



## Research paper

### Current international experience in drafting and implementing safety measures in vaccination delivery

**Abdyrakman Eshiev<sup>1</sup>, Ledi Necaj<sup>2</sup>, Aitbek Aaliev<sup>3</sup>, Mariela Geneva-Popova<sup>4</sup>,  
Stanislava Popova-Belova<sup>4</sup>**

<sup>1</sup> Department of Surgical Dentistry and Pediatric Surgical Dentistry, Osh State University, Kyrgyz Republic

<sup>2</sup> Department of Clinical Subjects and General Nursing, Nursing in Internal Disease, Pediatrics, University of Medicine, Tirana, Albania

<sup>3</sup> Department of Morphological Disciplines, S. Tentishev Asian Medical Institute, Kant, Kyrgyz Republic

<sup>4</sup> Department of Propedeutics of Internal Diseases, Medical University of Plovdiv, Bulgaria

#### ARTICLE INFO

##### Article history

Received: November 22, 2024

Accepted: January 10, 2025

Available online: August 27, 2025

##### Keywords

Adverse effects

Vaccination

COVID-19

Population immunization

Spontaneous reporting

Passive surveillance

##### Doi

<https://doi.org/10.29089/paom/199983>

##### User license

This work is licensed under a  
Creative Commons Attribution –  
NonCommercial – NoDerivatives  
4.0 International License.



#### ABSTRACT

**Introduction:** Vaccination remains a cornerstone in combating infectious diseases, and understanding the global strategies and disparities in vaccination delivery is critical for improving public health outcomes.

**Aim:** This study focused on analysing the approaches and best practices of global health organisations in designing and implementing safe vaccination of the population to prevent infectious diseases, reduce their prevalence, and minimize associated adverse events.

**Material and methods:** The scientific work was based on a comparison of official data on vaccination against Covid-19 in the USA, Bulgaria, Italy, and Europe.

**Results and discussion:** By the end of 2021, Italy and the USA achieved high vaccination rates, with over 80% of Italy's population and 65% of the US population receiving at least one dose. In contrast, Bulgaria, Romania, and Croatia had significantly lower rates, with revaccination coverage averaging below 25%. Strategies for combating diseases like polio, measles, and yellow fever were also found to be effective and safe, despite regional disparities in implementation.

**Conclusions:** The study highlights substantial disparities in vaccination rates between countries, emphasizing the need for targeted interventions in regions with low coverage. While international health organizations have ensured the safety and effectiveness of vaccination strategies, addressing these gaps is essential for improving global health equity and reducing the burden of infectious diseases.

## 1. INTRODUCTION

COVID-19 vaccination is essential owing to the persistent epidemic and the emergence of SARS-CoV-2 variants. Vaccination lowers mortality, morbidity, and severe cases, alleviating healthcare expenses and decreasing hospitalisations, especially among at-risk populations. Booster dosages are essential for maintaining immunity, reducing transmission, and preventing mutations that may result in more severe epidemics. Notwithstanding advancements, disparities in vaccination accessibility endure worldwide, highlighting the necessity for ongoing efforts to guarantee equitable distribution and counteract misinformation. As of early 2024, around 70.6% of the world population has gotten at least one COVID-19 vaccination dosage. Nevertheless, significant discrepancies persist: high-income countries frequently surpass 80% coverage, but certain low-income nations report figures as low as 32.7%.<sup>1</sup> The disparities arise from logistical challenges, vaccination reluctance driven by disinformation, and inadequate healthcare infrastructure. The research conducted by Ioannidis et al.<sup>2</sup> highlights the essential function of vaccination in averting fatalities and enhancing health outcomes throughout the epidemic, suggesting that millions of lives have been preserved thanks to worldwide immunisation initiatives.

The COVID-19 vaccination has substantially impacted public health by markedly decreasing morbidity and death linked to the virus. The analysis by Ioannidis et al.<sup>2</sup> indicates that immunisations have prevented around 2.5 million fatalities worldwide from December 2021 to October 2024, especially for elderly persons who are at greater risk for severe illness. This impact is crucial as healthcare systems persist in addressing the long-term consequences of the pandemic, encompassing the burden of lengthy COVID and the necessity for sustained healthcare resources. This study's findings emphasise that successful vaccination efforts not only preserve lives but also reduce the burden on healthcare systems overwhelmed by the epidemic. The economic advantages of vaccination encompass not just individual health results but also wider societal effects. Vaccination initiatives enhance worker stability by decreasing illness-related absenteeism and facilitating the safer reopening of enterprises and educational institutions. Countries with elevated immunisation rates have often seen more rapid economic recoveries than those with diminished rates.

A study by Rangelova et al.<sup>3</sup> conducted in Bulgaria evaluated adverse responses to COVID-19 vaccinations to enhance public confidence. Out of the 761 immunised patients, 469 received an mRNA vaccine, while 292 received an adenovirus vector vaccine. More than 89% of mRNA recipients and 93.8% of adenovirus recipients experienced at least one mild to severe adverse response, predominantly tiredness, headache, and myalgia, which subsided within days without necessitating medical intervention. A safety evaluation of a third mRNA vaccination dosage in the USA included 47,999 subjects.<sup>4</sup> It exhibited few severe adverse effects (0.01% for pericarditis), and no instances of anaphylax-

is were reported. Mild adverse effects were more prevalent with the third dosage compared to the second, encompassing tiredness, lymphadenopathy, headache, nausea, and myalgia. The third dose was considered safe, with significant adverse effects similar to those following the two doses.

Bonanni et al.<sup>5</sup> reviewed current data on the single administration of several vaccines in children. European countries and the USA widely use booster combined vaccines against tetanus, diphtheria, and pertussis, as well as vaccines against meningococcus and human papillomavirus in adolescents and adults. Immunisation for influenza, pneumococcal infections, and herpes zoster is advised for vulnerable populations and the elderly.<sup>6</sup> Adult vaccination rates are lower than those of children, despite the necessity of repeated doses for travellers. Simultaneous administration of vaccinations in both groups is safe and effective. Consequently, comprehensive vaccination initiatives for adolescents, adults, and the elderly can improve immunisation rates and diminish infectious illnesses within communities.

The current research is innovative in its examination of worldwide differences in COVID-19 vaccine coverage, specifically addressing the obstacles encountered by low-income nations and areas with lower immunisation rates, including Eastern Europe. While existing studies have highlighted the effectiveness and safety of COVID-19 vaccines, this research addresses the geographic and socio-economic factors influencing vaccine access, the role of misinformation in vaccine hesitancy, and the long-term public health and economic benefits of widespread vaccination. It provides fresh insights into the safety of booster doses and the efficacy of combination vaccination tactics to enhance coverage, particularly for at-risk populations, offering a thorough comprehension of the obstacles and advantages associated with attaining global immunisation objectives.

## 2. AIM

The aim of this study was to investigate the strategies and experiences of international medical organisations in the safe implementation of vaccination of the population against COVID-19 in the USA, Bulgaria, Italy, and European countries. Objectives: to collect statistical data and compare the experience of other countries to better understand the vaccination coverage in the population.

## 3. MATERIAL AND METHODS

The study was based on a comparison of official data in the design and implementation of vaccination measures against COVID-19 patients in the USA, Bulgaria, Italy and European countries. Data on general population vaccination against COVID-19, as well as elderly and at-risk groups in these countries, were taken into account. In addition, evidence-based information posted in reliable databases was searched. The practices of international medical organiza-

tions in the safe organization and delivery of population immunization against COVID-19 and other infectious diseases were reviewed.

The literature search was conducted for the period from 2020 to 2024. Publications were searched using keywords such as: vaccination safety, vaccination Bulgaria, vaccination implementation programmes, patient immunisation strategies, side effects, World Health Organization (WHO), vaccination strategies, population immunization, vaccination of at-risk groups, vaccination of patients with chronic diseases, immunization of children, immunization of premature babies, vaccination of pregnant women, vaccination of the elderly, measles, rubella, mumps, tuberculosis, Covid-19, yellow fever, tetanus, rabies, human papillomavirus, polio, diphtheria, herpes zoster, influenza, pneumococcal infection, vaccine safety and effectiveness, immunization adherence, Vaccine Adverse Events Reporting System, Centres for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), European Medicines Agency. The databases examined were PubMed, Scopus, Google Scholar, and ScienceDirect. The inclusion requirements required that articles be in English, readily accessible for reading, and relevant to the specified keywords; 61 of the 96 studies met the inclusion criteria.

Recent recommendations from the WHO and the United Nations International Children's Emergency Fund (UNICEF)<sup>7</sup> were reviewed. Systems that monitor the quality, side effects, efficacy, and safety of vaccines, such as the Vaccine Adverse Events Reporting System,<sup>8</sup> CDC,<sup>9</sup> FDA,<sup>10</sup> and European Medicines Agency (EMA),<sup>11</sup> were described. Population vaccination implementation strategies were evaluated, including the use of new-generation vaccines, training of health care personnel, raising public awareness of immunisation, and the use of reminder systems. The reasons why patients and parents of children do not vaccinate their children against avoidable infections were examined. Models for vaccinating animals against rabies, which can be life-threatening to humans, were evaluated. Vaccine safety in high-risk, vulnerable populations, infants and pregnant women, and frequent and extremely rare reactions to immunisation were studied.

## 4. RESULTS

### 4.1. Vaccination against COVID-19 in the USA, Bulgaria, Italy, Europe

WHO<sup>12</sup> established a strategy to attain worldwide COVID-19 vaccination, with the objectives of minimising mortality, alleviating health system loads, and reinstating socioeconomic activity. Despite certain achievements in vaccination objectives, considerable disparities in vaccine distribution remained in 2021, especially impacting vulnerable people in low-income nations. Estimates suggest that about 600,000 fatalities may have been averted if all countries had 40% vaccination coverage by the conclusion of 2021. In 2022, the supply of vaccines escalated, resulting in the administration

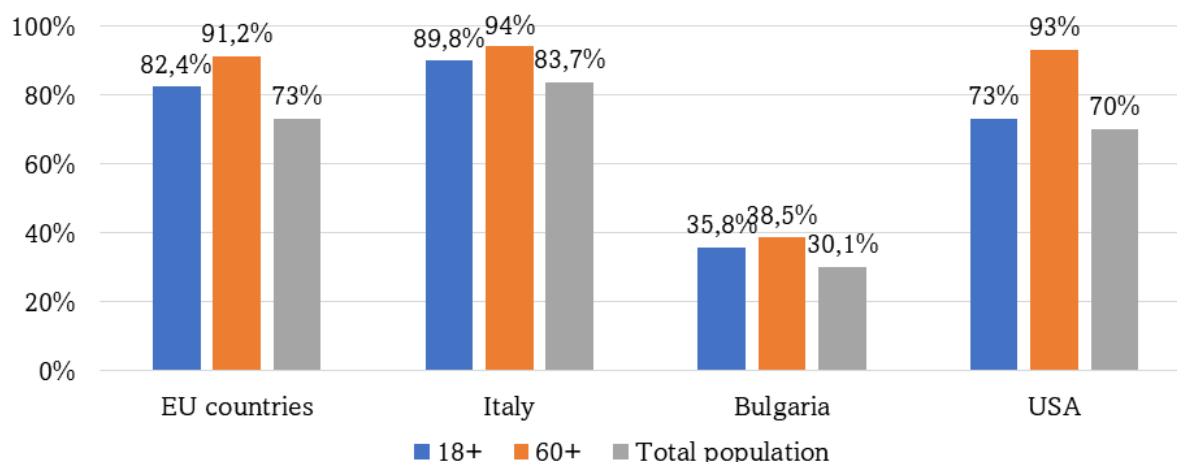
of approximately 12 billion doses worldwide, including 60% of the WHO member countries. Booster dosages become essential for protection against emerging variations. Vaccination rates among at-risk populations were insufficient, with only 25% of elderly adults completely immunised in low-income areas. This caused concerns over potential overlaps of COVID-19 waves with other respiratory disorders, compromising the capacity of health systems. The WHO underscored the significance of comprehensive vaccination protocols, including booster doses, to bolster protection against prevalent virus strains.

The U.S. response to COVID-19 vaccination has been focused on ensuring broad access and boosting public confidence. Key agencies, including the White House,<sup>13</sup> CDC, and FDA, implemented measures to expedite vaccine distribution. The FDA authorized COVID-19 vaccines for emergency use in late 2020 and played a crucial role in ensuring their safety, with vaccines from Pfizer and Moderna receiving approval.<sup>14</sup> By early 2022, over 215 million Americans were vaccinated, with high coverage among at-risk groups like the elderly and healthcare workers.<sup>15,16</sup> However, vaccination coverage remained lower in vulnerable communities with limited access to health services, requiring additional efforts by the government to ensure equal access to vaccination.

Bulgaria's COVID-19 immunisation plan prioritised vulnerable populations and the elderly, facilitating vaccines via national programs and accessible centres. By 2023, over 30% of the population was completely vaccinated, with more than 65% of persons aged 65 and older having received the vaccination, underscoring initiatives to safeguard vulnerable residents.<sup>17</sup> The government enhanced immunisation accessibility via health institutions and mobile units in isolated regions to augment coverage. Nonetheless, the first stages of the program were criticised for inadequately prioritising these demographics, resulting in elevated death rates among the elderly during the initial deployment from December 2020 to May 2021.

The vaccination strategy against COVID-19 in Italy intended a phased distribution of vaccines to different population groups, with the aim of achieving coverage of 80% of the population by September 2021.<sup>19</sup> The main risk groups that were prioritised for vaccination included people over 80 years of age; people with chronic diseases; people aged 70 to 79 years and 60 to 69 years; health and social service workers, and educational and law enforcement personnel. By September 2021, about 80% of the Italian population had received at least one dose of the vaccine.<sup>20</sup> Among those over 80 years of age and those with comorbidities, vaccination coverage was almost 100%.<sup>21</sup> Figure 1 illustrates the primary COVID-19 vaccination coverage across the European Union, Italy, Bulgaria, and the USA.<sup>22,23</sup>

Figure 1 illustrates significant differences in COVID-19 vaccination rates among several areas, indicating both achievements and obstacles in attaining comprehensive immunisation. The European Union and Italy have robust immunisation rates, indicating effective outreach to at-risk populations, particularly the elderly, who are more suscepti-



**Figure 1. Primary vaccination course coverage against COVID-19 in EU Countries, Italy, Bulgaria, and the USA.**

ble to severe COVID-19 consequences. The elevated vaccination rates indicate successful public health initiatives, strong healthcare systems, and considerable public confidence in vaccinations. Conversely, Bulgaria's vaccination rates are far lower. Bulgaria encounters considerable obstacles to attaining elevated immunisation rates, such as vaccine reluctance, disinformation, and even inadequate healthcare infrastructure. The disparity in vaccination rates between the general populace and older folks suggests that, although certain at-risk populations may have received priority, extensive outreach initiatives are necessary to encompass the whole community. The U.S. has a high vaccination rate among older persons (93%), although there exists a significant disparity in overall immunisation rates, with just 70% of the whole population immunised. Although prioritising vulnerable individuals, vaccination accessibility or acceptability among younger, less at-risk populations may remain problematic. It underscores the necessity for ongoing initiatives to enhance immunisation rates throughout all age demographics, especially with the emergence of new virus types.

As of early 2023, around 331 million individuals in Europe have received their main COVID-19 immunisation, representing 73% of the population.<sup>24</sup> 54.7% obtained their first booster, while just 14.1% and 1.7% finalised the second and third boosters, respectively. In adults, primary vaccination coverage attained 82.4%, with Portugal, Spain, and Denmark surpassing 85% owing to robust promotion for the aged and vulnerable populations, markedly decreasing mortality and hospitalisations. Conversely, Eastern European nations like Bulgaria and Romania had poor rates, with fewer than 25% of individuals obtaining their first booster, due to vaccination scepticism and restricted healthcare access. Variations in vaccination attitudes among nations indicate significant consequences for public health policies (Table 1).<sup>25,26</sup>

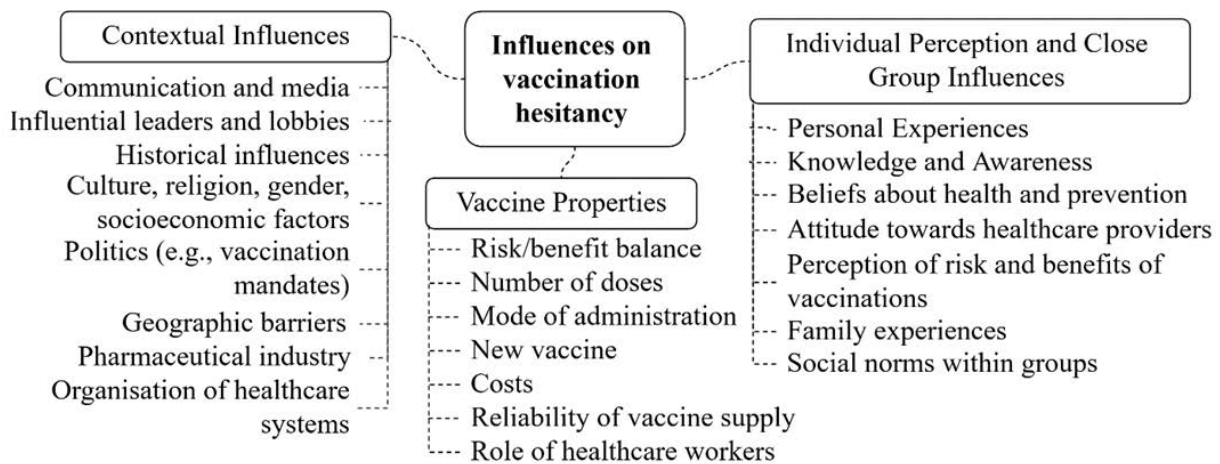
Bulgaria (51% hesitancy) and Latvia (45% hesitancy) demonstrate considerable scepticism towards vaccines, obstructing initiatives to attain herd immunity and manage infectious illnesses. This hesitance arises from historical scepticism towards government health initiatives, disinformation, and cultural influences that impact views on

**Table 1. Vaccine hesitancy and acceptance.**

Country	Vaccine hesitancy (%)	Vaccine acceptance (%)
Bulgaria	51	49
Latvia	45	55
Slovenia	40	60
Spain	23	77
Malta	15	85

vaccination safety. Nations exhibiting lower reluctance percentages, such as Malta (15%) and Spain (23%), have a more positive disposition towards vaccination, potentially improving immunisation rates and health outcomes, especially amid persistent public health crises like COVID-19. The pronounced disparities in vaccination hesitancy underscore the want for customised communication tactics; nations exhibiting significant resistance may necessitate focused educational initiatives to tackle particular apprehensions and foster confidence in vaccines. Economic, social, and political determinants profoundly affect public health outcomes, leading to discrepancies in vaccination rates. The restricted financing in Bulgaria obstructs efficient vaccination programs, while elevated out-of-pocket healthcare expenses hinder vaccine availability for low-income persons who prioritise acute healthcare requirements above preventative measures. Furthermore, entrenched distrust in public institutions intensifies vaccination hesitancy in Bulgaria, driven by a history of political instability and corruption. Widespread demonstrations against COVID-19 vaccinations signify popular concern about governmental overreach and vaccine safety. The proliferation of vaccine misinformation exacerbates public health challenges, while political instability hinders effective health communication and undermines faith in government actions.

The report highlights the efficacy of worldwide immunisation initiatives while exposing ongoing problems. Countries such as Italy have attained substantial vaccination coverage among vulnerable populations, but Bulgaria persists in facing challenges with low immunisation rates attributed to vaccine reluctance and insufficient healthcare infrastruc-



**Figure 2. Factors influencing vaccination hesitancy.**

ture. Addressing these gaps requires targeted public health activities to enhance vaccination adoption in areas with considerable hesitation. The work underscores the need for comprehensive vaccination protocols, including booster doses, to sustain immunity and avert COVID-19 outbreaks, promoting equitable vaccine availability as an essential element of pandemic response efforts.

#### 4.2. Studies from various countries that have investigated the safety of COVID-19

A research conducted in Poland examined the determinants affecting parents' choices to vaccinate their children against human papillomavirus (HPV) and COVID-19.<sup>27</sup> Findings indicated that several parents, including those in favour of vaccination, have insufficient understanding regarding these vaccinations. Favourable factors encompassed convictions on the safety and preventive advantages of vaccines against cancer and COVID-19. Younger parents exhibited more desire to vaccinate than older parents. Conversely, adverse impacts originated from misconceptions regarding immunisation, apprehensions about the HPV vaccination impacting children's sexual conduct, and parental age. The scheduling of vaccines was significantly influenced by perceptions of safety and efficacy, along with apprehensions over adverse effects. These and other factors are shown in Figure 2.<sup>27</sup>

Vaccine hesitancy is a complicated and diverse phenomenon that varies considerably according to the specific vaccine involved. Vaccination hesitancy is not homogeneous. Instead, factors such as the vaccine's technology, public perception, and the credibility of the information sources consumers trust shape it.<sup>28</sup> For example, mRNA vaccines, such as those created by Pfizer and Moderna, have encountered varying degrees of scepticism compared to conventional vaccinations. This reluctance frequently arises from apprehensions over the novelty of mRNA technology, with certain persons questioning its long-term safety and efficacy. People who subscribe to conspiracy theories are more likely to perceive mRNA vaccinations as objectionable, whereas those who depend on political leaders for health advice may hold varying opinions regarding vector-based or whole-vi-

rus vaccines such as AstraZeneca or Sinopharm.

The reluctance toward mRNA vaccinations might be compared to the more favourable perceptions of other vaccine types among specific communities. Study by Bussink-Voorend et al.<sup>29</sup> suggests that people may accept vector-based vaccinations if they come from reliable sources or have a longer history of use. Individuals who initially refuse one vaccination may subsequently take another, influenced by their assessments of safety and efficacy. This variety underscores that vaccination hesitancy is not only a uniform rejection but a complex spectrum wherein individuals may accept certain vaccines while declining others, influenced by their foundational beliefs and experiences. Additionally, overarching social variables, such as faith in healthcare systems and governmental organisations, influence vaccination hesitancy. Distrust in public health communications or widespread disinformation can significantly increase vaccination hesitancy across all vaccine categories in these areas. Survey by Khankeh et al.<sup>30</sup> indicates that apprehensions over side effects and the perceived hazards linked to new vaccinations are widespread, especially in nations with lower vaccination rates. This suggests that, although mRNA vaccines have particular obstacles, the fundamental factors leading to vaccination reluctance are generally relevant to all vaccine categories.

Aidalina and Khalsom<sup>31</sup> analysed COVID-19 vaccine distribution models in Malaysia, demonstrating that mass immunisation programs were the most cost-effective relative to no vaccination and universal vaccination methods compared to risk-stratified models. Policies with elevated immunisation expenses encompassed that emphasising enhanced vaccine effectiveness, vaccination rates, and the targeting of at-risk populations. The study highlighted the necessity for improved vaccine manufacturing and expedited distribution networks to immunisation centres. In France, Couderc et al.<sup>32</sup> conducted a study on COVID-19 immunisation among older cancer patients, comprising 150 participants with an average age of 81. The immunisation rate was 82.6%, with minor adverse effects reported by 15.9% following the first dosage and 23.4% after the second. The morbidity rate of COVID-19 was 5.1% in vaccinated patients, in contrast to 16.7% in unprotected

individuals. Of the 22 vaccinated patients evaluated for antibodies, 68% exhibited antibody development within 21 days following the initial dosage, demonstrating that vaccination initiatives for cancer patients are both efficacious and safe.

Gil-Díaz et al.<sup>33</sup> performed a trial in Spain with 62 individuals who had a history of cerebral venous sinus thrombosis (CVST) and got COVID-19 vaccines. Of the individuals, 69.4% received the Pfizer-BioNTech vaccine, 11.3% received Moderna, 11.3% received ChAdOx1, and 8.1% received Janssen. After 30 days, there were no recurrences of CVST, and one unrelated death occurred (1.6%), affirming the safety of immunisation in this cohort. In Italy, Bellomo et al.<sup>34</sup> examined anaphylaxis associated with COVID-19 vaccinations, observing that although experts recommend caution for individuals with a history of anaphylaxis, the CDC advocates for vaccination in those with immediate-type allergic reactions, contingent upon a 30-minute monitoring period post-vaccination. Frequent side effects encompass erythema and fever, but anaphylaxis remains rare. Study in India by Garg and Paliwal<sup>35</sup> indicated that although vaccinations are often well-accepted, mild adverse effects such as weariness and pain are prevalent. Significant neurological effects, including CVST, were predominantly observed in women after receiving vector vaccinations, whereas mRNA vaccines were associated with Bell's palsy and herpes zoster. Zavala-Jonguitud and Pérez-García<sup>36</sup> documented a case of delirium in an 89-year-old patient following immunisation, ascribed to age and pre-existing problems rather than the vaccine. The patient achieved complete recovery after treatment modifications. The effect of vaccination on the occurrence of delirium was due to age, polypragmasy and other reasons that became risk factors for this patient.

Studies suggest that COVID-19 vaccines, encompassing mRNA and vector-based variants, are predominantly safe and well-tolerated. Nonetheless, apprehensions over possible adverse consequences such as allergy and neurological diseases remain, especially within specific demographics. Vaccine hesitancy is shaped by disinformation, insufficient understanding, and socio-political influences, shown in parental reluctance to immunise children. The results confirm that vaccination initiatives, particularly for high-risk groups, have markedly decreased morbidity and death, highlighting the essential function of vaccinations in public health. The research advocates for the resolution of safety issues by efficient communication and transparent safety oversight to preserve public confidence in immunisation programs.

#### **4.3. International organisations and the introduction of vaccination against other infectious diseases in the population**

In 2020, the WHO formulated an immunisation strategy for 2021–2030, partnering with different countries and organisations to utilise data from prior epidemics.<sup>37</sup> This approach seeks to synchronise initiatives at national, regional, and global levels to guarantee holistic health and well-being for all demographics, irrespective of age, gender, or socioeconomic position. Primary objectives are the eradication

of polio, the elimination of newborn tetanus in 40 nations, the eradication of measles and rubella across five regions, a 90% reduction in cholera mortality, and a substantial decrease in chronic viral hepatitis B infections and mortality by 2030. The strategy aims for a 75% decrease in mortality from vector-borne illnesses, the eradication of yellow fever outbreaks, and enhanced outcomes for meningitis patients. The plan includes annual vaccines for seasonal influenza and a decrease in rabies infections resulting from animal bites.

The WHO and UNICEF<sup>7</sup> cooperate to evaluate country immunisation coverage via yearly evaluations that encompass surveys and data assessments.<sup>38</sup> They assess coverage for many vaccinations, including DTP, polio, hepatitis B, and measles, to track immunisation in children. Collaboration between the WHO and UNICEF in addressing vaccine misinformation is an essential element of the global immunisation plan detailed in the 'UNICEF Immunization Roadmap to 2030'.<sup>37</sup> This collaboration seeks to address substantial issues presented by disinformation, which may critically undermine public confidence in vaccinations and obstruct immunisation initiatives. WHO and UNICEF established a principal project, the 'Misinformation Management Guide'<sup>39</sup> to assist health systems in effectively combating disinformation. To improve vaccination acceptability, WHO and UNICEF educate healthcare professionals, leverage social media for accurate information distribution, and include local influencers. They examine national immunisation data to pinpoint regions with substantial misunderstandings and customise communication tactics accordingly. Through the assessment of public sentiment via surveys and social media, they modify their strategies to enhance community engagement in vaccine discourse, eventually seeking to cultivate faith in global immunisation initiatives.

The Vaccine Adverse Event Reporting System<sup>8</sup> in the USA monitors vaccination adverse effects, accepting reports from healthcare professionals, manufacturers, and the public. In 2021, it received more than 900,000 reports about COVID-19 immunisations, indicating increased public involvement. Following vaccine approval by the CDC<sup>9</sup> and FDA,<sup>10</sup> the Vaccine Adverse Events Reporting System persists in monitoring adverse events to detect novel or infrequent responses, evaluate common side effects, and ascertain risk factors. The key objectives are the surveillance of vaccination safety, the identification of regional or product-specific concerns, and the facilitation of emergency response initiatives.

In Europe, safety and side effects after vaccination are monitored by the EMA.<sup>11</sup> During the coronavirus pandemic, the EMA was involved in overseeing the monitoring of vaccine safety.<sup>40</sup> The EMA monitored the occurrence of thrombosis with thrombocytopenia syndrome associated with adenoviral vector vaccines, myocarditis, or pericarditis following vaccination with RNA vaccines. These problems were quickly identified and analysed, and refinements minimised the risk through the use of evidence, clinical expertise, and regulatory tools.

International organisations like the WHO and UNICEF have formulated extensive initiatives to enhance global im-

munisation rates and tackle the issues presented by infectious illnesses. The WHO's immunisation strategy for 2021–2030 establishes lofty objectives, such as the eradication of polio, elimination of neonatal tetanus, and the decrease of mortality from illnesses like cholera and hepatitis B. These endeavours are augmented by international endeavours to oversee and enhance vaccination coverage, especially through the yearly evaluations performed by UNICEF. Moreover, entities such as the vaccination Adverse Events Reporting System and the EMA are integral to vaccination safety, diligently monitoring adverse effects and responding to public apprehensions. These techniques together seek to enhance vaccine acceptability, diminish disinformation, and guarantee fair access, all of which are crucial for attaining widespread immunisation and advancing global public health outcomes.

#### 4.4. Adverse reactions to immunization

A study by De Camargos et al.<sup>41</sup> monitored adverse reactions to vaccination in children from birth to 9 years of age. About 0.008% of cases of vaccination errors, such as failure to follow age recommendations, were identified. Of this number, 91.8% did not result in severe adverse events, and 56% were children under 1 year of age. Of the symptoms, 72% were local or systemic reactions, and 41% were fever. The work showed that despite the errors, vaccination of children was safe and effective.

A case of an anaphylactic reaction to the measles, rubella, and mumps vaccine in a patient who was sensitive to gelatin was described in a scientific paper by Miller et al.<sup>42</sup> Although such vaccines are usually well tolerated, allergic reactions can occur to additives or residual components in the vaccine. This scientific work has shown that the rare occurrence of anaphylaxis to an additive component of the vaccine is possible. Therefore, the patient's medical history should be carefully reviewed before immunization. A group of scientists, Winkelmann et al.,<sup>43</sup> studied the side effects, safety, and efficacy of vaccination in 222 patients with multiple sclerosis. Of these, 76.6% were women and 23.4% were men; 89.6% had a relapsing form of the underlying disease. Of the vaccines with which the patients were immunised, 56.3% were influenza vaccines and 33.8% were tetanus vaccines. Multiple sclerosis symptom severity decreased from 0.63 to 0.38 in the follow-up year. Side effects were reported in 19.2% of patients who received vaccines, of which 65.2% had local manifestations and 34.8% reported influenza-like reactions. This study showed that inactivated non-live vaccines are safe, effective, and well-tolerated in patients with multiple sclerosis.

In a scientific paper by Meleis et al.,<sup>44</sup> a case was described in which a 50-year-old man with a history of arthritis with psoriasis developed bilateral paraesthesia of the lower extremities 7 days after vaccination against herpes zoster. On CT scan, the patient had signs of acute transverse myelitis. In the hospital, he developed ventricular tachycardia with loss of consciousness. After prolonged selection of treatment, the patient noted improvement after plasmapheresis. The causes of these conditions could not be determined, but

a postvaccine aetiology could not be excluded. The description of adverse symptoms for the development of safe immunisation strategies for the population is an important point. Given that vaccines are indicated for at-risk and vulnerable populations, the study of this topic should be at a high level. This will help vaccine developers to optimise vaccines to improve safety, efficacy, and tolerability.

Lataster<sup>45</sup> rigorously analysed the changing perceptions and social attitudes around mRNA COVID-19 vaccinations. Once seen as revolutionary, attitudes have altered with the advent of fresh studies. Initial research indicated significant efficacy and safety. However, later studies highlighted issues about long-term effectiveness, especially in relation to emerging variations and the necessity for booster vaccinations. Lataster underscores the evolving scientific consensus, with several specialists expressing concerns over the longevity of protection conferred by mRNA vaccines and the possibility of side consequences, particularly following numerous booster doses. This change in comprehension has affected public perception, resulting in heightened vaccination reluctance stemming from persistent concerns over safety, adverse effects, and long-term health consequences. These discoveries highlight the necessity of clear communication and ongoing surveillance of vaccination safety to preserve public confidence in mRNA vaccines, which are vital in the worldwide effort against COVID-19.

Healthcare professionals are essential in addressing adverse vaccination responses and educating patients about potential hazards. They must be educated to identify and manage allergic reactions, including anaphylaxis, and do comprehensive pre-vaccination evaluations to ascertain contraindications. Observing patients for a minimum of 15 minutes following immunisation is essential for the prompt identification of adverse reactions. Establishing explicit strategies for managing typical responses and thorough documentation to the Vaccine Adverse Event Reporting System is crucial. Healthcare practitioners must transparently convey the hazards linked to vaccinations, encompassing prevalent side effects and infrequent severe responses, while assuring patients of the stringent safety assessments vaccines undergo before licensure. Creating an atmosphere conducive to enquiries cultivates trust and motivates patients to express concerns, while supplying written materials about potential side effects empowers them to make educated choices.

The studies underscore the predominantly safe and efficacious characteristics of vaccinations, with the majority of adverse effects being minor and transient. Nonetheless, few yet serious responses, including anaphylaxis and neurological complications, have been recorded, underscoring the necessity for comprehensive pre-vaccination evaluations and continuous surveillance. These findings highlight the imperative for explicit communication from healthcare practitioners regarding potential adverse effects and ongoing monitoring to guarantee vaccination safety.



## 5. CONCLUSIONS

- (1) Italy achieved one of the highest vaccination rates in Europe, with 80% of the population receiving at least one dose by the end of 2021, and nearly 100% coverage among those over 80 years old.
- (2) The U.S. vaccinated 65% of its population by early 2022, with over 90% coverage among those over 65 and high rates among healthcare workers.
- (3) Average vaccination coverage in the European Union was 73%, with first booster doses reaching 54.7%, but Bulgaria, Romania, and Croatia had significantly lower revaccination rates (below 25%).
- (4) Bulgaria had one of the lowest overall vaccination rates in Europe (30%), though coverage among those over 65 years was above 65%.
- (5) Strategies that increased vaccination rates included public education, reminder mechanisms, incentives, policy optimization, and free workplace immunization.
- (6) Special vaccination campaigns targeted homeless people and animals, reducing risks of infection among humans.
- (7) Vaccination of high-risk groups, such as pregnant women and elderly patients, showed high safety and efficacy, with mostly mild to moderate adverse events.
- (8) Rare severe adverse events, including anaphylaxis and neurological symptoms, were identified and require further research.
- (9) A limitation was the lack of comprehensive data on vaccination in Bulgaria, suggesting the need for more detailed future studies.

## Conflict of interest

None declared.

## Funding

None declared.

## References

- <sup>1</sup> UNDP. *Global Dashboard for Vaccine Equity Data Futures Exchange*. 2021. <https://data.undp.org/insights/vaccine-equity>. Accessed: January 5, 2025.
- <sup>2</sup> Ioannidis JPA, Pezzullo AM, Cristiano A, Boccia S. Global estimates of lives and life-years saved by COVID-19 vaccination during 2020–2024. *medRxiv*. 2024;24316673. <https://doi.org/10.1101/2024.11.03.24316673>.
- <sup>3</sup> Rangelova V, Raycheva R, Sariyan S, Kevorkyan A. Reporting adverse events of COVID-19 vaccines: The case of Bulgaria. *PLoS One*. 2022;17(6):e0269727. <https://doi.org/10.1371/journal.pone.0269727>.
- <sup>4</sup> Niesen MJM, Pawlowski C, O'Horo JC, et al. Surveillance of safety of 3 doses of COVID-19 mRNA vaccination using electronic health records. *JAMA Netw Open*. 2022;5(4):e227038. <https://doi.org/10.1001/jamanetworkopen.2022.7038>.
- <sup>5</sup> Bonanni P, Steffen R, Schelling J, et al. Vaccine co-administration in adults: An effective way to improve vaccination coverage. *Hum Vaccin Immunother*. 2023;19(1):2195786. <https://doi.org/10.1080/21645515.2023.2195786>.
- <sup>6</sup> Mo Y, Zeng J, Xiao C, et al. Effectiveness and safety of pneumococcal vaccines used alone or combined with influenza vaccination in dialysis patients: A systematic review and meta-analysis. *Vaccine*. 2020;38(47):7422–7432. <https://doi.org/10.1016/j.vaccine.2020.09.080>.
- <sup>7</sup> UNICEF. UNICEF Immunization Roadmap To 2030: The priorities for immunization through the end of this decade. 2024. <https://www.unicef.org/documents/unicef-immunization-roadmap-2030>. Accessed: January 5, 2025.
- <sup>8</sup> Vaccine Adverse Events Reporting System. <https://vaers.hhs.gov/index.html>. Accessed: January 5, 2025.
- <sup>9</sup> Centers for Disease Control and Prevention. <https://www.cdc.gov/about/cdc/index.html>. Accessed: January 5, 2025.
- <sup>10</sup> Food and Drug Administration. <https://www.fda.gov>. Accessed: January 5, 2025.
- <sup>11</sup> European Medicines Agency. <https://www.ema.europa.eu/en/about-us>. Accessed: January 5, 2025.
- <sup>12</sup> World Health Organization. Global COVID-19 Vaccination Strategy in a Changing World: July 2022 update. 2022. <https://www.who.int/publications/m/item/global-covid-19-vaccination-strategy-in-a-changing-world-july-2022-update>. Accessed: January 5, 2025.
- <sup>13</sup> The White House. National COVID-19 Preparedness Plan. 2024. <https://www.whitehouse.gov/covidplan>. Accessed: January 5, 2025.
- <sup>14</sup> Food and Drug Administration. Emergency Use Authorization. <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>. Accessed: January 5, 2025.
- <sup>15</sup> Centers for Disease Control and Prevention. Product Info by U.S. Vaccine. 2024. <https://www.cdc.gov/vaccines/covid-19/info-by-product/index.html>. Accessed: January 5, 2025.
- <sup>16</sup> Wong MK, Brooks DJ, Ikejezie J, et al. COVID-19 mortality and progress toward vaccinating older adults – World Health Organization, Worldwide, 2020–2022. *MMWR Morb Mortal Wkly Rep*. 2023;72(5):113–118. <http://dx.doi.org/10.15585/mmwr.mm7205a1>.
- <sup>17</sup> Reuters. Bulgaria: World coronavirus tracker and maps. 2022. <https://www.reuters.com/graphics/world-coronavirus-tracker-and-maps/countries-and-territories/bulgaria>. Accessed: January 5, 2025.
- <sup>18</sup> World Health Organization. Bulgaria: Country Health Profile 2023. 2023. <https://euro.who.int/publications/m/bulgaria-country-health-profile-2023>. Accessed: January 5, 2025.
- <sup>19</sup> National COVID-19 vaccination plan. Epicentro. 2021. <https://www.epicentro.iss.it/en/vaccines/covid-19-vaccination-plan>. Accessed: January 5, 2025.
- <sup>20</sup> Italy: World coronavirus tracker and maps. Reuters. 2022. <https://www.reuters.com/graphics/world-corona->



- virus-tracker-and-maps/countries-and-territories/italy. Accessed: January 5, 2025.
- 21 COVID-19 Vaccines. AIFA. 2024. <https://www.aifa.gov.it/en/vaccini-covid-19>. Accessed: January 5, 2025.
  - 22 US Coronavirus vaccine tracker. 2024. <https://usafacts.org/visualizations/covid-vaccine-tracker-states>. Accessed: January 5, 2025.
  - 23 European Centre for Disease Prevention and Control (ECDC). 2023. COVID-19 Vaccine Tracker. <https://vaccinetracker.ecdc.europa.eu/public/extensions/Covid-19/vaccine-tracker.html#uptake-tab>. Accessed: January 5, 2025.
  - 24 Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA. ECDC. 2023. <https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-deployment-plans>. Accessed: January 5, 2025.
  - 25 Kozlovskiy S, Bilenko D, Kuzheliev M, Ivanyuta N, Butenko V, Lavrov R. Comparison and Assessment of Factors Affecting the COVID-19 Vaccination in European Countries. *Probl Ekorozv.* 2021;16:26–33. <https://doi.org/10.35784/pe.2021.2.03>.
  - 26 Toshkov D. What accounts for the variation in COVID-19 vaccine hesitancy in Eastern, Southern and Western Europe? *Vaccine.* 2023;41(20):3178–3188. <https://doi.org/10.1016/j.vaccine.2023.03.030>.
  - 27 Zastawna B, Milewska A, Załuska R, Kozłowski R, Zastawna M, Marczak M. Analysis of parents' attitudes and knowledge toward immunization and how these factors influence their decisions to vaccinate their children against Human Papilloma Virus (HPV). *Medicina.* 2023;59(10):1755. <https://doi.org/10.3390/medicina5910175>.
  - 28 Kutasi K, Koltai J, Szabó-Morvai Á, Röst G, Karsai M, Biró P, Lengyel B. Understanding hesitancy with revealed preferences across COVID-19 vaccine types. *Sci Rep.* 2022;12:13293. <https://doi.org/10.1038/s41598-022-15633-5>.
  - 29 Bussink-Voorend D, Hautvast JLA, Vandeberg L, Visser O, Hulshar MEJL. A systematic literature review to clarify the concept of vaccine hesitancy. *Nat Hum Behav.* 2022;6:1634–1648. <https://doi.org/10.1038/s41562-022-01431-6>.
  - 30 Khankeh H, Pourebrahimi M, Hosseinabadi-Farahani M, et al. Comparison of vaccine hesitancy during the low and high points of COVID-19 in a population under international sanctions: A longitudinal mixed-methods study in Iran. *Front Public Health.* 2023;10:958899. <https://doi.org/10.3389/fpubh.2022.958899>
  - 31 Aidalina M, Khalsom S. COVID-19 vaccination: A systematic review of vaccination strategies based on economic evaluation studies. *Med J Malaysia.* 2023;78(3):411–420.
  - 32 Couderc AL, Ninove L, Nouguerède E, et al. Acceptance, efficacy, and safety of COVID-19 vaccination in older patients with cancer. *J Geriatr Oncol.* 2022;13(6):850–855. <https://doi.org/10.1016/j.jgo.2022.05.002>.
  - 33 Gil-Díaz A, Gil-Hernández A, Lozano-Jiménez AI, Benítez-Peña J, Conde-Martel A. Safety of COVID-19 vaccination in patients with previous cerebral venous sinus thrombosis. *Thromb Res.* 2021;209:84–85. <https://doi.org/10.1016/j.thromres.2021.12.004>.
  - 34 Bellomo RG, Gallenga CE, Caraffa A, Tetè G, Ronconi G, Conti P. Anaphylaxis is a rare reaction in COVID-19 vaccination. *J Biol Regul Homeost Agents.* 2021;35(3):839–842. [https://doi.org/10.23812/bellomo\\_edit\\_3\\_21](https://doi.org/10.23812/bellomo_edit_3_21).
  - 35 Garg RK, Paliwal VK. Spectrum of neurological complications following COVID-19 vaccination. *Neurol Sci.* 2022;43:3–40. <https://doi.org/10.1007/s10072-021-05662-9>.
  - 36 Zavala-Jonguitud LF, Pérez-García CC. Delirium triggered by COVID-19 vaccine in an elderly patient. *Geriatr Gerontol Int.* 2021;21(6):540. <https://doi.org/10.1111/ggi.14163>.
  - 37 Vaccines and immunization. WHO. 2020. [https://www.who.int/health-topics/vaccines-and-immunization#tab=tab\\_3](https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_3). Accessed: January 5, 2025.
  - 38 Immunization dashboard: Global reported cases of vaccine-preventable diseases (VPDs). WHO. 2023. <https://immunizationdata.who.in>. Accessed: January 5, 2025.
  - 39 Misinformation Management Guide: Guidance for addressing a global infodemic and fostering demand for immunization. WHO. 2020. <https://vaccinemisinformation.guide>. Accessed: January 5, 2025.
  - 40 Durand J, Dogné J, Cohet C, Browne K, Gordillo-Marañón M, Piccolo L, et al. Safety monitoring of COVID-19 vaccines: Perspective from the European Medicines Agency. *Clin Pharmacol Ther.* 2023;113(6):1223–1234. <https://doi.org/10.1002/cpt.2828>.
  - 41 De Camargos SM, Oliveira MLS, Luvisaro BMO, Silva TPRD, Souza JFA, Vimieiro AM, et al. Adverse event following immunization or vaccination in children in Minas Gerais: 2015 to 2020. *Rev Bras Epidemiol.* 2023;26:e230056. <https://doi.org/10.1590/1980-549720230056>.
  - 42 Miller CK, Mendoza JC, Coop CA. Anaphylaxis to MMR vaccine mediated by IgE sensitivity to gelatin. *Mil Med.* 2020;185(9–10):e1869–e1871. <https://doi.org/10.1093/milmed/usaa058>.
  - 43 Winkelman A, Metze C, Zettl UK, Loebermann M. Side effects following vaccination in multiple sclerosis: A prospective, multi-centre cohort study. *Sci Rep.* 2023;13:14480. <https://doi.org/10.1038/s41598-023-41271-6>.
  - 44 Meleis MM, Hahn SB, Carraro MN, Deutsch AB. Extensive longitudinal acute transverse myelitis complicated by pulseless ventricular tachycardia and recent shingles vaccination. *Am J Emerg Med.* 2023;68:213.e1–213.e3. <https://doi.org/10.1016/j.ajem.2023.04.033>.
  - 45 Lataster R. Scientific views around mRNA based covid vaccines are changing, but to what end?. *Pol Ann Med.* 2024;31(2):158–161. <https://doi.org/10.29089/paom/193801>.