025

Year	Median percentage change from 2021, %	Q1 of percentage change, %	Q3 of percentage change, %	p value
2022	-2.50	-17.81	17.02	0.55
2023	-2.96	-16.04	10.67	0.39
2024	-3.90	-15.45	16.90	0.49
2025	-17.75	-30.39	-0.10	0.00

Note. Percentage changes represent changes in regional HBV immunization relative to 2021. Q1 and Q3 represent the first and third quartiles of the regional percentage-change distribution. P values were obtained using paired Wilcoxon signed-rank tests comparing each year with 2021.

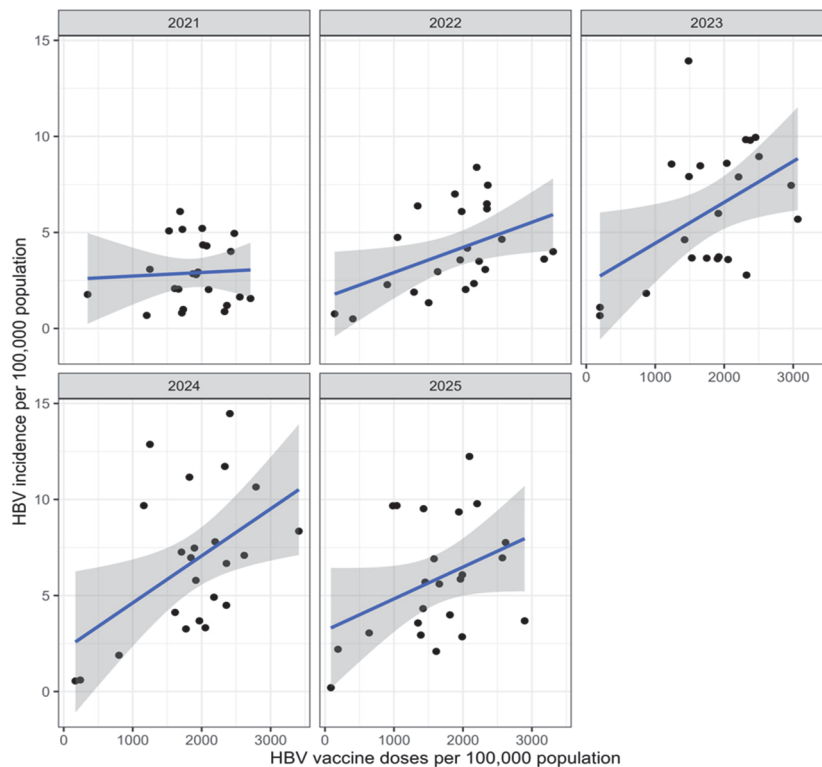


Fig. 4. Correlation analysis between regional HBV immunization rates (per 100,000 population) and HBV incidence rates (per 100,000 population).

Results of correlation analysis between regional HBV immunization rates (per 100,000 population) and HBV incidence rates (per 100,000 population) are presented in Figure 4. In 2021, no significant correlation was observed between vaccine administration and HBV incidence (Spearman's $\rho = -0.024$, $p = 0.914$). In contrast, significant positive correlations were identified in 2022 ($\rho = 0.491$, $p = 0.017$) and 2024 ($\rho = 0.427$, $p = 0.042$), while the associations in 2023 ($\rho = 0.401$, $p = 0.058$) and 2025 ($\rho = 0.369$, $p = 0.084$) were also positive but did not reach statistical significance.

The lagged correlation analysis, assessing the association between regional immunization rates in a given year and HBV incidence rates in the subsequent year, similarly showed positive correlations.

The lagged correlation was statistically significant for 2022 immunization versus 2023 incidence ($\rho = 0.422$, $p = 0.045$) and for 2024 immunization versus 2025 incidence ($\rho = 0.415$, $p = 0.049$), whereas the associations for 2021–2022 ($\rho = 0.368$, $p = 0.084$) and 2023–2024 ($\rho = 0.404$, $p = 0.056$) were not statistically significant. Overall, higher regional immunization rates were unexpectedly associated with higher, rather than lower, HBV incidence rates, both within several individual years and with a one-year lag.

Thus, HBV immunization remained broadly comparable with the pre-war level during 2022–2024, whereas a substantial and statistically significant reduction became evident in 2025, together with increased regional variability.

Discussion. Our study results showed that routine childhood vaccination remains the cornerstone of HBV prevention in Ukraine, although wartime has somewhat disrupted its implementation. The annual number of pediatric doses administered decreased significantly from 700,088 in 2021 to 565,336 in 2025. A statistically significant decrease in regional vaccination volumes (by 17.75 %, $p <$

0.001) occurred only in 2025, while levels in 2022–2024 fluctuated without significant deviations from the pre-war 2021 baseline.

This decline was accompanied by sharp regional polarization, as evidenced by an increase in the coefficient of variation (from 27.58 % in 2021 to 43.98 % in 2025) and the ratio of the interquartile range to the median. This geographic disparity is due to a significant decrease in child vaccination rates in the eastern and southern regions directly affected by active hostilities (such as Luhansk, Donetsk, and Kherson), in contrast to the western regions, which managed to maintain or even increase vaccination rates. Although official data for 2024 indicate a relatively high coverage of the annual target, real humoral protection may be significantly lower. A prospective study of Ukrainian refugee children in Poland showed that although 83.2 % were reported as vaccinated, only 64.9 % had a protective antibody titer to HBs antigen ≥ 10 IU/L, with protection dropping below 50 % in adolescents aged 15–18 years [13]. Although immunological memory often persists despite low antibody levels, this rapid decline

in humoral immunity during adolescence, coinciding with the onset of sexual activity and higher risk of infection, highlights the urgent need for targeted screening programs and supplementary immunization.

While childhood immunization remains adequate, although facing growing regional challenges, the situation among the adult population shows a somewhat different dynamic. In relative terms, adult (≥ 18 years) immunization has experienced a remarkable threefold increase, increasing from 11,119 doses in 2021 to a peak of 43,990 in 2023, and then stabilizing at 34,242 doses in 2025. However, despite this relative increase, the absolute volume of adult vaccination remains low and completely insufficient compared to the real needs of the population. State-funded free HBV vaccination in Ukraine is systematically provided to newborns and children within the framework of the National Immunization Program; adults must purchase vaccines at their own expense or meet narrow epidemiological or professional indications (military personnel, rescuers, medical workers, and others) [4].

Consequently, the vast majority of the adult civil population remains fully susceptible to HBV. This vulnerability is underscored by serological data from Ukrainian migrants in Germany where 74 % of those examined, mostly adults, lacked sufficient protective antibodies [1]. Therefore, the observed increase to only 30,000–44,000 adult vaccine doses per year – this is a tiny number that cannot provide herd immunity to millions of susceptible adult residents of Ukraine [11].

Beyond the baseline deficits in adult vaccination coverage, our analysis revealed another unexpected trend in how immunization dynamics are associated with reported infection rates. A key finding was a significant positive correlation between regional immunization rates and HBV incidence, observed both synchronously in 2022 and 2024, and with a one-year lag in the 2022–2023 and 2024–2025 periods. Although epidemiological theory suggests that higher immunization rates should correlate with lower incidence, this positive association reflects the diagnostic realities of wartime. First, Ukraine has seen a significant expansion of HBV screening: in 2024 alone, over 1.1 million people were tested (with a positivity rate of 1.2 %). Second, mandatory screening and enhanced medical surveillance in the Ukrainian Armed Forces have successfully identified numerous previously undiagnosed cases of latent chronic HBV. This has led to an increase in the number of reported cases, peaking in 2024 at 4.03 cases per 100,000 population, compared to the pre-war baseline of 3.57–3.71 [10]. Regions with intensive screening, large military and civilian hospitals, and high concentrations of internally displaced persons naturally recorded both higher HBV incidence rates and higher vaccination rates among high-risk groups (healthcare, rescue and military personnel). Thus, the positive correlation reflects a “detection effect” and the targeted allocation of vaccination resources to epidemic

hotspots, rather than a failure of immunization itself. However, the lack of an impact of vaccination on HBV incidence primarily indicates gaps in the vaccination of adults born before 2000 who were not vaccinated as children. These data highlight the urgent need to expand vaccination among the adult population as a key component of preventive epidemiological surveillance programs.

The consequences of these internal epidemiological shifts extend far beyond national borders. The displacement of millions of Ukrainians (mostly women and children) across Europe has resulted in a significant epidemiological and economic burden on the healthcare systems of receiving countries. A striking example can be seen in Poland, where the proportion of imported cases of chronic HBV or HBV at an undetermined stage increased from 7 % in 2023 to 9.9 % in 2024, with the vast majority of them associated with arrivals from Ukraine [12]. This highlights how low adult immunization rates in Ukraine and wartime epidemiological shifts create cross-border public health challenges, forcing European countries to rapidly implement targeted screening and supplementary vaccination programs for displaced people.

Taken together, these data demonstrate that the traditional child-focused vaccination model is insufficient in wartime settings and should be reconsidered to include widespread immunization of adults. The key population groups currently at risk are adults, particularly military personnel and mobilized civilians. Since mobilization predominantly affects men aged 25–60 years, born long before the introduction of universal newborn HBV vaccination in 2000–2001, they are highly susceptible to the virus. Active combat, high trauma rates, emergency surgeries or blood transfusions exponentially increase the risk of parenteral transmission. Frontline healthcare workers, rescue workers, and displaced populations face similarly extreme risks. International benchmarks point a clear path forward: in 2022, the US Advisory Committee on Immunization Practices (ACIP) updated its guidelines to recommend universal HBV vaccination for all adults aged 19–59 years, eliminating the need for specific risk factor screening [16]. Optimizing the universal adult vaccination strategy in Ukraine – with priority given to mobilized groups, healthcare workers, and emergency services personnel – is an urgent, vital task under martial law. This will not only protect people in high-risk areas, but also significantly reduce the national burden of chronic hepatitis B and its complications.

An important limitation of this study is that we calculated the HBV vaccination rate (per 100,000 population) from 2022 to 2025 based on official population data as of early 2022, which are only available on the website of the National Statistics Service of Ukraine. Data on HBV incidence (per 100,000 population), provided by the Public Health Center of the Ministry of Health of Ukraine, were also calculated accordingly. The war in Ukraine has led to significant demographic changes and large-scale

population migration, resulting in an actual decline in the permanent population in regions close to the front lines and population growth in western regions. Despite this limitation, the data indicate a downward trend in the total number of vaccine doses administered during the war and critically low vaccination coverage among adult civilians, with no

clear evidence of an association between vaccination rates and HBV incidence. The findings provide an overview of changes in HBV vaccination during the war in Ukraine, highlighting major gaps in adult immunization and the need to strengthen active vaccination of the adult population during ongoing hostilities.

Conclusion

The results of the study demonstrate a decrease in the annual number of pediatric doses and critically low HBV vaccination for adult civilians during the war time in Ukraine. Regional variability in the HBV vaccination became significant and regional differences increased by 2025 with the greatest reductions in childhood vaccination in the eastern and southern regions most affected by the war, while several western regions maintained or increased vaccination levels. The observed relationship between HBV vaccination and incidence HBV infection likely reflects the complex effects of wartime population displacement, expanded screening, and differences in healthcare access rather than a direct effect of vaccination on incidence. These findings highlight the need to maintain childhood immunization, widespread immunization of adults, and strengthen HBV surveillance during and after the war.

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