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COVID-19 Vaccine Hesitancy:
A Tale of Two Pandemics

HABILITATION THESIS

HYGIENE, PREVENTIVE MEDICINE AND EPIDEMIOLOGY

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ABSTRACT

The global health landscape has recently been challenged by two overlapping pandemics: COVID-19 and vaccine hesitancy. These dual crises have complicated each other, creating a vicious cycle that has necessitated timely and evidence-informed interventions. Vaccine hesitancy holds deep historical roots, with disputes arising since Edward Jenner introduced the first smallpox vaccine in the late 18th century; however, misinformation and complacency in the modern era have exacerbated this phenomenon. The COVID-19 outbreak has created a complex interplay with vaccine hesitancy, posing profound challenges for health systems worldwide.

The present thesis explored COVID-19 vaccine hesitancy through seven cross-sectional studies spanning diverse population groups in the Czech Republic and internationally during primer vaccination campaigns (winter–summer 2021) and booster vaccination campaigns (winter–spring 2022). This thesis is divided into two sections. The first comprises three studies conducted in the Czech Republic among university students (study II), pregnant and lactating women (study III), and healthcare professionals (study IV). The second section comprises four studies undertaken among dental students in 22 countries (study I), German university students and academics (study V), Polish healthcare professionals and students (study VI), and the Algerian general adult population (study VII). In total, 13,966 participants were surveyed using validated instruments adapted from theoretical models, including the WHO-SAGE matrix model, socio-ecological model, and health belief model.

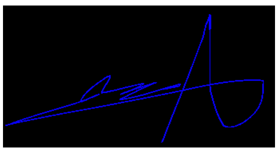
The findings of this thesis revealed that vaccine hesitancy was higher among females, younger adults, and those distrusting vaccine safety/effectiveness evidence. However, altruism and collective responsibility emerged as significant motivators for acceptance. The studies advocate addressing knowledge gaps through compassionate communication, emphasising vaccine benefits while respecting diverse perspectives. They suggest vaccine mandates should be judiciously implemented based on transparent risk-benefit analysis and ethical considerations, as mandates could potentially harden hesitancy if imposed non-consensually. Overall, the findings underscore nuanced, multi-level strategies to foster vaccine acceptance.

This thesis makes several original contributions. Firstly, the large sample provides robust, generalisable findings. Secondly, the timing during critical stages of primer/booster rollout offers policymakers timely evidence to navigate the pandemic response. Thirdly, using validated instruments and advanced statistical techniques, including machine learning, enhances analytic rigour. Fourthly, the diverse populations surveyed facilitate global comparisons of vaccine attitudes and associated sociodemographic factors. Lastly, adherence to reporting guidelines and ethical principles augments methodological strength.

In conclusion, this thesis delivers pivotal insights into combatting two converging pandemics—COVID-19 and vaccine hesitancy. These lessons hold enduring relevance as public health continues to confront infectious diseases and vaccine hesitancy worldwide. This work underscores the importance of compassionate communication, community-focused motivators, and respect for personal healthcare choices in fostering vaccine acceptance.

DECLARATION

I hereby declare that this thesis is a product of my independent research, conducted using only the resources cited in the bibliography. I affirm that the work presented herein is my own, except where explicitly stated otherwise. I further declare that this thesis has not been submitted for any other academic award.



Brno, July 24th, 2023 — Abanoub Riad, PhD, DDS, FRSPH

TABLE OF CONTENTS

Vaccine Hesitancy: A Pervasive Global Health Threat

On January 10th, 2019, the World Health Organisation (WHO) released a list of the top ten threats to global health that need to be tackled alongside its new quinquennial strategic plan (2019 – 2023), which aimed to expand health coverage, increase health emergency protection, and enhance well-being [1]. One of these threats is vaccine hesitancy which is defined by the WHO's Strategic Advisory Group of Experts on Immunization (SAGE) as the "*delay in acceptance or refusal of vaccination despite the availability of vaccination services*" [2,3]. The WHO recognises vaccine hesitancy as a growing challenge that is limiting vaccine coverage and contributing to an estimated 1.5 million child fatalities annually from vaccine-preventable diseases [2,4].

I.I. Historical Footage

Vaccine hesitancy is not a new phenomenon. It has been a recurring issue throughout the history of vaccination, dating back to the time when Dr Edward Jenner introduced the smallpox vaccine in the late eighteenth century [5]. Prior to Jenner's discovery, variolation, a method of inoculating with smallpox to prevent the disease, was practised by Chinese physicians for quite a long time but was neither safe nor consistent due to misdiagnoses and the risk of spreading other diseases, such as syphilis [5,6]. This was a pre-existing challenge for Jenner, which was coupled with his poor understanding of the mechanism of action and the optimal dose of his new cowpox-based product [6]. The first petition against Jenner's work came in 1797 from the Royal Society, which rejected his short communication about the innovative experiment he made on an 8-year-old boy who was protected against smallpox through the by-products of cowpox lesions [6]. Despite this initial disapproval, Jenner continued his experiments and included 23 volunteers before he published his results in a booklet titled "*An Inquiry into the Causes and Effects of the Variolae Vaccinae*" a couple of years later [7]. Jenner is also accredited for coining the term "*vaccination*", which he used to distinguish between his new cowpox-based product and the classic variolation procedure [6,7].

In the beginning, vaccination faced religious opposition, with critics arguing that it was an arrogant attempt to avoid divine punishment and that injecting animal materials into the human body was a direct violation of God's will [8,9]. This mirrored earlier debates about variolation, but vaccines were also challenged by the concerns that they would cause "Cow-Mania" [9]. In 1805, Dr William Rowley published a book titled "*Cow-pox Inoculation: No Security Against Small-pox Infection",* in which he detailed the adverse effects of the smallpox vaccine on children [10]. He highlighted the case of an 'ox-faced boy' with distorted facial features and a girl covered in painful sores, attributing their conditions to Jenner's vaccine [10]. On the other hand, several physicians supported Jenner's vaccine and actively disseminated it among their patients [6]. Within this extensively polarised landscape, vaccines slowly gained popularity and became a scientifically proven method to control smallpox epidemics and gradually replaced variolation [6,8]. Figure 1

Figure 1. Illustration from 'Cow-Pox Inoculation No Security Against Small-Pox Infection' by W. Rowley. Image courtesy of the Wellcome Collection. Public Domain Mark.

The 1840 Vaccination Act, "*An Act to extend the Practice of Vaccination*", was the first legislative intervention in the United Kingdom (UK) to set up public vaccination services, primarily through the Poor Law medical practitioners [11,12]. This act outlawed variolation


THE ANTI-VACCINATOR,
And Advocate of Cleanliness.
MONTREAL, OCTOBER, 1885.
SMALL-POX.

Figure 2. Cover of 'The anti-vaccinator, and advocate of cleanliness.' Contributor: Alexander Milton Ross, 1832-1897. Published in Montreal, 1885. National Library of Medicine Digital Collections.

and made vaccination free of charge for everyone [12]. The second Vaccination Act that was passed in 1853 mandated compulsory vaccination for all infants within their first three months, with penalties for non-compliant parents, including fines or imprisonment. Therefore, this act was met with immediate resistance, inciting violent riots in various towns and leading to the formation of the first-ever anti-vaccination group, the Anti-Vaccination League (AVL), in London [13]. The third Vaccination Act of 1867 extended compulsory vaccination to the age of 14 and added new restrictions and penalties for non-compliance [13,14]. In response to this new law, Richard Butler Gibbs established the Anti-Compulsory Vaccination League (ACVL) with a seven-point mission statement, "*National Anti-Compulsory Vaccination Reporter*", asserting that parliament had overstepped its bounds by making good health a crime, punishable by fine or imprisonment, thereby infringing on the rights of parents to protect their children from the disease [13]. Moreover, Gibbs strongly criticised the parliament for significantly violating civil liberties by compromising them in the name of public health [11,13]. Figure 2

During the Victorian era, the anti-vaccination movement spread to other European countries and crossed the Atlantic to North America. In 1879, the Anti-Vaccination Society of America was established following the visit of William Tebb, a vocal British anti-vaccinationist who held several positions in the UK anti-vaccination organisations [13,15]. The number of United States (US) anti-vaccination organisations increased rapidly between 1879 and 1900, including the New England Anti-Compulsory Vaccination League (1882) and the Anti-vaccination League of New York City (1885) [15,16]. Following the 1902 smallpox outbreak in Cambridge, Massachusetts, all residents were mandated to be vaccinated. Henning Jacobson, a city resident, refused, arguing that the law violated his personal rights, which led to criminal charges and a local court battle that he lost and appealed to the US Supreme Court. In 1905, the Supreme Court ruled in the state's favour, marking the first Supreme Court case concerning state power in public health law [16]. Figure 3

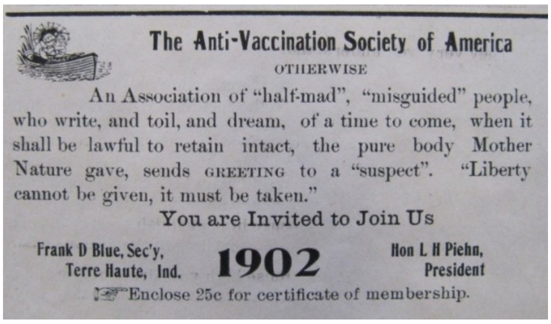


Figure 3. Anti-Vaccination Society of America advertisement from 1902. Anti-Vaccination Society of America via The College of Physicians of Philadelphia. Public domain.

In Europe, the anti-vaccination movement flourished during the second half of the nineteenth century, with Stockholm serving as a notable example, where vaccination rates dropped to a mere 40% in contrast to the 90% coverage in rural Sweden, thereby disrupting herd immunity [17]. Despite persistent warnings from health authorities about the inevitable risks of vaccination rejection, these advisories were largely disregarded. Nevertheless, the advent of a new epidemic smallpox wave in 1874 rekindled the perception of risk among the city's population, thus leading to a resurgence in vaccination uptake and cessation of anti-vaccination activities [17]. In contrast to the UK, where vaccination was largely considered an individual decision, Germany, with its tradition of medical police and state responsibility for health, adopted mandatory vaccination early on, with the Kingdom of Bavaria introducing it as early as 1807 [18]. This early adoption sparked a robust debate in the mid-nineteenth century, fuelled by concerns about vaccines' waning effectiveness and potential side effects. Key figures in this debate included Michael Reiter, who defended the necessity and enforcement of vaccination, and Carl Nittinger, who viewed compulsory vaccination as a violation of individual liberty [18]. Despite this controversy, compulsory vaccination remained a cornerstone of public health policy in Germany throughout the century [18].

Between 1920 and 1970, the introduction of new vaccines for diseases such as tuberculosis, yellow fever, whooping cough, tetanus, and polio significantly reduced childhood mortality. However, several incidents during this period led to public concerns about vaccine safety and effectiveness [19]. The Cutter Incident in 1955, where several batches of the polio vaccine contained the active virus, resulted in over 250 polio cases and laid the basis for distrust in the pharmaceutical industry [20]. Additionally, between 1955 and 1963, it was estimated that 10-30% of polio vaccines in the US were contaminated with Simian Virus 40 (SV40), suspected to cause human cancers [20]. In 1976, a campaign to encourage vaccination against swine flu led to a slight increase in Guillain-Barré Syndrome (GBS) cases [21]. The safety of the diphtheria, tetanus, and pertussis (DTP) vaccination program was also questioned in the mid-1970s, leading to a rapid decline in immunisation rates and subsequent whooping cough outbreaks in the UK [22,23]. Moreover, in 1998, a *Lancet* report published by Andrew Wakefield alleging a link between the measles, mumps, and rubella (MMR) vaccine and autism sparked widespread media coverage and a drop in MMR vaccination, despite the lack of supportive evidence and subsequent retraction of the paper [24]. These controversies have shaped the public perception of vaccines and led to changes in vaccine manufacturing, regulation, and compensation programs for vaccine-related complications [25].

I.II. Global Burden of Vaccine Hesitancy

The extensive burden of vaccine hesitancy, which affects both high-income and low-and-middle-income countries, leads to the under-utilisation of effective vaccination services. This, in turn, results in gaps in immunisation coverage and triggers outbreaks of vaccine-preventable diseases. Importantly, this issue is not confined to childhood vaccinations but also significantly impacts adult vaccinations [26].

Vaccine-preventable Diseases (VPDs) are infectious diseases for which immunisation can provide effective prevention. The WHO identifies 25 such VPDs globally that hold the potential for realistic control and even eradication. Despite this, these diseases continue to circulate at varying levels and significantly contribute to the global disease burden [27]. In 2021, the global vaccination coverage declined to 81% compared with 86% in 2019, primarily due to the unprecedented pressure of the COVID-19 response; this led to 25 million children missing essential lifesaving vaccines [28]. Table 1 presents the most common VPDs, their clinical sequela, vaccination coverage levels in 2021, and global burden.

Table 1. Summary of vaccine-preventable disease (VPDs) clinical sequela, vaccination coverage and global burden.

Disease	Sequela	Vaccination Coverage [1]	Global Burden
Haemophilus influenzae type b (Hib)	Causes meningitis and pneumonia.	192 member states. Global coverage (3 doses): 71%	Global Hib incidence is 1.13/100k child-years, with a case-fatality ratio of 11.21% [29].
Hepatitis B	A viral infection that targets the liver.	190 member states. Global coverage (3 doses): 80%.	HBV affects 296M globally, leading to 331K cirrhosis and 192K liver cancer deaths in 2019 [30].

Human papillomavirus (HPV)	It causes cervical cancer in women, other types of cancer, and genital warts in both men and women.	116 member states. Global coverage (first dose, girls): 15%.	Global HPV prevalence is 11.7%, with high rates in Africa and Oceania, but most cases are asymptomatic and transient. Annually, HPV causes 630K cancer cases (4.5% of all cancer cases), with the majority (83%) being cervical cancer [31].
Meningitis A	Often deadly infection that leaves 1 in 5 affected individuals with long-term devastating sequela.	350M people in 24 out of the 26 countries in the African meningitis belt had been vaccinated with MenAfriVac.	In 1990, meningococcus was the leading aetiology for meningitis deaths, with an estimated 193K globally. Meningitis A caused 85% of meningitis epidemics in the meningitis belt before mass vaccination introduction in 2010 [32,33].
Measles	A highly contagious disease that can lead to blindness, encephalitis, or death.	Global coverage (1st dose): 81%. Global coverage (2nd dose): 71%.	In 2021, measles caused 128K deaths, primarily in unvaccinated or under-vaccinated children under 5 [34].
Mumps	A highly contagious virus that causes painful swelling at the side of the face under the ears, fever, headache, and muscle aches.	123 member states.	In 2021, 225K incident cases were reported, with more than half of them (53.4%) coming from China alone [35].
Pneumococcal diseases	Including pneumonia, meningitis, and febrile bacteraemia, as well as otitis media, sinusitis, and bronchitis.	154 member states. Global coverage (3 doses): 51%	In 2019, 2.5M deaths were caused by pneumococcal disease, with *S. pneumoniae* leading to 300K deaths, mainly among children under 5 [36,37].
Poliomyelitis	A highly infectious viral disease that can cause irreversible paralysis.	80% of infants received three doses. Coverage of infants receiving their first dose of inactivated polio vaccine (IPV): 79%.	Wild poliovirus cases dropped by 99% since 1988, from 350K to 6 cases in 2021. The COVID-19 pandemic delayed the global eradication of polio [38]. As of 2022, wild poliovirus type 1 persists only in Pakistan and Afghanistan [39].
Rotaviruses	The most common cause of severe diarrhoeal disease in young children.	118 member states. Global coverage: 49%	Globally, 25M outpatient visits and 2M hospitalisations are attributed to rotaviruses, mainly among children under 5 [40]. In 2019, 19.11% of deaths from diarrhoea were caused by rotavirus [41].
Rubella	A viral disease that can cause foetal death or congenital rubella syndrome if infection occurs during early pregnancy.	173 member states. Global coverage: 66%	In 2019, congenital rubella syndrome (CRS) incidence was highest in Africa (64/100K live births) and Eastern Mediterranean (27/100K). Global annual CRS cases significantly dropped from 121K in 1996 to 32K in 2019 [42].
Yellow fever	Acute viral haemorrhagic disease transmitted by infected mosquitoes.	36 / 40 of high-risk regions. Coverage in high-risk regions: 47%.	In 2013, yellow fever in Africa resulted in an estimated 130K cases and 78K deaths, with vaccination campaigns reducing cases and deaths by 27% [43].

ƚ Vaccination coverage rates presented are extracted from the Global Health Observatory (GHO) 2021 reports [28].

The eradication of VPDs is a crucial public health target, yet it confronts numerous obstacles, with vaccine hesitancy standing as a paramount concern. As the incidence of VPDs declines due to successful vaccination campaigns, so too does the perceived susceptibility to these diseases. Paradoxically, this renders vaccines victims of their own success. When individuals weigh the potential side effects against the benefits of immunisation, the perceived risk often overshadows the substantial advantages of vaccination, leading to an unfortunate decline in vaccine acceptance [44].

The assumption that vaccine hesitancy is less prevalent in low-income countries due to the high burden of VPDs is misleading. This resistance is often disease-specific and vaccine-specific, as seen in northern Nigeria and parts of northern India, where communities refused polio vaccines despite low disease incidence [45]. Factors beyond epidemiology, such as local socio-political dynamics, demographic factors, and competing health problems, significantly influence vaccine acceptance [44].

In addition to the persistent burden of VPDs that is current and largely attributable to vaccine hesitancy, several modelling studies attempted to measure the cost of vaccine hesitancy on communities. Mesa *et al.* 2023 developed a compartmental metapopulation model of measles transmission to investigate the societal costs of vaccine hesitancy, using measles in England as a case study. Their findings revealed that even low levels of vaccine refusal could impose a significant societal burden, with an estimated societal loss of GBP 292 million and a disease burden of 17,630 quality-adjusted life-years over a 20-year period [46].

Another study by Mesa *et al.* 2022 explored the potential impact of vaccine hesitancy on controlling the COVID-19 pandemic by combining an epidemiological model of SARS-CoV-2 transmission with data on vaccine hesitancy from population surveys. The study found that in countries with high vaccine hesitancy, mortality over a two-year period could be up to 7.6 times higher compared to an ideal vaccination uptake if non-pharmaceutical interventions (NPIs) are relaxed [47]. Yakum *et al.* 2016 calculated the economic burden attributable to VPDs among US adults, estimating a total cost of approximately $9 billion in 2015 alone. The study found that unvaccinated individuals were responsible for almost 80%, or $7.1 billion, of this financial burden [48].

In the context of HPV vaccination, Simms *et al.* 2020 estimated the impact of vaccine hesitancy in Japan, where HPV vaccine coverage dropped to less than 1% following reports of adverse events [49]. The study found that the vaccine crisis from 2013 to 2019 could result in an additional 24,600–27,300 cases and 5,000–5,700 deaths over the lifetime of cohorts born between 1994 and 2007, compared to if coverage had remained at around 70% since 2013 [49].

I.III. Conceptualisation of Vaccine Hesitancy

In a recent systematic review of Bussink-Voorend *et al.* 2022 that included 422 studies aiming to clarify the concept of vaccine hesitancy, three predominant conceptualisations of vaccine hesitancy emerged. These include cognitions or affect (expressing concerns, doubts, or questions and showing reluctance or unsureness about vaccination), behaviour (ranging from delay or refusal of vaccines to accepting all vaccines), and decision-making (describing individuals who are undecided or indecisive and those seeking more information to make the right decision about vaccination) [50]. The review also revealed that the concept of vaccine hesitancy is often intertwined with other concepts, such as confidence or trust, complacency, and convenience, which are usually identified as determinants of vaccine hesitancy [50].

The review also found that the conceptualisation of vaccine hesitancy varied according to the research field and vaccine type—conceptualisations focusing on decision-making predominated in public health and social science fields. In terms of cognitions or affect, terms like 'beliefs' and 'concerns' were used across all fields, while 'reluctance', 'doubts', and 'questions' were mostly used in the public health field. On the other hand, conceptualising vaccine hesitancy as a behaviour occurred in all research fields. The review found no significant differences in the conceptualisation of vaccine hesitancy between studies focusing on general vaccination and those specific to childhood vaccines [50].

I.IV. Theoretical Models of Vaccine Hesitancy

Vaccine hesitancy is a complex psychosocial phenomenon that necessitates contemporary examination through validated models; therefore, behavioural models are pivotal in vaccine hesitancy research [51]. These models provide a streamlined understanding of the diverse reasons for vaccine hesitancy, including complacency, inconvenience, lack of confidence, and rational calculation. Identifying these determinants guides tailored interventions aiming to increase vaccine uptake. For instance, emphasising motivation for the complacent, removing barriers for those finding vaccination inconvenient, and incentivising the calculative can be more effective and economical than solely trying to persuade those lacking vaccination confidence [51].

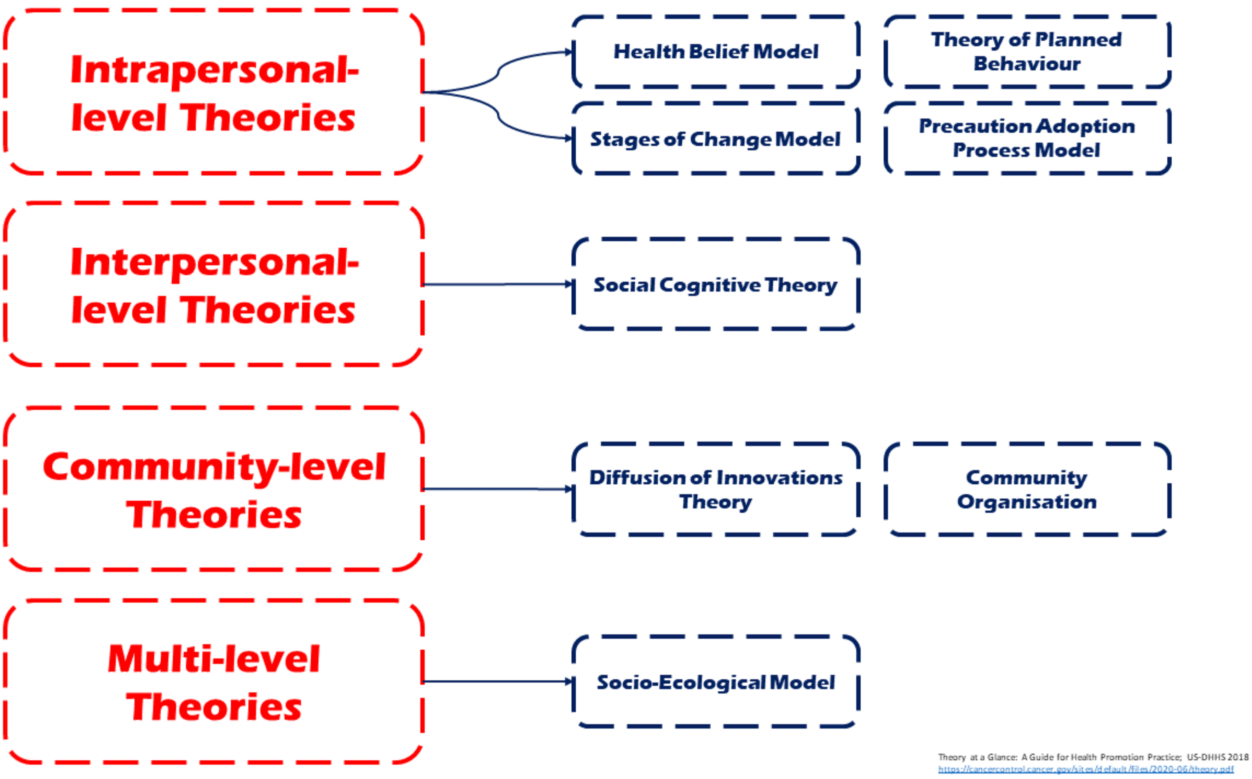
The behavioural models used to examine vaccine hesitancy can be categorised into:

i) generic models, which can be adapted to various health behaviours, including vaccination decisions, and

ii) specific models, which are specifically designed for vaccination decisions.

The generic models are based on a wide range of health promotion theories, including individual or intrapersonal-level theories, e.g., the Health Belief Model (HBM), the Theory of Planned Behaviour (TPB), the Stages of Change (Transtheoretical Model), and the Precaution Adoption Process Model (PAPM), interpersonal-level theories, e.g., the Social Cognitive Theory (SCT), community-level theories, e.g., the Diffusion of Innovations Theory (DOI), and Community Organisation and Other Participatory Models, and multi-level theories, e.g., the Socio-Ecological Model (SEM) [52]. Figure 4

Figure 4. Health Promotion Theories Applicable to Vaccine Hesitancy Research.



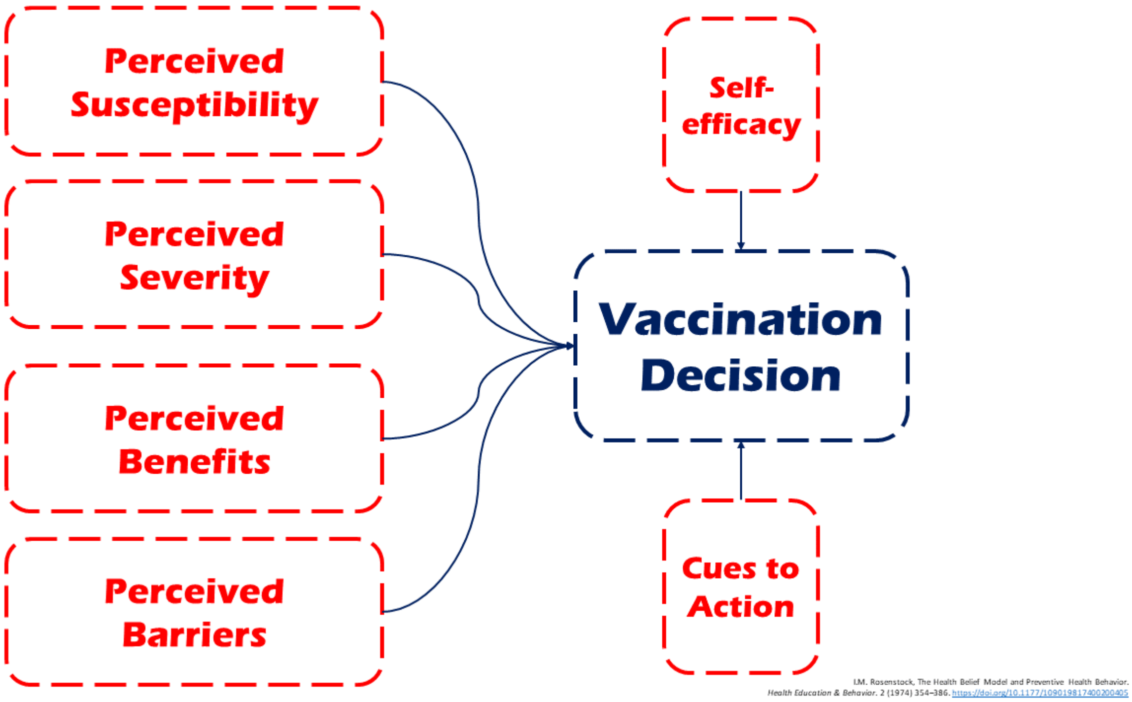
a) Health Belief Model (HBM)

Developed in the 1950s by social psychologists at the US Public Health Service, the HBM is one of the earliest and most commonly used models to explore health behaviour change. The HBM posits that people's beliefs about health problems, including perceived susceptibility, perceived severity, perceived benefits, perceived barriers, the presence of a stimulus or cue to action, and self-efficacy collectively determine their engagement in health-promoting behaviour [53,54]. Figure 5

A recent systematic review by Limbu *et al.* 2022 was conducted on the COVID-19 vaccine hesitancy studies that were based on the HBM [55]. The review included 16 studies, mostly cross-sectional studies, with 30,242 participants, and found that perceived barriers and perceived benefits were the key constructs of the HBM significantly linked to vaccine hesitancy. Specifically, an increase in perceived benefits was associated with a decrease in vaccine hesitancy, while an increase in perceived barriers was linked to an increase in vaccine hesitancy. Other HBM constructs, such as perceived susceptibility, cues to action, perceived severity, and self-efficacy, were also inversely related to vaccine hesitancy [55].

In the context of measles vaccination, a study by Smith *et al*. 2011 using the HBM found a significant correlation between US parents' beliefs about vaccines, including perceived susceptibility and perceived benefits, and their decisions to delay or refuse vaccines for their children, thereby affecting the children's vaccination coverage at 24 months [56]. This study underscored the critical role of addressing parental perceptions about vaccine safety, susceptibility to diseases, and the benefits of vaccines in improving vaccination coverage [56]. Similarly, a study in Israel by Grinberg *et al.* 2021 used the HBM to investigate the factors influencing mothers' decisions to vaccinate their children against measles. The study found that mothers' intentions to vaccinate were significantly influenced by their perceived benefits of the vaccine and the perceived severity of the disease [57].

Figure 5. Health Belief Model (HBM) Adapted to Vaccine Hesitancy Research.



Donadiki *et al.* 2014 conducted a cross-sectional study using the HBM to understand the reasons for the refusal of the human papillomavirus (HPV) vaccine among Kenyan female university students [58]. The study found that students who perceived high barriers to vaccination viewed no general or specific benefits to the vaccine and had high scores for 'general perceived barriers' were more likely to report being unvaccinated. The study concluded that the HBM constructs were useful in understanding vaccination intentions and uptake, highlighting the need for health promotion campaigns to enhance perceived benefits and reduce perceived barriers to HPV vaccination [58]. Following this, Mehta *et al*. 2013 designed and evaluated an intervention based on the HBM to increase the intent of HPV vaccination among US college male students [59]. This randomised controlled trial showed that the HBM-based intervention was effective in increasing self-efficacy for taking the vaccine, reducing perceived barriers, and enhancing perceived severity, thus promoting positive attitudes toward HPV vaccination [59].

Additionally, in the context of influenza vaccination, Chen *et al.* 2011 surveyed 2,778 Taiwanese caregivers using the HBM and found that the perceived susceptibility, perceived benefits, perceived barriers, and cues to action were the most significant predictors of vaccination [60]. Coe *et al.* 2012 conducted a cross-sectional survey-based study among US college students to understand their intentions to receive the novel H1N1 vaccine [61]. Perceived severity, perceived barriers, and cues to action through healthcare providers' recommendations were the most significant predictors of the vaccination decision of the participating students [61]. When applying HBM in the context of the 2022 monkeypox outbreak, Riad *et al.* 2022 found that the cues to action and perceived susceptibility were the most important constructs to predict vaccination acceptance among Czech healthcare professionals (HCPs) [62].

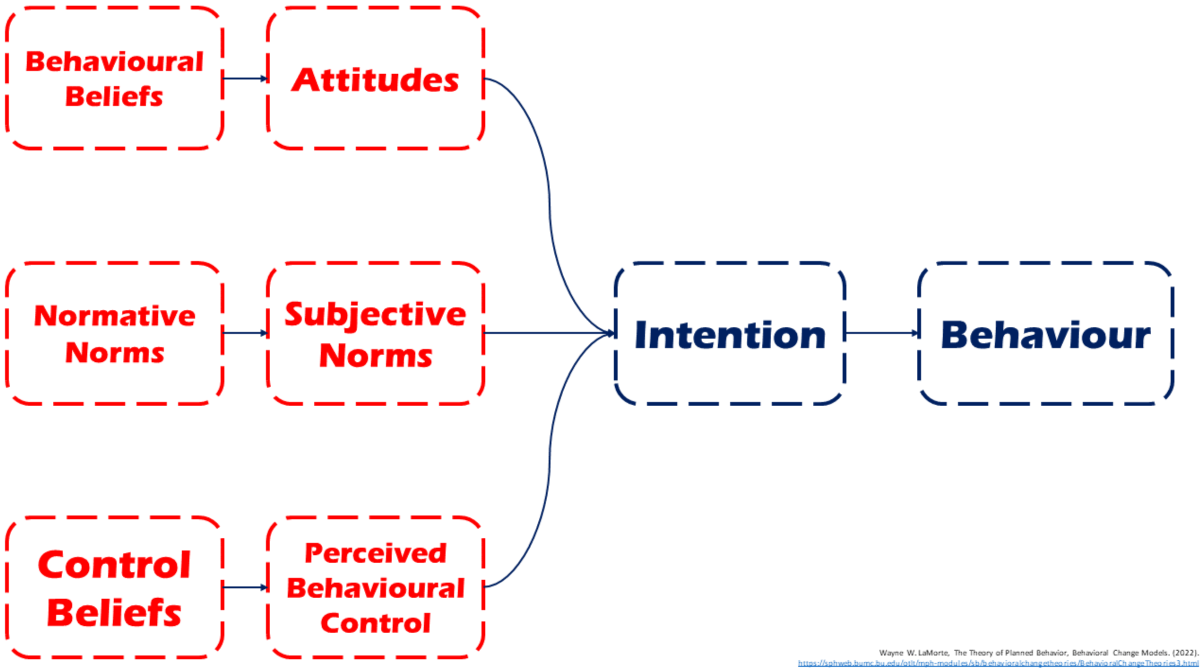
b) Theory of Planned Behaviour (TPB)

The Theory of Planned Behaviour (TPB) is a psychological framework that was proposed by Icek Ajzen in 1985 as an extension of the Theory of Reasoned Action (TRA), which Ajzen had developed with Martin Fishbein in the late 1970s [63]. The three components of the TPB are attitude (an individual's positive or negative evaluation of the behaviour), subjective norms (the perceived social pressure to perform or not perform the behaviour), and perceived behavioural control (the individual's belief about their ability to perform the behaviour) [63,64]. The theory has been applied to various domains, such as consumer psychology, social psychology, and health psychology, including vaccine hesitancy research [65,66]. Figure 6

In a study by Yahaghi *et al.* 2021, the TPB, supplemented with fear of COVID-19 and perceived COVID-19 infectability, was used to explain the intention to get vaccinated among a representative sample of 10,843 participants in Qazvin, Iran. The study revealed that perceived behavioural control, subjective norms, attitudes, and perceived COVID-19 infectability significantly explained individuals' intention to get vaccinated [67]. Likewise, in a study by Dou *et al.* 2022, the TPB was used to examine the vaccination intentions of 405 Chinese citizens, where subjective norms and perceived behavioural control were positively related to vaccination intention for the whole sample [68]. Nonetheless, attitudes were only related to males' intentions, while subjective norms were only related to females' intentions, suggesting that gender-specific strategies may be needed to boost vaccination intentions [68].

Additionally, Fan *et al.* 2021 conducted a cross-sectional survey-based study among 3,145 students from 43 universities in mainland China to predict students' intentions to uptake COVID-19 vaccination using the extended TPB [69]. The study found that students' knowledge and risk perception of COVID-19 positively influenced their attitude towards the uptake of the vaccine. However, subjective norms and perceived behavioural control were not significant predictors for the intention to uptake COVID-19 vaccination [69].

Figure 6. Theory of Planned Behaviour (TPB) Adapted to Vaccine Hesitancy Research.



In the context of HPV vaccination, Fisher *et al.* 2013 applied the TRA and TPB to understand vaccination intentions among Canadians in the vaccination age, where they found that both vaccination attitudes and perceptions of social support significantly influenced the intentions to be vaccinated in the coming semester [70]. Likewise, Askelson *et al.* 2010 conducted a study on a random sample of US mothers in rural areas to assess their intentions to vaccinate their daughters against HPV using the TPB [71]. The study revealed that attitudes were the strongest predictor of mothers' intentions to vaccinate, with subjective norms also influencing intention; however, mothers' risk perceptions, experience with STIs, and beliefs about the vaccine encouraging sexual activity were not related to intention [71]. Similarly, Catalano *et al.* 2016 found that attitudes and subjective norms were the most significant predictors of HPV vaccination intention among US college male students [72].

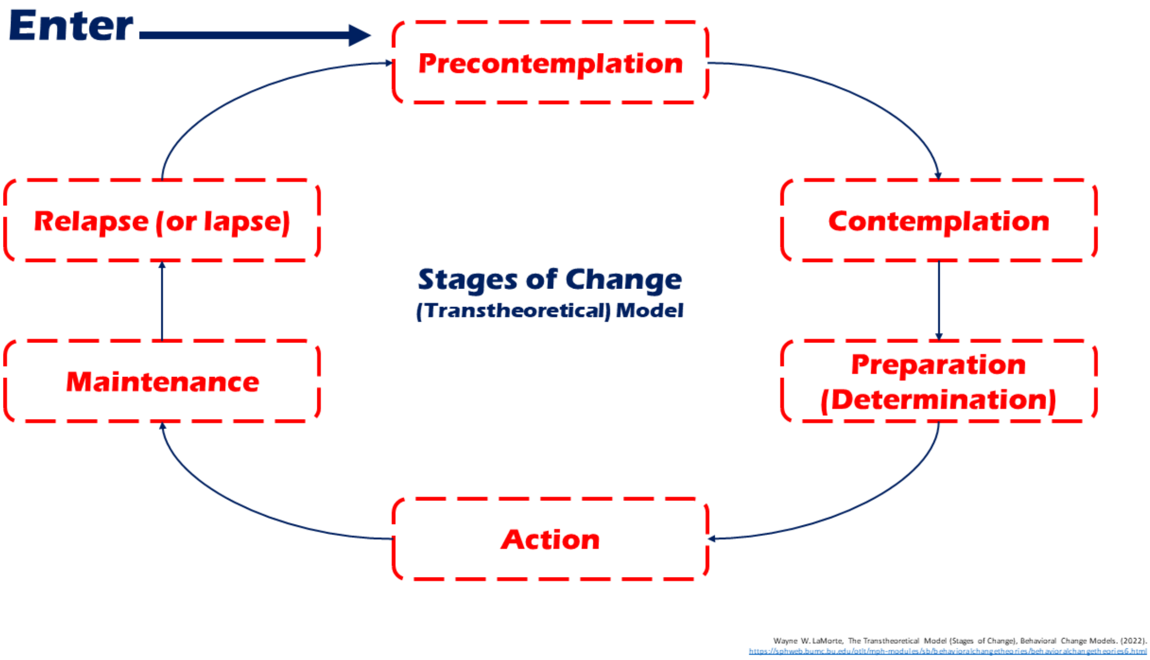
Addressing influenza vaccination, Chu *et al.* 2021 utilised the TPB to evaluate the vaccination intentions among US adults during the COVID-19 pandemic [73]. The study revealed that participants' attitudes towards the benefits of the vaccine and the influence of physicians' recommendations, a component of subjective norms, significantly contributed to the intention to get vaccinated, emphasising the crucial role of healthcare professionals in shaping vaccination intentions [73]. Likewise, Agarwal 2014 revealed that attitudes, subjective norms, and perceived behavioural control contributed to H1N1 vaccination intention among US university students [74].

c) Transtheoretical Model (TTM)

The Transtheoretical Model (TTM), or the Stages of Change Model, was created by Prochaska and DiClemente in the late 1970s to understand the process of intentional behaviour change [75,76]. The model was initially used to study smoking cessation but

has since been applied to a wide range of health behaviours, including physical exercise, alcohol consumption, and vaccine hesitancy [76–78]. It consists of several key constructs, i.e., stages of change, processes of change, decisional balance, and self-efficacy. The stages of change constitute the core of the model and include precontemplation (not ready to make a change), contemplation (considering a change), preparation/determination (ready to make a change), action (actively making changes), maintenance (sustaining the change over time), and termination/relapse (no desire to return to unhealthy behaviours and sure they will not relapse) [75,76]. Figure 7
The TTM is based on the assumption that people do not change behaviours quickly and decisively, but rather, change in behaviour occurs continuously through a cyclical process [76,79]. Therefore, the TTM is used in public health interventions to assess an individual's readiness to act on new healthier behaviours and provides strategies or processes of change to guide individuals [79]. The model suggests that effective interventions need to be stage-matched; that is, they need to target the specific barriers and facilitators that are relevant to each stage of change. Nevertheless, it has also been criticised for its linear approach to behaviour change and the lack of clarity in the definition and measurement of the stages of change. Despite these criticisms, the TTM remains a valuable tool for understanding and promoting behaviour change [75,76].

Figure 7. Transtheoretical Model (TTM) Adapted to Vaccine Hesitancy Research.



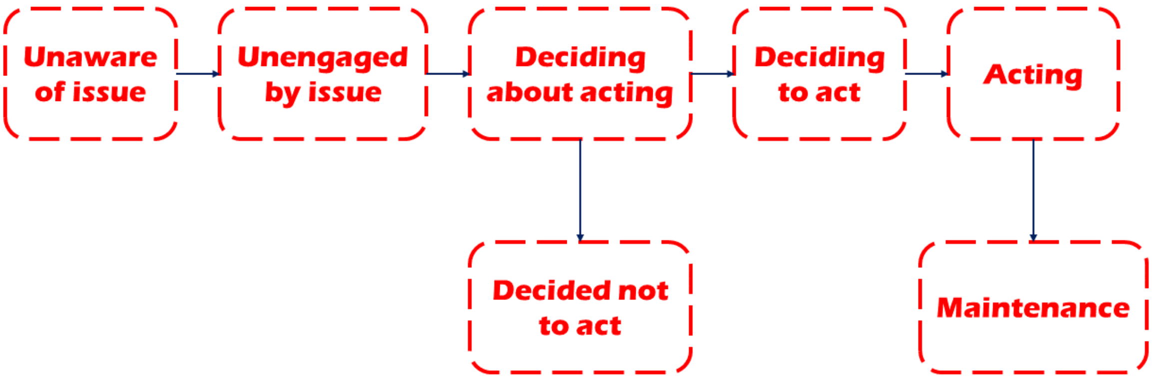
In a series of studies by Lipschitz *et al.* (2013) and Fernandez *et al.* (2016), the TTM was applied to understand HPV vaccination intentions among college students [80,81]. The studies validated TTM measures of decisional balance and self-efficacy for seeking the HPV vaccine, revealing that attitudes towards undergoing HPV vaccination and perceptions of social support for undergoing HPV vaccination contributed uniquely to the prediction of both women's and men's intentions to be vaccinated [80]. These findings underscore the value of TTM in vaccine hesitancy research, providing reliable and valid measures that can be used in TTM-tailored interventions to promote HPV vaccine uptake among college students [81]. In line with these findings, Stein *et al.* 2015 conducted a cross-sectional study among undergraduate nursing students and found a moderate correlation between attitudes/beliefs about HPV vaccination and stages of change [82]. The students with more favourable attitudes/beliefs about HPV vaccination were more likely to either be in the process of getting vaccinated or had already been vaccinated and while there was no statistical difference in attitudes/beliefs about the HPV vaccine between males and females, males were less likely to have made efforts to be vaccinated compared with females [82].

In the context of COVID-19 vaccination, Lachance-Grzela *et al.* 2022 conducted a study in New Brunswick, Canada, to identify determinants of vaccination intentions [83]. The individuals who intended to get vaccinated were more likely to report lower levels of mistrust toward authorities, higher perceived scientific consensus, and higher perceived severity of COVID-19, suggesting that addressing these factors could help move individuals from the contemplation stage to the preparation stage of change, thereby increasing vaccination uptake [83].

d) Precaution Adoption Process Model (PAPM)

The Precaution Adoption Process Model (PAPM) is a psychological model developed by Neil D. Weinstein in 1988 and has since been widely used in public health research to understand health behaviours, including vaccine hesitancy [84,85]. The PAPM consists of seven stages: unaware of the issue, unengaged by the issue, deciding about acting, decided not to act, decided to act, acting, and maintenance [86,87]. Each stage represents a different point in the decision-making process, and individuals can move forward or backward through these stages. The model suggests that different interventions may be needed at each stage to move individuals towards action [86,87]. However, the PAPM also has some limitations, such as the lack of specific variables or mechanisms that explain the transition between stages, the possibility of stage regression or skipping, and the difficulty of measuring stage membership. Therefore, the PAPM should be used in combination with other theories and methods that can complement its strengths and address its weaknesses [88]. Figure 8

Figure 8. Precaution Adoption Process Model (PAPM) Adapted to Vaccine Hesitancy Research.



Glanz K.; Rimer B.K.; Viswanath K. The Precaution Adoption Process Model. In *Health Behavior and Health Education*; 4th ed. Jossey-Bass: Hoboken, NJ, 2008. https://www.med.upenn.edu/hbhe4/part2-ch6-overview.shtml

Building upon the utility of the PAPM, Lee *et al.* 2015 conducted a study to explore the factors influencing HPV vaccination adoption stages among female university students in South Korea [89]. They identified age, economic status, doctor's recommendation, and perceived severity of cervical cancer as key drivers in transitioning from unawareness to decision-making. Furthermore, perceived benefits and self-efficacy were crucial in progressing to the action stage, thus underscoring the necessity for robust

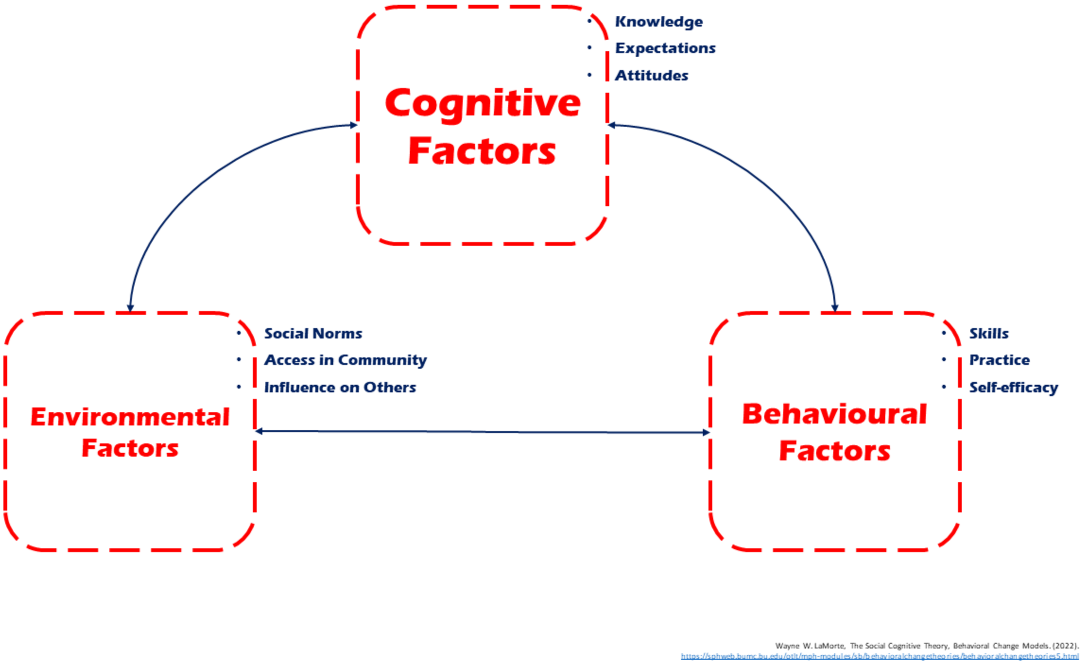
HPV vaccination campaigns and tailored strategies that emphasise health beliefs and self-efficacy [89]. Similarly, Barnard *et al.* 2017 employed the PAPM to examine HPV vaccine knowledge, attitudes, and uptake among college students in the US [90]. Their study found that while most students had a basic understanding of HPV, their perceptions of susceptibility to the virus were low, and the majority of unvaccinated students were in the early stages of decision-making related to vaccination, indicating the need for educational interventions and prompts from healthcare providers to increase HPV vaccination rates [90]. In Canada, Tatar *et al.* 219 employed the PAPM to examine HPV-related attitudes, beliefs, and knowledge longitudinally and to identify the psychosocial factors influencing HPV vaccine acceptability among parents [91]. The parents categorised as "flexible" hesitant (i.e., unengaged/undecided) showed changes over time in their HPV-related attitudes, behaviours, knowledge, and intentions to vaccinate, with factors such as greater social influence to vaccinate, increased HPV knowledge, higher family income, white ethnicity, and lower perception of vaccine-related harms being associated with higher HPV vaccine acceptability [91].

In the context of COVID-19 vaccination, Meyer *et al.* 2023 applied the PAPM to understand decision-making about the COVID-19 booster vaccine in England [88]. The majority of the participants had decided to have the booster vaccine, while a small percentage were unengaged or undecided, with factors such as beliefs in their immune system, employment status, income, vaccine knowledge, previous vaccine experience, subjective norms, anticipated regret, and academic qualifications significantly associated with these stages of decision-making [88].

e) Social Cognitive Theory (SCT)

The Social Cognitive Theory (SCT) is a psychosocial model developed by Albert Bandura in 1986 as an expansion of his 1960s works on the Social Learning Theory (SLT) [92]. According to the SCT, the likelihood of a person changing a health behaviour is influenced by three main factors: self-efficacy, goals, and outcome expectations [52]. Figure 9

Figure 9. Social Cognitive Theory (SCT) Adapted to Vaccine Hesitancy Research.



Evolving from the SLT, the SCT integrates self-efficacy and combines cognitive, behaviourist, and emotional models, thereby creating a versatile framework for behaviour change across diverse scenarios, where the six key components of the SCT include [52,93]

i) reciprocal determinism (the dynamic interaction between the person, the behaviour, and the environment),
ii) behavioural capability (knowledge and skill to perform a given behaviour),
iii) observational learning (learning by observing others' behaviours and the outcomes of those behaviours),
iv) reinforcements (responses to a person's behaviour that increase or decrease the likelihood of recurrence),
v) expectations (anticipated outcomes of a behaviour), and
vi) self-efficacy (confidence in one's ability to take action and overcome barriers).

The SCT has several limitations, including its assumption that environmental changes automatically lead to personal changes, which may only sometimes hold true. Additionally, the theory's loosely organised structure, based on the dynamic interplay between person, behaviour, and environment, leaves ambiguity about the extent of influence each factor has on behaviour, and its heavy focus on learning processes overlooks biological and hormonal predispositions that may impact behaviours. Furthermore, SCT does not sufficiently address emotion or motivation, and its broad scope can make it challenging to operationalise in its entirety [93].

In Canada, Catalano et al. 2016 applied the SCT to predict the intentions of unvaccinated college women to receive the HPV vaccine within the next six months [94]. The study revealed that self-control and situational perception were significant predictors of HPV vaccination intentions, suggesting that these SCT constructs could be targeted to increase HPV vaccination rates among this population [94]. Likewise, Priest *et al.* 2015 found that situational perception and self-control were significant predictors of vaccination intentions among female university students in the US, accounting for 22% of the variance in behavioural intentions to get vaccinated within the next six months, indicating that these SCT constructs could be targeted to increase HPV vaccination rates among the university females [95].

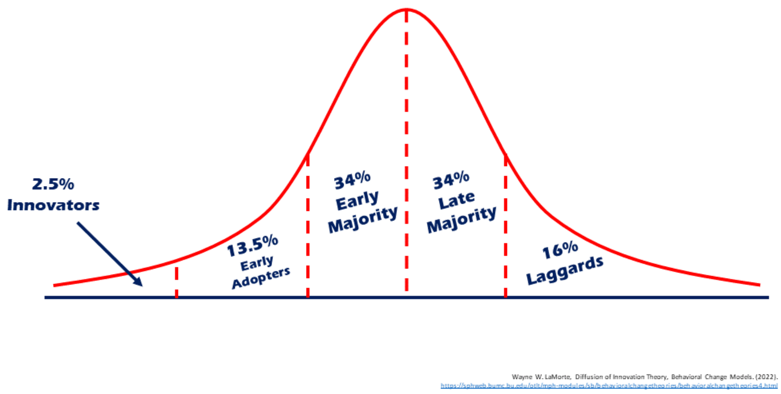
In the context of COVID-19 vaccination, AlSaeed *et al.* 2021 found that significant predictors of vaccine rejection among Saudi adults were reciprocal determinism (nationality, income, and previous COVID-19 infection), behavioural capability (knowledge about vaccine safety), self-efficacy (registration for vaccination), and observational learning (vaccination uptake following friends and family members), thus highlighting the potential of SCT in developing strategies to increase COVID-19 vaccine uptake [96]. Similarly, a study conducted in China by She *et al.* 2022 revealed that physical and self-evaluative outcome expectations, self-efficacy, norms, and job satisfaction were all significantly associated with the intention to get vaccinated, suggesting that health promotion interventions aiming to improve vaccine uptake among healthcare workers should focus on these factors [97]. In the US, Zhu *et al.* 2022 used the SCT to understand parental attitudes towards vaccinating their children against COVID-19 [98]. The personal factors, such as having younger children and identifying as Republican, along with the behavioural factor of conservative news use, were significantly associated with negative attitudes towards health officials and lower vaccination intentions, highlighting the role of political polarisation and media use in vaccine uptake [98].

f) Diffusion of Innovations Theory (DOI)

The Diffusion of Innovations Theory (DOI) is a psychosocial theory developed by E.M. Rogers in 1962 that explains how new ideas or products spread through a population or social system over time [99,100]. The DOI identifies five stages of the diffusion process: awareness, persuasion, decision, implementation, and confirmation. It also categorises potential adopters into five groups based on their willingness to adopt an innovation: innovators, early adopters, early majority, late majority, and laggards [99]. Therefore, the theory suggests that different strategies are needed to reach different groups and to overcome barriers to adoption. Figure 10

In the context of public health, DOI has been used to understand and promote the adoption of health behaviours, including vaccination intentions, especially with newly developed vaccines [101]. According to Rosen and Goodson, the DOI can be effectively applied to understand the role of school nurses as opinion leaders in promoting HPV vaccination among youth [102]. In line with this proposition, Cohen *et al.* 2013 conducted 83 in-depth interviews with 18-26-year-old women to understand the disparities in knowledge, attitudes, and practices between HPV vaccine adopters and non-adopters according to the DOI framework [103]. The study underscored the importance of targeted risk communication strategies, supportive social influences, and interpersonal networks in accelerating the diffusion of the HPV vaccine while also highlighting the role of erroneous beliefs and safety concerns as barriers to vaccine uptake [103]. In Indonesia, the use of celebrities as opinion leaders in HPV vaccination campaigns has been found to significantly influence the millennial generation's acceptance of the vaccine, according to a study on the Indonesia Cervical Cancer Prevention Coalition's strategies [104]. The study highlighted that the celebrities' role in the social system makes the vaccination message more relevant, memorable, reliable, and trustworthy, although it also acknowledges the need for interpersonal communication [104]. Building on this, a study applied the DOI to examine correlates of HPV and cancer knowledge and intention to vaccinate against HPV among African American adolescent females, demonstrating that the DOI model effectively integrates all factors influencing HPV vaccine uptake and provides an optimal framework to explain HPV knowledge and vaccination intent in this population [105].

Figure 10. Diffusion of Innovations Theory (DOI).



In the context of COVID-19 vaccination, Mo *et al.* 2021 used the DOI to understand vaccination intentions among university students in mainland China [106]. The perceived efficacy of the COVID-19 vaccine, use of social media for vaccine-related information, openness to experience, and descriptive norms were all positively associated with the intention to receive the vaccine, with the associations being stronger among those with lower levels of openness to experience [106]. Additionally, the study

by Hunter-Mullis *et al.* 2022 found that early adoption of the COVID-19 vaccine among adults in rural Indiana was significantly associated with the perceived attributes of trialability, relative advantage, and compatibility, as per the DOI [107]. The study also revealed that age and political ideology were significant moderators of complexity and relative advantage, respectively, suggesting that health education strategies should focus on building trust in vaccine safety, increasing the short-term benefits of vaccination, and promoting relatability to personal values [107].
Expanding further, Hensel *et al.* 2011 utilised the DOI to examine the adoption of new vaccination administration techniques among perinatal nurses, specifically the shift away from aspirating for blood return prior to intramuscular immunisation [108]. The majority of nurses were still in the knowledge phase regarding this change, with the primary barrier to adoption being a lack of knowledge, thus underscoring the importance of effective communication, organisational factors, and the nature of the innovation itself in promoting change [108].

g) Community Organisation Model (COM)

The Community Organisation Model (COM) is a participatory decision-making process that empowers communities to improve their health through active participation of the community in identifying key health issues and strategies to address them [109,110]. The COM, which includes the collective identification of problems and the development of strategies, is integral to health education and promoting preventive behaviours like vaccination [111]. Through fostering empowerment, individuals and communities can gain better control over their health, driving the adoption of preventive measures and promoting a more proactive approach to health outcomes [111]. According to Rothman's classification, community organising can be divided into three types: locality development, social planning, and social action. Locality development emphasises the process, focusing on group identity and capacity building, while social planning is task-oriented and relies on expert problem-solving. Social action combines both elements, aiming to enhance the community's problem-solving capacity and effect tangible changes to address social injustices [112]. Table 2 summarises the common concepts that are present in the different approaches, which are referred to as community organisation [52].

Table 2. Summary of Community Organisation Model (COM) Common Features.

Feature	Description
Empowerment	A proactive process wherein individuals gain control and command over their personal lives and their communities.
Community Capacity	Traits inherent to a community which impact its ability to recognise, rally around, and tackle problems.
Participation	Involvement of community members as equivalent contributors, embodying the principle, "Never perform tasks for others that they can undertake themselves".
Relevance	Community organisation that commences "from the existing state or conditions of the people".
Issue Selection	Identification of immediate, specific, and attainable goals for modification that galvanise and reinforce community power.
Critical Consciousness	Understanding of the social, political, and economic dynamics that lead to societal challenges.

In a recent scoping review of 38 studies conducted by Kadariya *et al.* 2023, it was found that community involvement significantly impacts various health outcomes, including lifestyle habits, sexual and reproductive health, healthcare access and equity, and management of substance abuse and chronic diseases, although the models of community organising differed across the studies [113]. No single model or framework was shown to be universally superior in effecting positive social change in health through community organising. The review emphasised the necessity for standardisation in the implementation and evaluation of these programs and the vital role of partnerships between public and non-governmental sectors in sustaining community-driven health promotion efforts [113]. Additionally, Santilli *et al.* 2016 demonstrated that employing a robust community organising approach in community health needs assessment resulted in reliable data, enhanced access to residents, and leverage of community-driven interventions, thereby underscoring the significance of community engagement in health needs assessment [114].

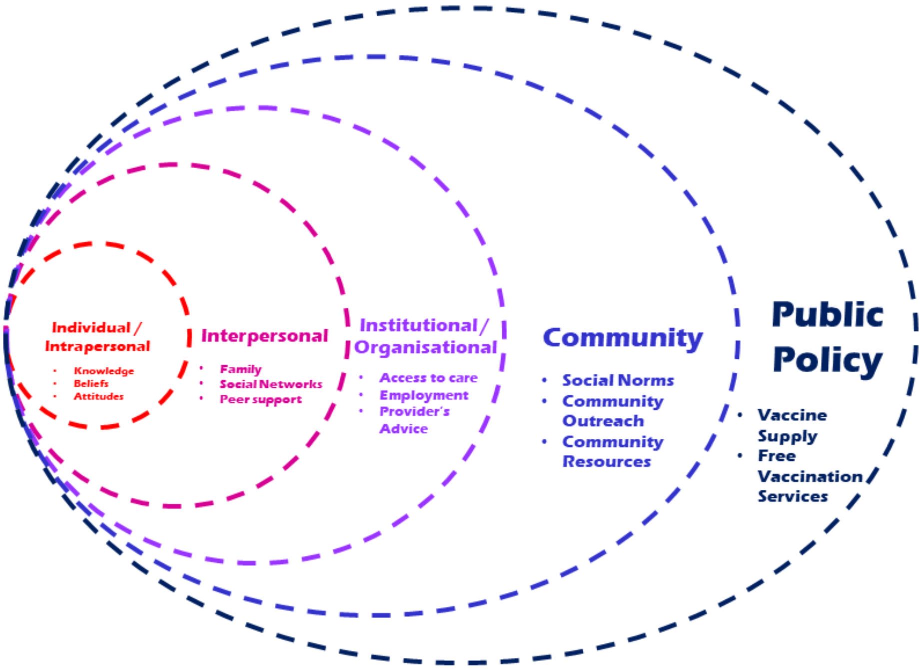
h) Socio-Ecological Model (SEM)

The socio-ecological model (SEM), first introduced by Urie Bronfenbrenner in the 1970s, is a multi-level framework used to understand the complex interplay of individual, interpersonal, community, and societal factors that shape behaviours, including health behaviours [115]. SEM's core tenet is that behaviour is affected by multiple levels of influence: individual or intrapersonal level (knowledge, attitudes, behaviours), interpersonal or social level (family, friends, peers), organisational level (institutions, structures, systems), community level (relationships among organisations), and public policy level (national laws and regulations). These levels are interconnected, meaning changes in one level can impact the others [116]. Figure 11

In public health and health promotion research, SEM has been instrumental in designing interventions that target multiple levels of influence, thereby increasing their effectiveness. For example, interventions aimed at reducing tobacco use have targeted individual behaviours (smoking cessation aids), interpersonal influences (peer and family support), organisational policies (smoke-free workplaces), community norms (anti-smoking campaigns), and public policies (tobacco taxes) [117].

In a recent systematic review by Al-Jayyousi *et al.* 2021, it was found that the factors influencing public attitudes towards COVID-19 vaccines spanned the different levels of the SEM, including sociodemographic characteristics, individual factors, and social and organisational aspects, along with certain characteristics of the COVID-19 vaccines themselves [118]. Understanding these diverse elements that shape public attitudes is crucial for planning effective, evidence-based multilevel interventions to enhance global vaccine uptake [118]. Further cementing the importance of the SEM, a US-based study examined parents' intention to vaccinate their children against COVID-19 [119]. It revealed that factors such as parents' vaccination status, trusted information sources, and the age of children significantly influenced vaccination intentions, suggesting the need for dyadic programs promoting both child and parent vaccination and highlighting the potential effectiveness of peer diffusion strategies, particularly among parents expressing vaccination uncertainty [119]. Likewise, a study on pregnant and lactating women in Kenya used the SEM to explore the complex decision-making process concerning COVID-19 vaccination [120]. The study identified numerous factors influencing vaccination decisions, including contextual influences such as myths, interpersonal norms, and religion, individual and group influences like safety and risk perception, and vaccine-specific issues such as availability, accessibility, and eligibility [120]. Riad *et al.* 2021 applied the SEM in a multi-centre, multi-national cross-sectional survey-based study investigating factors influencing COVID-19 vaccination willingness among dental students. The machine learning analysis suggested five important predictors: the economic level of the country where the student resides and studies, the individual's trust in the pharmaceutical industry, misconceptions of natural immunity, beliefs about the risk-benefit ratio of vaccines, and attitudes towards novel vaccines [121]. The country's economic level was a contextual predictor, with the remaining factors being individual predictors, emphasising the multi-level influences on vaccination willingness in accordance with SEM principles. These insights underscore the importance of tailored communication strategies to increase vaccine demand [121].

Figure 11. Socio-Ecological Model (SEM) Adapted to Vaccine Hesitancy Research.



Theory at a Glance: A Guide for Health Promotion Practice; US-DHHS 2018
https://cancercontrol.cancer.gov/sites/default/files/2020-06/theory.pdf

The specific models are particularly designed to explore the psychosocial determinants underpinning vaccination intentions, willingness, or behaviours. These models, limited to the intrapersonal and interpersonal levels, include the WHO-SAGE Matrix Model, the 3-C model (confidence, complacency, convenience), the 5-C model (confidence, complacency, convenience, calculation, collective responsibility), the 7-C model (confidence, complacency, convenience, calculation, collective responsibility, compliance, conspiracy), and the 5-A model (access, affordability, awareness, acceptance, activation) [122,123]. It is pivotal to differentiate these theoretical models from psychometric instruments such as the multi-dimensional vaccine hesitancy scale (MVHS) and parent attitudes about childhood vaccines (PACV). While these models serve as a source of inspiration and guidance for such instruments, they are not to be conflated with them [50,124].

i) The WHO-SAGE Matrix Model

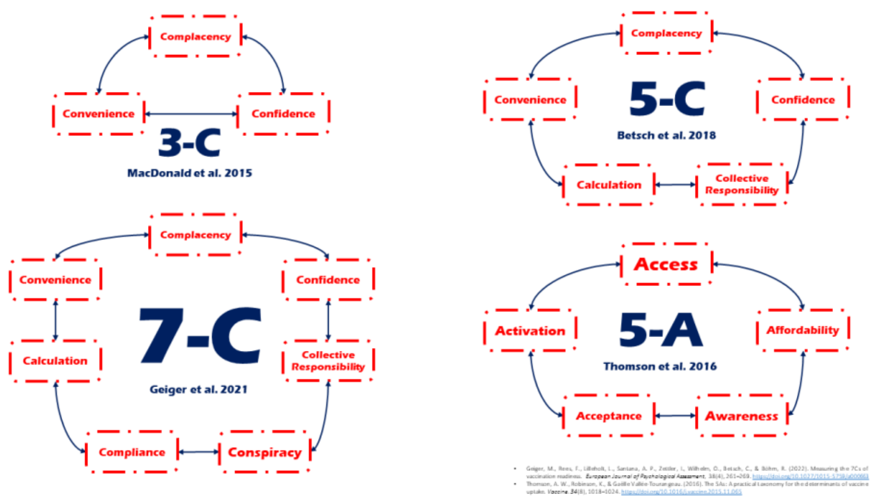
In 2012, the WHO-SAGE was tasked to develop a definition and explanatory framework for vaccine hesitancy as a response from the WHO to the decaying levels of vaccine coverage globally [125–127]. The first-ever specific model developed to explain vaccine hesitancy was the WHO-SAGE Matrix Model, which comprises three core categories influencing vaccination behaviour [126]. The first category, "Contextual Influences", includes factors such as historical, sociocultural, environmental, health system/institutional, economic, or political elements. The second, "Individual and Group Influences", encompasses personal perception of the vaccine or influences that arise from social or peer dynamics. The final category, "Vaccine/Vaccination-specific Issues", deals with aspects directly related to vaccines or their usages, such as the mode of administration or the vaccination schedule. This matrix model provides a thorough framework for identifying and understanding the diverse elements contributing to vaccine hesitancy [126]. Figure 12

Figure 12. WHO-SAGE Matrix Model of Vaccine Hesitancy [126].

j) The 3-C Model

The 3-C model was developed by the WHO-SAGE in 2014 to simplify their initial matrix model [3]. This model delineates three primary factors contributing to vaccine hesitancy: Confidence, Complacency, and Convenience [127]. The 3-C model identifies "Confidence" as trust in vaccine effectiveness, safety, delivery systems, and the integrity of policymakers. "Complacency" arises when perceived risks of VPDs are low, diminishing the perceived need for vaccination. Finally, "Convenience" encompasses the accessibility, affordability, and comprehensibility of vaccines and their delivery services. The influence and interaction of these factors can vary between countries, within a country, and over time, creating a dynamic and complex environment for vaccine acceptance [127]. Figure 13

Figure 13. The 3-C, 5-C, 7-C, and 5-A Models of Vaccine Hesitancy.



Research indicates a limitation of the 3-C model in its application to specific vaccines, as general vaccine confidence does not necessarily correlate with acceptance of particular vaccines like the influenza vaccine [128]. Therefore, the model may require vaccine-specific adjustments to account for unique factors such as strain variability and disease severity misconceptions [128].

k) The 5-C Model

The 5-C model was proposed in 2018 by Cornelia Betsch and her team at the University of Erfurt, Germany, as an advancement over the preceding models like the 3-C model [129]. Betsch's team introduced two unique dimensions, "calculation" and "collective responsibility", in response to the need for a more nuanced understanding of vaccination behaviours [129].

'Calculation' highlights the role of extensive information-seeking, particularly online, in an individual's vaccination decision-making process. This aspect acknowledges the influence of the digital age on health-related decisions and conflicting information sources. On the other hand, 'collective responsibility' encapsulates an individual's acknowledgement of the wider societal implications of their vaccination decisions. It encompasses the concept of herd immunity, underlining the role of individual vaccinations in protecting the broader community, particularly those who are unable to receive vaccinations themselves [129]. Figure 13

By incorporating these new dimensions, the 5-C model serves as a valuable tool for crafting targeted interventions to enhance vaccine uptake [130]. Nevertheless, the 5-C model has limitations when applied to various vaccines. Notably, the "calculation" factor, indicative of extensive information-seeking behaviour, did not influence vaccine uptake for single-dose pneumonia and shingles vaccines. This suggests that the model's applicability may vary depending on the specific vaccine under consideration [131].

l) The 7-C Model

The 7-C model, also known as Vaccination Readiness, was first developed in 2020, extending the 5-C model by adding two new components: compliance and conspiracy [123]. The model was developed by researchers including Mattis Geiger Cornelia Betsch, Robert Böhm, and others, and was funded by grants from the Lundbeck Foundation, University of Copenhagen and the German Research Foundation [132]. The model went through several iterations in its development to improve its psychometric properties and refine the definitions of its components based on empirical studies [123,133]. Figure 13

"Compliance" refers to the support for societal monitoring and sanctioning of people who are not vaccinated, embodying the idea of enforcement of vaccination as a societal norm. Also, "Conspiracy" represents the tendency towards conspiracy thinking and belief in fake news related to vaccination, indicating the influence of misinformation and unfounded theories on vaccination readiness [123].

m) The 5-A Model

The 5-A model of vaccine hesitancy, also known as the 5As taxonomy, was developed by Angus Thomson in 2016. The model is structured around five core dimensions: Access, Affordability, Awareness, Acceptance, and Activation. The "Access" component refers to the availability and convenience of vaccination services. "Affordability" addresses the financial cost associated with obtaining vaccines. "Awareness" involves information and knowledge about vaccines and vaccination programs. "Acceptance" relates to the attitudes, beliefs, and perceptions about vaccines

and their importance, while "Activation" captures interventions that prompt or nudge people towards getting vaccinated, such as SMS reminders [134]. Figure 13
The 5As taxonomy has already been used to facilitate mutual understanding of the primary determinants of suboptimal vaccine coverage within inter-sectorial working groups, serving as a valuable tool in developing targeted and effective solutions to improve vaccination rates [122].

I.V. Drivers of Vaccine Hesitancy

Vaccine hesitancy embodies a multifaceted and context-dependent decision-making process; thus, identifying and understanding its determinants is an inaugural step for effective interventions in communities [135]. The WHO-SAGE Matrix Model of 2014 provides a list of potential drivers of vaccine hesitancy, which are summarised in Table 3. Based on this model, the WHO-SAGE developed a compendium of survey questions to scrutinize the root causes of vaccine hesitancy. However, there is still a need for these questions to be validated across low, middle, and high-income settings, with the findings subsequently disseminated to aid future refinement of such tools [125,126]. Additionally, the WHO EUR Guide to Tailoring Immunisation Program (TIP) emerges as a promising instrument. Primarily, TIP supports the identification and prioritisation of vaccine-hesitant populations, diagnoses the barriers to vaccination, and aids in designing context-specific, evidence-informed responses to vaccine hesitancy [135].

Table 3. The WHO-SAGE Matrix Model of Vaccine Hesitancy Determinants [125].

Level	Determinant	Description
Contextual Influences	Communication and Media Environment	Media platforms shape perceptions about vaccines, either positively or negatively, while enabling influential individuals and groups to sway public sentiment.
	Influential Leaders, Gatekeepers, and Anti- or Pro-vaccination Lobbies	Opinions of community figures like religious authorities or celebrities significantly impact attitudes towards vaccination, affecting acceptance or hesitancy.
	Historical Influences	Past experiences, such as the Trovan trial in Nigeria, can erode public trust, influencing vaccine acceptance, especially when coupled with the influence of leaders and media.
	Religion/Culture/Gender/Socio-economic	Religious doctrines, cultural norms, and gender biases can interact to shape attitudes towards vaccination, contributing to vaccine hesitancy.
	Politics/Policies (Mandates)	Government-imposed vaccination mandates can incite hesitancy, driven by opposition to enforced vaccination, independent of safety concerns.
	Geographic Barriers	Despite trust in vaccines and health services, geographical inaccessibility to healthcare facilities can contribute to vaccine hesitancy.
	Pharmaceutical Industry	Perceived prioritisation of profit over public health in the pharmaceutical industry, leading to distrust, can spur vaccine hesitancy, which can extend to government entities if they are viewed as influenced by industry interests.
Individual & Group Influences	Experience with Past Vaccination	Previous interactions with vaccinations, either negative or positive, can sway vaccine hesitancy or acceptance. Personal or second-hand experience with Vaccine-Preventable Diseases (VPD) or Adverse Events Following Immunization (AEFI) can be decisive.
	Beliefs, Attitudes about Health and Prevention	The notion that natural immunity is superior or that alternative health practices can substitute vaccination can induce vaccine hesitancy.
	Knowledge/Awareness	Vaccination decisions are influenced by the level of awareness, accurate knowledge, or misinformation. Proper knowledge does not guarantee acceptance, and misperceptions can still result in acceptance, despite causing hesitancy.

	Health System and Providers' Trust and Personal Experience	Trust in authorities and prior experiences with healthcare processes influence vaccine acceptance. Complicated procedures or unfavourable personal interactions can trigger hesitancy.
	Risk/benefit (Perceived, Heuristic)	Perceptions of risk, or lack thereof, affect vaccine acceptance. Complacency arises when disease risk is seen as low, reducing the perceived need for vaccination.
	Immunisation as a Social Norm vs. Not Needed/ Harmful	Social norms and peer influences significantly affect vaccine acceptance or hesitancy.
Vaccine-Specific Influences	Risk/benefit (Scientific Evidence)	Scientific data on risk/benefit, and a history of safety issues can induce hesitancy, even if these issues have been addressed. Incidents such as adverse effects from certain vaccines can evoke such responses.
	Introduction of a New Vaccine or a New Formulation	Hesitancy may arise towards a new vaccine due to perceived insufficient testing or the belief that it is unnecessary. Conversely, a high perceived risk of the vaccine-preventable disease can promote acceptance.
	Mode of Administration	The method of vaccine delivery can influence hesitancy, with convenience and fear factors playing a role. For instance, oral or nasal methods might be preferred over injections due to fear or distrust in healthcare worker's competency.
	Design of Vaccination Program / Mode of Delivery	Hesitancy can be influenced by the delivery approach, such as door-to-door campaigns or inconvenient healthcare center hours.
	Reliability and/or Source of Vaccine Supply	Confidence in the vaccine supply system and its origin can impact vaccine acceptance. Hesitancy can occur if there is distrust in the continuity of the supply or the source's integrity.
	Vaccination Schedule	Despite understanding the importance of preventing diseases, individuals may resist adhering to recommended schedules, due to factors like frequency or age of vaccination.
	Costs	Financial constraints can cause hesitancy even if there is confidence in the vaccine and delivery system. Conversely, freely provided vaccines might be perceived as less valuable.
	Role of Healthcare Professionals	Healthcare professionals serve as role models, and their hesitation due to lack of confidence in a vaccine's safety or necessity can influence patients' willingness to vaccinate.

In May 2022, the WHO released its inaugural position paper on the behavioural and social drivers (BeSD) of vaccine uptake, introducing novel tools and indicators to assess these drivers for both childhood and COVID-19 vaccinations [136]. The BeSD of vaccination are defined as "beliefs and experiences specific to vaccination that are potentially modifiable to increase vaccine uptake". However, these drivers often go unmeasured or, if measured, lack validity, conceptual clarity, and comparability across different contexts, limiting the ability to track trends and make cross-country comparisons [137]. Existing measures frequently oversimplify the issue, focusing on individual perspectives while overlooking social influences and practical matters associated with vaccination [136].

The BeSD framework of 2022 outlines four primary domains that influence vaccination: "Thinking and Feeling", "Social Processes", "Motivation", and "Practical Issues". Each domain is characterised by specific, modifiable, and measurable elements tied to vaccination.

i) **Thinking and Feeling:** This domain encompasses individuals' cognitive and emotional responses towards vaccines and vaccine-preventable diseases. Key constructs within this domain include attitudes towards vaccines, beliefs about the safety and effectiveness of vaccines, and trust in the medical system.

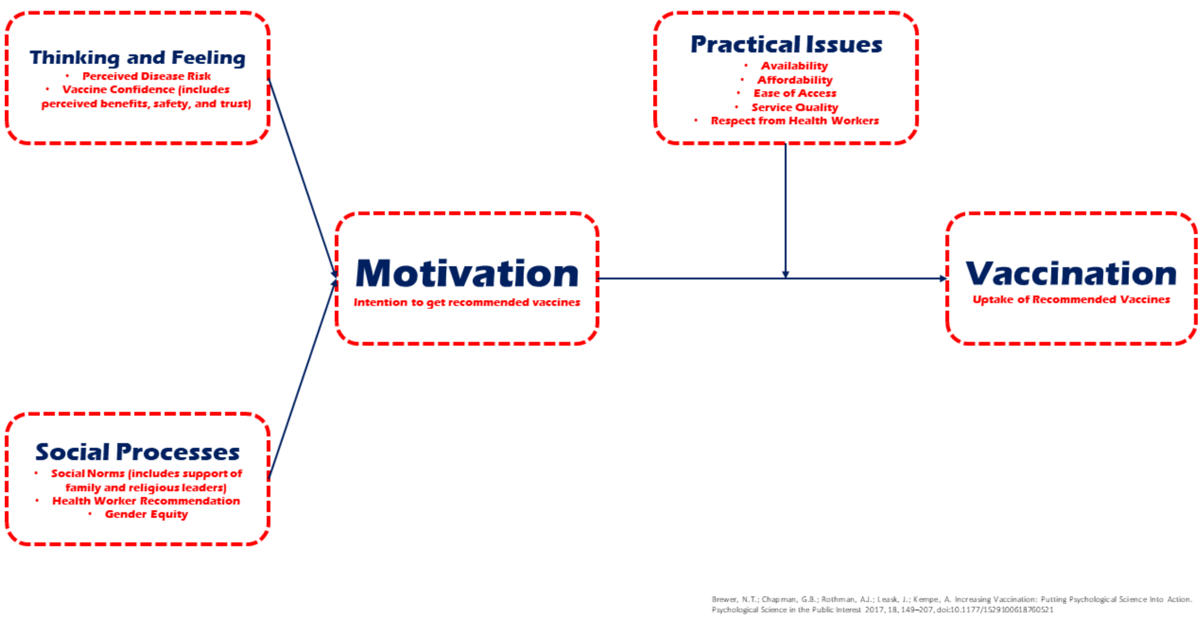
ii) **Social Processes:** This domain involves social norms and recommendations concerning vaccination. It can include the influence of one's community, family, or peer group on vaccination decisions, as well as the impact of broader social norms or cultural beliefs about vaccination.

iii) **Motivation:** This domain refers to individuals' willingness, intention, or hesitancy to get vaccinated. Here, 'Vaccine Hesitancy' is defined as a conflicted or opposing attitude towards vaccination. This includes individuals who are unsure about getting vaccinated or who may refuse vaccination altogether.

iv) **Practical Issues:** This domain concerns the logistical aspects of getting vaccinated. This could include barriers to access such as distance to the clinic, cost of transport, availability of vaccines, or the convenience and ease of the vaccination process.

In this framework, significant constructs within each domain, such as vaccine confidence in “Thinking and Feeling” and vaccine hesitancy in “Motivation”, have been identified and defined. Vaccine confidence is described as the trust in the efficacy, safety, and reliability of vaccines, whereas vaccine hesitancy is characterised as a conflicted or opposing attitude towards vaccination, inclusive of intentions and willingness. This updated definition separates hesitancy from the resulting behaviour, in contrast to what was laid down earlier by the WHO-SAGE in 2014 when vaccine hesitancy was defined as the delay of vaccination, thus providing a more precise understanding and measurement of behaviours and their multiple influences [138]. Figure 14

Figure 14. The Behavioural and Social Drivers (BeSD) of Vaccination Framework [137,138].



I.VI. Strategies to Address Vaccine Hesitancy

Addressing vaccine hesitancy is an imperative task in today's global health landscape. Through understanding and implementing a multitude of strategies, we can confront this challenge and promote a broader acceptance of vaccination.

In the systematic review of Jarrett *et al.* 2015, strategies implemented across diverse global contexts to address vaccine hesitancy were assessed. The review, encompassing both peer-reviewed articles from 2007 to 2013 and grey literature up to October 2013, found that few strategies had been evaluated for their impact on vaccination uptake or changes in knowledge, awareness, or attitude [139]. The review classified the interventions into three major categories: a) dialogue-based interventions, b) non-financial incentives, and c) reminder-recall interventions.

Dialogue-based interventions, including engagement of religious or traditional leaders, social mobilisation, and use of mass and social media, generally showed positive impacts in addressing vaccine hesitancy, although these varied in success and were notably dependent on proper targeting, understanding of the target audience, and effective management, as summarised in Table 4.

Table 4. Dialogue-based Interventions for Vaccine Hesitancy [139].

Intervention	Description
Religious/Traditional Leaders' Involvement	By engaging religious or traditional leaders, this intervention aims to eliminate misconceptions and build trust. Success hinges on understanding the target audience, fostering open discourse, and integrating with existing community structures.
Social Mobilisation	Aimed at specific vaccine-resistant populations, social mobilisation efforts can yield positive results through targeted, multi-level communication.
Social Media	Utilising social media platforms can encourage adherence among those already partaking in vaccination schedules. However, vigilant management is necessary to avoid exploitation and the approach may not reach the most hesitant or marginalized groups.
Mass Media	Mass media campaigns can raise health service awareness in under-informed populations, but success may be constrained by underlying complexities that require more personalized interventions.
Communication Tool-Based Training for Healthcare Workers	Communication tools for healthcare workers can foster better vaccine uptake, especially for certain vaccines like EPI and DTP3. The strategy's effectiveness, often linked to one-way communication, varies depending on the level and nature of vaccine hesitancy.
Information-Based Training for Healthcare Workers	Despite often showing limited improvements in overall vaccination uptake, information-based training for healthcare workers has resulted in notable successes for specific vaccines such as HepB and DTP/OPV, possibly linked to increased healthcare worker confidence.

Non-financial incentives like food supplies demonstrated a notable impact on vaccine uptake in low-income communities by addressing basic needs and fostering confidence. However, the singular use of reminder-recall interventions showed limited effectiveness due to the multifaceted nature of vaccine hesitancy. Thus, a multi-component approach employing multiple strategies and focusing on increasing knowledge and awareness of various vaccines was found to be more effective across different income settings [139].

Research indicates that health literacy also plays a vital role in shaping vaccination attitudes and behaviours. As evidenced by a recent study on HIV health literacy among Czech adolescents, school type and gender impacted knowledge levels, indicating certain groups may be more vulnerable to low literacy regarding infections like HIV [140]. Such findings underline the need to account for demographic factors and context when addressing knowledge gaps related to vaccine hesitancy.

Healthcare providers play a critical role in combating vaccine hesitancy; and their attitudes, knowledge, and practices significantly influence their patients' vaccine acceptance; however, as the study by Agrinier *et al.* 2017 indicated, discrepancies can arise between their personal vaccine practices and the recommendations they make for their patients [141]. To maintain the success of vaccination programs, it is essential to identify and understand vaccine hesitancy among healthcare providers and develop tailored strategies to address it [142].

In the context of COVID-19 vaccination, overcoming vaccine hesitancy—fuelled by rapid vaccine development, misinformation, polarised socio-political climate, and logistical challenges—was crucial to the success of vaccination programs [143]. Despite the evident value of vaccines during lethal COVID-19 surges, achieving widespread vaccination necessitated multilevel, evidence-based strategies to encourage behavioural changes. Survey research showed significant vaccine hesitancy in the US, indicating that an effective healthcare system response, in conjunction with policy and community initiatives, is crucial to ensuring vaccine uptake. Interpersonal, individual-level, and organisational interventions, guided by social, behavioural, communication, and implementation science, could play a vital role in bridging this gap and boosting population adoption of COVID-19 vaccination [143]. Table 5 summarises the evidence-based interventions suggested by Rutten et al. 2021 to address COVID-19 vaccine hesitancy, stratified according to the SEM structure (individual, interpersonal, organisational, community and policy) [143].

Table 5. Rutten's Interventions Proposed to Address COVID-19 Vaccine Hesitancy [143].

Level	Intervention	Description
Intrapersonal/ Individual	Frame Messages in Terms of Gain	By emphasizing the benefits of vaccination, a technique known as gain-framing, patient education materials can effectively promote prevention. It focuses on the positive outcomes of vaccination, such as protection for oneself and one's family.
	Offer Novel Information about the Disease	Offering unique insights about COVID-19, rather than explicitly trying to counter common misconceptions, can be more effective. This approach involves tailoring patient reminders and addressing common patient barriers and concerns.
	Appeal to Altruism and Prosocial Behaviour	Communicating that vaccination is a way of protecting one's family or community can also effectively promote vaccination. Appeals to altruism and social responsibility have been found to be impactful.
	Address Patient Barriers and Counter Misperceptions	Addressing patient concerns directly and providing factual alternative narratives can help overcome vaccine hesitancy. If correcting misconceptions about the vaccine is needed, it is crucial to frame messages in a way that resonates with the audience's values, and avoid repeating misinformation.
Interpersonal	Clinician Recommendations	Clinician suggestions significantly boost vaccination rates, as healthcare providers are generally the most trusted sources of information, especially concerning COVID-19.
	Strong Recommendations	The strength and quality of a clinician's recommendation influence vaccination rates, potentially enhancing vaccine confidence and reducing safety concerns.
	Presumptive, Announcement-style Language	Observational studies and clinical trials suggest that using assertive language (e.g., "Today you will be getting your vaccine") rather than participatory language leads to higher vaccination acceptance.
Organisational / Institutional	Standing Orders	Standing orders enable nurse-led vaccinations without individual orders by clinicians. This method enhances vaccination accessibility and streamlines the process, overall increasing the vaccination rates.
	Audit and Feedback	Audit and feedback interventions provide regular presentations of vaccination performance metrics to clinicians. This systematic appraisal of vaccination rates leads to improvements in coverage. The addition of peer performance or benchmark performance metrics can also promote normative behaviour among clinicians.

	Reminders / Recalls	This strategy involves direct communication with patients to inform them that a vaccination is due, coming due, or past due. Reminders and recalls have consistently shown effectiveness in boosting vaccination rates.
	Point-of-care Prompts	Point-of-care prompts are alerts about recommended vaccinations during clinical encounters. These prompts can be based on the review of current vaccination records or through electronic clinical decision support, and they are proven to be effective in enhancing vaccination rates.
Community & Public Policy	Reducing Out-of-pocket Expenses	This policy-level strategy decreases the patient's financial burden related to vaccinations, indirectly aiding in overcoming vaccine hesitancy by facilitating a positive context for additional clinical measures.
	Offering Vaccination Programs in Schools and Child Care Centres	Implementing vaccination schemes in educational institutions improves accessibility, thus indirectly easing vaccine hesitancy by providing a supportive milieu for further clinical strategies.

In conclusion,

- Vaccine hesitancy is a major global health issue, leading to approximately 1.5 million child deaths annually from preventable diseases.
- The roots of vaccine hesitancy can be traced back to the late 18th century, around the time of the smallpox vaccine's introduction.
- Theoretical models of vaccine hesitancy are classified as general models that are adapted to vaccine hesitancy research, e.g., HBM, TPB, and SEM, and specific models that were designed particularly for the vaccination context, e.g., WHO-SAGE Matrix Model, 3-C, and 5-A.
- The WHO's 2022 behavioural and social drivers (BeSD) framework identifies four key domains influencing vaccination decisions: Thinking and Feeling, Social Processes, Motivation, and Practical Issues.
- Multi-component interventions are proven to be the most effective in addressing vaccine hesitancy.

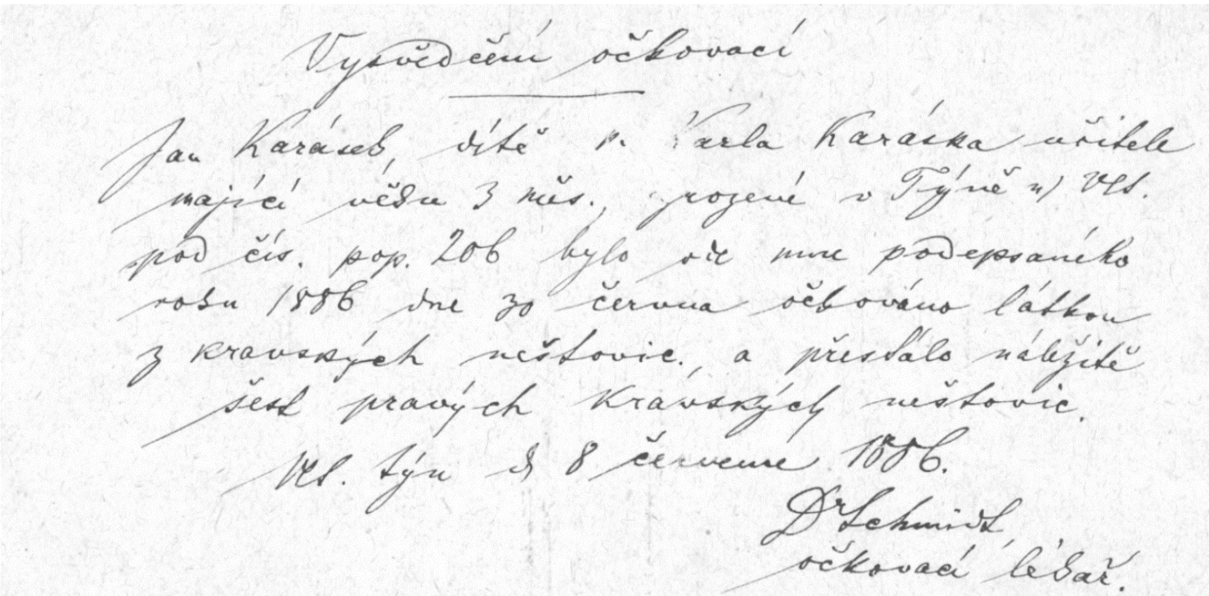
Exploring Vaccine Hesitancy: Insights from the Czech Republic

II.I. Vaccine Story: From Austro-Hungarian Empire to Today

The history of immunisation in the Czech Republic, historic Bohemia, can be traced back to the reign of Maria Theresa in the 18th century when the practice of variolisation, a precursor to modern vaccination, was introduced to combat smallpox epidemics [144–146]. Following the contraction of smallpox by Maria Theresa in 1767, which also led to the death of her daughter Josefa and the wives of Joseph II, the inception of variolation trials in 1768 demonstrated effectiveness, providing immunity to four imperial children. Despite these initial successes, the practice encountered considerable resistance due to public apprehension, medical malpractice, and the financial burden it imposed on local authorities. The commencement of the first structured variolation programme in 1800 in Brunn am Gebirge, precipitated by enhancements in variolation techniques and increased bureaucratic regulation, marked significant progress in public health within the region [144–146].

Initiated in 1821, compulsory smallpox vaccination was instituted under an imperial decree by the Austrian emperor, František I, representing the first legal mandate for vaccination in the region [147]. This extensive immunisation against smallpox persisted for the ensuing 160 years until global eradication of the disease prompted the cessation of the vaccination programme in the Czechoslovak Socialist Republic (CSSR) in 1980 [147,148]. Figure 15

Figure 15. Copy of smallpox vaccination certificate (1886) issued for a recently vaccinated three-month-old Jan Karasek [148].


Vysvědčení očkovací
Jan Karásek, dítě p. Karla Karáska učitele
mající věku 3 měs., rozené v Týně n/ Vlt.
pod čís. pop. 206 bylo od mne podepsaného
roku 1886 dne 30 června očkováno látkou
z kravských neštovic, a přestálo náležitě
šest pravých kravských neštovic.
Vl. Týn d. 8 července 1886.
Dr Schmidt
očkovací lékař.

Following Louis Pasteur's pioneering work on rabies vaccination in the 1880s, the practice of immunisation against the disease was first introduced in Bohemia in 1918 [147]. Additional compulsory immunisations were implemented in 1946 for diphtheria, 1947 for tuberculosis, 1952 for tetanus, 1958 for whooping cough, 1960 for cerebral palsy, 1969 for measles, 1986 for rubella, 1987 for mumps, and finally in 2001 for viral hepatitis B and Haemophilus influenzae B [149]. Table 6 summarise the compulsory vaccines in the Czech Republic (historic Bohemia) in chronological order [150].

Table 6. List of vaccines in the Czech Republic in chronological order [148,150].

Vaccine	Discovery	Implementation in the Czech Republic
Smallpox Vaccine	1796: Edward Jenner	1821: Imperial Decree 1919 – 1980: Mandatory
Rabies Vaccine	1885: Louis Pasteur	1918: Prophylaxis
Cholera Vaccine	1894: Waldemar Haffkine	Unspecified
Typhoid Vaccine	1896: Richard Pfeiffer and Almroth Wright	Unspecified
BCG Vaccine	1921: Albert Calmette and Camille Guérin	1923: Introduced 1953: Mandatory 2010: Limited to high-risk groups only
Diphtheria Vaccine	1923: Alexander Glenny and Gaston Ramon	1946: Mandatory 1958: DiTePe
Pertussis Vaccine	1923: Thorvald Madsen	1951: Mandatory 1958: DiTePe
Tetanus Vaccine	1927: Gaston Ramon and Christian Zoeller	1958: DiTePe
Yellow Fever Vaccine	1932: Andrew Sellards and Jean Laigret	Unspecified
Influenza Vaccine	1937: Jonas Salk	Unspecified
Tick-born Encephalitis Vaccine	1949: Smorodincev	1987: Introduced
Inactivated Polio Vaccine	1954: Jonas Salk	1957: Introduced
Oral Polio Vaccine	1957: Albert Sabin	1960: Introduced
Measles Vaccine	1960: John Enders	1969: Introduced / Mandatory
Rubella Vaccine	1962: Meyer and Parkman	1982: 12-year-old (mandatory) 1986: 2-year-old (mandatory)
Mumps Vaccine	1966 – 1968: Maurice Hilleman	1987: Introduced / Mandatory
Meningitis C Vaccine	1968: Emil Gotschlich	1995: Introduced
Meningitis A Vaccine	1971: Emil Gotschlich	1995: Introduced
Varicella Vaccine	1973: Michiaki Takahashi	Unspecified
Hepatitis B Vaccine	1976: Philippe Maupas	1982: Introduced (risk groups)
Human Papilloma Virus Vaccine	1990: Ian Frazer and Jian Zhou	2012: Recommended (13-14-years-old girls) 2018: Recommended (boys)
COVID-19 Vaccine	2020 - 2022	2020: Introduced

Serological surveys in the Czech Republic, which started in the 1960s, were conducted annually until 1988, after which the frequency was adjusted to 5 to 12 years due to epidemiological and financial considerations [151]. These surveys have informed immunisation policies, enabled rapid disease elimination, like polio, and provided insights into population immunity and disease incidence to shape public health interventions [151].

Mass vaccination policies in the Czech Republic successfully eliminated the incidence of VPDs such as polio and diphtheria, dramatically reducing them from hundreds of cases in 1955 to zero by 2005 [150]. Moreover, the comprehensive immunisation programs also led to a profound decrease in mortality rates for all VPDs, effectively reducing deaths from few hundreds in the mid-20th century to virtually none by the early 21st century [152]. Table 7

Table 7. Number of Detected and Mortality Cases of VPDs in the Czech Republic (1945 – 2005) [150,152].

Number of Detected Cases of VPDs in the Czech Republic (1955 – 2005)								
Year	**Polio**	**Diphtheria**	**Pertussis**	**Tetanus**	**Measles**	**Rubella**	**Mumps**	**Tuberculosis**
1955	133	1,232	30,402	27	42,246	0	0	1,683
1965	0	21	657	1	22,591	8,763	47,559	198
1975	0	1	16	0	17,998	3,059	100,553	58
1985	0	0	35	0	26	68,024	58,063	46
1995	0	0	14	0	1	420	5,303	67

2000	0	0	187	0	9	749	120	21
2001	0	0	124	3	6	894	107	0
2005	0	0	330	0	0	5	747	6
Number of Mortality Cases of VPDs in the Czech Republic (1945 – 2005)								
Year	**Polio**	**Diphtheria**	**Pertussis**	**Tetanus**	**Measles**	**Rubella**	**Mumps**	**Tuberculosis**
1945	16	828	433	85	160	0	3	749
1950	13	139	166	57	179	0	1	306
1955	3	81	46	18	42	1	2	53
1960	1	13	4	1	48	1	0	11
1961 – 1970	0	12	12	1	291	1	4	26
1971 – 1980	0	0	0	0	0	0	3	3
1981 – 2000	0	0	0	0	0	0	1	1
2000 – 2005	0	0	1	0	0	0	0	0

In the last few decades, the Czech Republic has witnessed an increase in anti-vaccination sentiments, coinciding with the rise of freedom of speech that followed the dissolution of the Soviet Union. The internet, media, and social networks have contributed to the propagation of these views, with notable opponents including physician Ludmila Eleková, Tomáš Lebenhart, Jan Vavrečka, and natural scientist Anna Strunecká [153]. Their main arguments can be summarised in the following points:

A) The incidence of childhood infectious diseases is extremely low.
B) The post-vaccination complications rates of vaccines are high.
C) Vaccination, they argue, poses a greater risk than the diseases themselves.
D) In most developed Western countries, vaccination is voluntary and not compulsory.

These arguments are presented to support their claim that mandatory vaccination should be abolished, despite the fact that in countries where vaccination is only voluntary, a decrease in the vaccination rate has been observed, which has led to reduced collective immunity and consequently the occurrence of smaller or larger epidemics of infectious diseases [154].

Organisations like Paracelsus and Rozalio have emerged to give structure to these views, both advocating for the end of compulsory vaccination [155–157]. Paracelsus, established in 2002, draws from foreign sources and online materials to further their cause. Rozalio, on the other hand, founded in 2007, states they are not against vaccination per se, but against compulsory vaccination, championing the individual's freedom of choice [155]. Together with the League of Human Rights, they have proposed amendments to the law and have amassed a significant social network following [157]. However, the discourse has been complicated by concerns over the unavailability of monovalent measles vaccines, with some parents refusing the MMR vaccine, despite the established effectiveness and safety of combined vaccines [158].

Table 8 enumerates Rozalio organisation's twenty proposed changes to the vaccination policies in the Czech Republic, which span five categories: adjustments to the vaccination schedule, vaccination in educational institutions, a long-term strategy for safer vaccination, choice of vaccine suppliers and their availability and reimbursement, and changes to advisory bodies. These changes include recommendations such as delaying the initiation of vaccination, allowing for more flexibility in vaccine scheduling for children, expanding the list of contraindications, providing comprehensive health monitoring of vaccinated individuals, ensuring better vaccine availability, and optimising the composition of the National Immunization Commission (NIKO) [158].

Table 8. A list of 20 claims proposed by Rozalio [158].

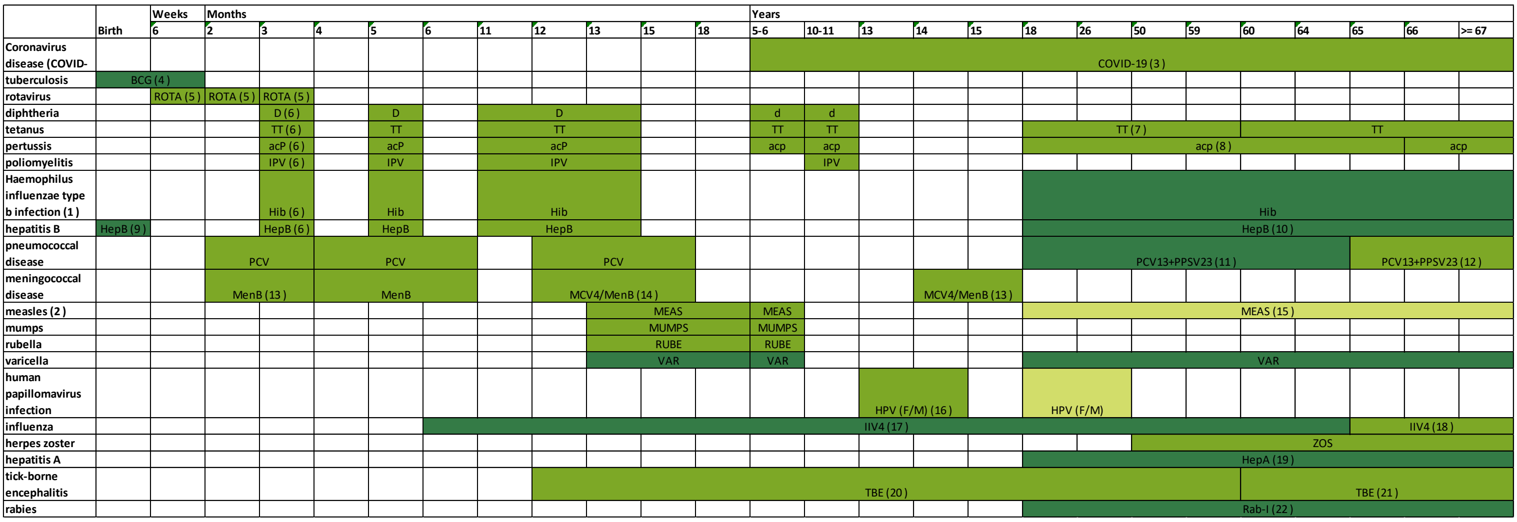
Category	Claim

Alterations to the Vaccination Schedule	1) Suggestion to separate the administration of hexavaccine and pneumococcal vaccines.
	2) Proposal to delay the initiation of vaccination to the 12th week of a child's life.
	3) Advocacy against setting an upper limit of 18 months for MMR vaccination.
	4) Proposal to introduce a single-disease measles vaccine to ensure vaccine availability.
	5) Suggestion to delay hepatitis B vaccination to between 12 and 13 years of age, introducing the possibility of using specific combinations of vaccines in infancy.
	6) Proposal to adjust the vaccination rules for premature infants, shifting to a higher gestational age and a 2+1 scheme.
Vaccination in Educational Institutions	7) Advocacy for private kindergartens and children's groups to accept children without vaccination limitations.
	8) Proposal to eliminate the vaccination requirement for recuperation actions.
Safer Vaccination - A Long-term Strategy	9) Suggestion to expand the list of contraindications.
	10) Advocacy for vaccinating children only when they are in a favourable health condition.
	11) Proposal for comprehensive health monitoring of vaccinated individuals.
	12) Advocacy for expanding centres for vaccination of stigmatized children and adults.
	13) Suggestion to educate doctors about vaccination and potential adverse effects.
	14) Proposal to add a leaflet to each vaccination card with post-vaccination behaviour advice, potential adverse reactions, and a space for parents to note concerning reactions.
Selection of Vaccine Suppliers, Their Availability, and Reimbursement	15) Advocacy for better vaccine availability and more alternatives for compulsory vaccination.
	16) Proposal for vaccines to be reimbursed up to the price of the state-funded vaccine.
	17) Advocacy for greater state involvement in selecting vaccine suppliers.
	18) Proposal to ban advertisements for specific vaccines.
Advisory Bodies	19) Suggestion to optimize the composition of the National Immunization Commission (NIKO).
	20) Proposal to form a working group composed of laypeople and experts.

II.II. Present-Day Vaccination Coverage in the Czech Republic

As of April 2023, the vaccination calendar of the Czech Republic comprises nine mandatory vaccines for children including diphtheria, tetanus, pertussis, polio, hepatitis B, Haemophilus influenzae type b (Hib), measles, mumps, and rubella, while BCG for only high-risk children. In addition, HPV, pneumococcal and meningococcal vaccines are only recommended [159]. Figure 16

Figure 16. Vaccination Calendar of the Czech Republic, ECDC Vaccine Scheduler [159].

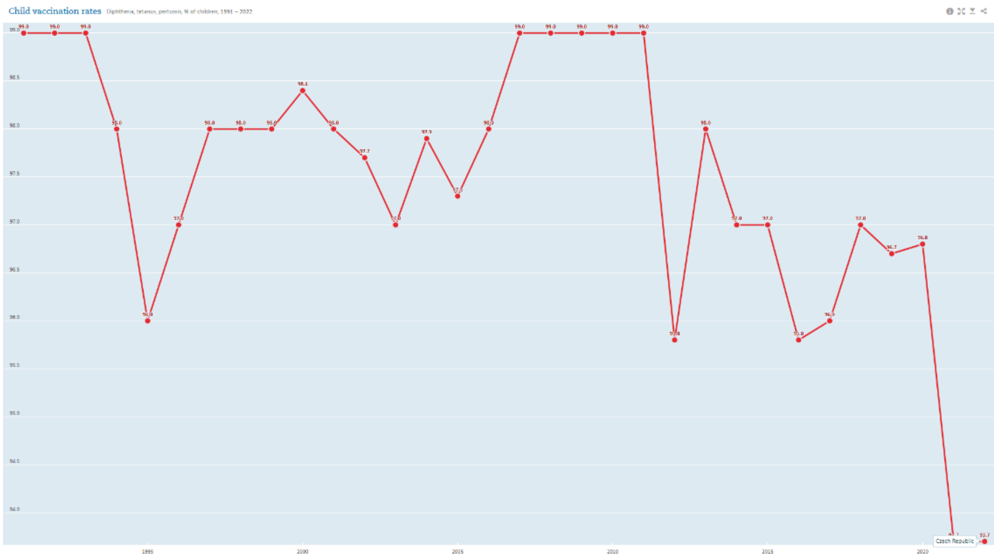


1. Vaccinations for specific risk groups are covered by health insurance.
2. Mandatory measles vaccination for newly employed at infectious or dermatovenerological wards aged 18 and above.
3. Reference link

4. At-risk babies receive specific vaccinations from 4 days to 6 weeks after birth.
5. Certain vaccinations are only recommended and not funded by National Health system or insurance.
6. Hexavalent vaccine's first dose is given end of 2nd month, with two months intervals for next, and the third at 11-13 months of child's age.
7. Booster dose given between 25-26 years of age, then every 10 - 15 years.
8. Pertussis vaccination is recommended from the 27th gestational week of every pregnancy.
9. Babies born to HBsAg-positive mothers receive first dose within 24 hours of birth by law.
10. Mandatory 3 doses of a specific vaccine for certain at-risk groups with no history of vaccination.
11. Any PCV or PPSV23 is recommended for various high-risk groups.
12. Reference link
13. MenB and MCV4 vaccines are covered by health insurance for immune-disordered individuals of all ages, and small infants.
14. From January 2022, MenB and MCV4 vaccinations will be funded under certain conditions.
15. Reference link
16. 3rd dose of MenB. Vaccination rules are the same as point 13-14.
17. Catch-up vaccinations for those newly admitted to infectious or dermatovenerological wards.
18. Gender-neutral vaccination for 13-14-year-olds is covered by health insurance since September 2019.
19. Vaccination for at-risk groups of any age is recommended and covered by insurance.
20. Certain vaccinations are recommended and covered by health insurance.
21. General recommendation for whole population: 2 doses if susceptible and no history of vaccination.
22. Recommended vaccinations: 3 doses, re-vaccination every 3-5 years. Not funded by National Health system.

According to the latest report of the Organisation for Economic Co-operation and Development (OECD), the level of diphtheria, tetanus, and pertussis (DTP) vaccination coverage of 2022 in the Czech Republic was 93.7% which is the lowest since 1991 (99%). Moreover, the level of measles vaccination coverage was 96.6% in 2022 as compared to 98% in 1991 [160]. Figure 17

Figure 17. Diphtheria, Tetanus, and Pertussis (DTP) Vaccination Coverage in the Czech Republic [160].



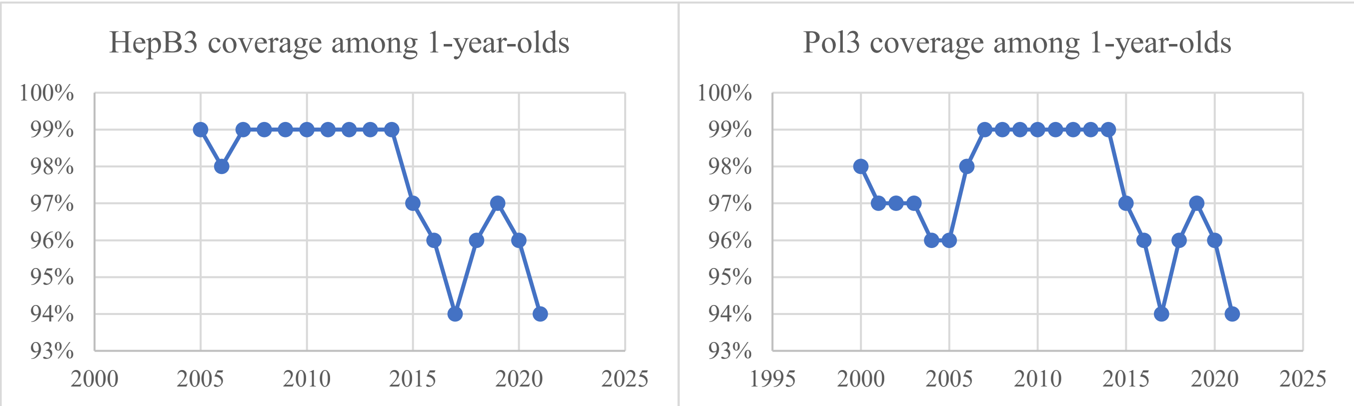
Other mandatory childhood vaccinations exhibited a steady decline over the last two decades, such as Hepatitis B vaccine (HepB3) that declined from 99% in 2005 to 94% in 2021, and polio vaccine (Pol3) from 98% in 2000 to 94% in 2021. Figure 18

The recent review of Chlíbek *et al.* 2021 demonstrated that insufficient vaccine imports in the Czech Republic have led to limitations in vaccination coverage, exemplified by the projected maximum coverage of 10.1% for influenza in the 2021/2022 season [161]. This coincides with a decrease in vaccinations among certain groups in 2020, including those aged 65 and over and institutionalised persons, due to various factors such as the COVID-19 pandemic. Coverage was also low among chronically ill patients. Comparatively, there was a decrease in tetanus vaccinations but a small increase in vaccination against tick-borne encephalitis in 2020. However, nearly half of those vaccinated failed to complete the basic vaccination schedule [161].

In a study conducted across 29 European countries, it was found that mandatory vaccination policies were associated with higher vaccination coverage and lower measles incidence rates [162]. However, only the Czech Republic and Latvia offered options for nonmedical vaccination exemptions, requiring either receipt of vaccination information or a written refusal, a practice which can potentially undermine the effectiveness of such policies by opening avenues for non-compliance [162].

Smetana *et al.* 2017, discovered a potential gap in measles protection among adults in the Czech Republic, despite the country's implementation of measles vaccination in the National Immunization Program since 1969 [163]. The study found that measles antibody seropositivity decreases over time after vaccination, and this, coupled with a limited natural booster and an initially one-dose vaccination schedule, might leave adults born after the implementation of vaccination less protected against measles [163].

Figure 18. Hepatitis B (HepB3) and polio (Pol3) Vaccination in the Czech Republic [28].

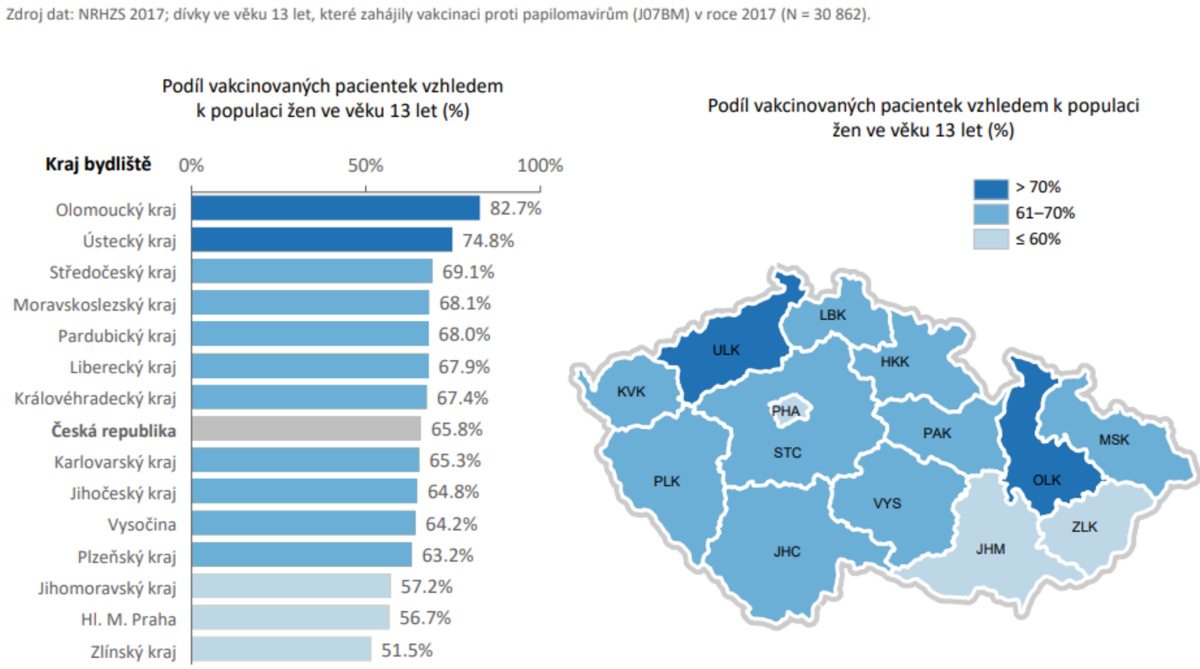


Moreover, Duval *et al.* 2016 highlighted a considerable disparity in vaccination coverage between Roma and non-Roma children in Central Europe [164]. While the Czech Republic had a higher-than-average coverage at 95.3%, the likelihood of Roma children being vaccinated remained significantly lower. This underscores the need for in-depth understanding of vaccination factors among the Roma and policies enhancing their healthcare access [164].

In the review of Nguyen-Huu *et al.* 2020 on HPV vaccination, the Czech Republic was noted for its facilitative measures to boost vaccine uptake [165]. The country adopted a gender-neutral vaccination strategy, providing the vaccine free of charge for the target groups. Furthermore, unlike many regions, parental consent was not mandated for vaccination in the Czech Republic, potentially easing access to the vaccine. Nevertheless, despite these measures, the Czech Republic maintained only a moderate VCR [165].

In 2017, coverage of HPV vaccination in the Czech Republic showed regional disparities, as the proportion of vaccinated 13-year-old females relative to the total female population varied across different regions. Olomouc region had the highest rate (82.7%), followed by Ústí nad Labem region (74.8%) and Central Bohemian region (69.1%), while Zlín region had the lowest rate (51.5%), followed by Prague the capital city (56.7%) and South Moravian region (57.2%) [166]. Figure 19

Figure 19. HPV Vaccination Coverage of 13-year-old Females in the Czech Republic [166].



Regarding seasonal influenza vaccination, Blank *et al.* 2018 observed a significant variation in vaccination coverage rates (VCRs) across Europe, with the VCR for HCPs in the Czech Republic being notably the lowest at 7% [167]. In addition, the VCR among those living with medical risk conditions in the Czech Republic was also on the lower end at 20% [167]. This pattern was noticed during the 2007/08 season, with those over 65 years in the Czech Republic presenting a notably low influenza vaccination coverage rate of 13.9%, likely influenced by the lack of full vaccine subsidy [168]. Considering the comparatively higher vaccination uptake among high-risk groups in other European countries, it becomes evident that enhanced efforts are necessary, especially in countries like the Czech Republic, where vaccinations are not fully subsidised or even partially so [168].

Kynčl *et al.*'s 2023 study highlighted an extremely low influenza vaccination coverage of less than 2% among pregnant women in a Prague maternity hospital, despite them being a priority group in the Czech Republic [169]. The researchers emphasised the need for increased awareness and implementation of vaccination recommendations in routine antenatal practice to boost vaccination rates [169].

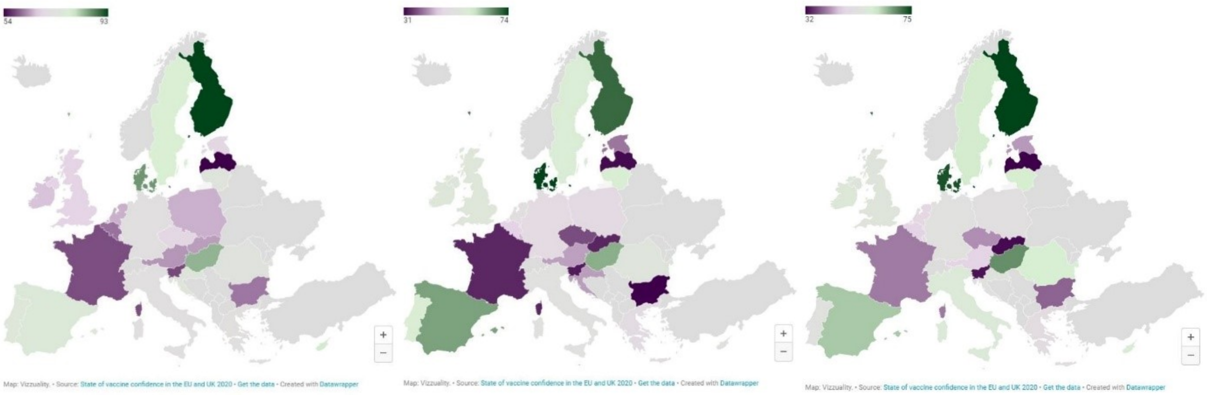
II.III. Benchmarking Vaccine Hesitancy: A European Perspective

To understand the dynamics of vaccine hesitancy more comprehensively in the Czech Republic, it is necessary to examine it within the broader European context. This cross-national comparison provides a robust framework for identifying patterns and deviations in vaccine attitudes. As an illustration of this broader context, the “State of Vaccine Confidence in the EU” project was launched in 2018 to monitor trends of public trust in vaccines across the EU member states and the UK [170]. Under the management of the Vaccine Confidence Project™ (VCP) at the London School of Hygiene & Tropical Medicine (LSHTM) and in collaboration with the Health and Food Safety Directorate-General of the European Commission, the project employs a broad array of methodologies such as large-scale surveys and in-depth analyses, aiming to intricately map out the landscape of vaccine attitudes [170].

According to the "State of Vaccine Confidence in the EU" 2022 report, in the Czech Republic, higher levels of education correlated with increased agreement in the general importance, safety, and effectiveness of vaccines and their compatibility with beliefs [171]. On the topic of confidence in the seasonal influenza vaccine, the Czech Republic was among the countries with the lowest agreement that this vaccine aligns with personal or religious beliefs. Interestingly, Czech healthcare professionals also reported one of the lowest likelihoods of recommending the seasonal influenza vaccine and the COVID-19 vaccine to pregnant women, with only 60.5% and percentages under 90%, respectively [171].

In the 2020 report, the Czech Republic exhibited the most significant gender disparities in the EU, with females showing less overall confidence in vaccines compared to their male counterparts [172]. Also, general practitioners (GPs) in the Czech Republic were found to be among the least likely to recommend MMR (measles, mumps, and rubella), seasonal influenza, and HPV (human papillomavirus) vaccines to patients. The study revealed that only 68% of surveyed GPs in the Czech Republic would recommend the HPV vaccine, the lowest among all 28 countries surveyed [172]. Additionally, 69%, 36%, and 42% of Czechs strongly agreed that vaccines were important, safe, and effective, respectively. This made the Czech Republic in the 14th, 23rd, and 22nd position out of 28 countries, respectively [173]. Figure 20

Figure 20. Public Confidence in Vaccines in 2020 in Europe [173].



a) vaccines are important; b) vaccines are safe; c) vaccines are effective

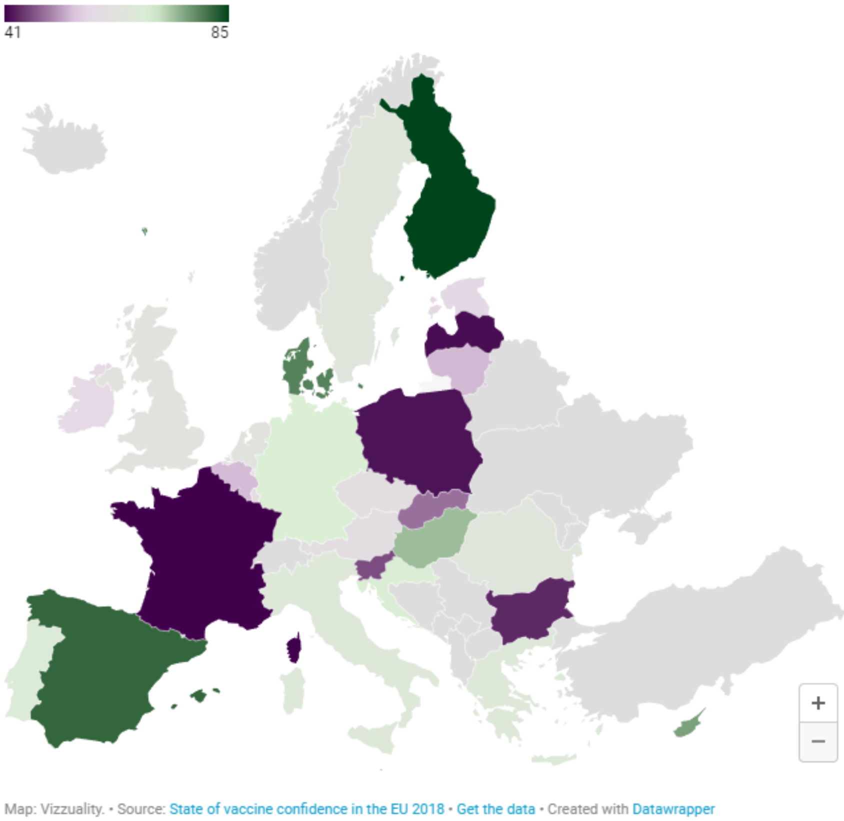
The 2018 report revealed that the Czech Republic has witnessed a decrease in confidence in the safety of vaccines among its public and GPs populations since 2015 [174]. More specifically, 36% of Czech GPs surveyed did not agree that the MMR vaccine was safe, and 29% did not believe it was important. Furthermore, the report indicated a significant gender disparity in the Czech Republic, with females being less likely than males to agree that vaccines are safe. Lastly, only 25.2% of GPs in the Czech Republic stated that they were likely to recommend the seasonal influenza vaccine to pregnant women [174]. Additionally, 61% of Czechs strongly agreed that vaccines were important, safe, and effective. This put the Czech Republic in the 15th position out of 28 countries [174]. Figure 21

Mascherini *et al.* 2022 analysed a survey of 29,755 participants from all 27 EU member states and found a significant correlation between heavy social media usage and increased COVID-19 vaccine hesitancy [175]. Within this pan-European assessment, the Czech Republic emerged as the sixth highest in terms of vaccine refusal rate (29.7%) after Bulgaria (59.6%), Latvia (45.7%), Croatia (41.2%), Slovenia (39%), Poland (32.5%), and Lithuania (31%), thus underscoring the urgency to address vaccine hesitancy within the Czech context [175].

In a recent study by Wester *et al.* 2022, frequent prayer was found to correlate with increased COVID-19 vaccine hesitancy among older adults in Europe [176]. Notably, the Czech

Republic was among the countries where this correlation was evident. However, in a contrasting scenario, Slovakia exhibited a different pattern, where frequent prayer was associated with lesser vaccine hesitancy, underlining the complexity of this issue across neighbouring contexts.

Figure 21. Public Confidence in Vaccines in 2018 in Europe [174].



Another recent study evaluated the interplay of vaccine hesitancy and political populism across Europe, the Czech Republic, alongside Germany, Portugal, Belgium, and Hungary, exhibited a medium position in populism and medium-low levels of distrust [177]. The researchers noted that Eastern European countries such as the Czech Republic and Hungary, with a history of vaccine development dating back to the 1950s, showed higher perceived usefulness of vaccines, potentially influenced by their experiences during the Cold War [177].

The study by Agosti *et al.* 2022 found that vaccine hesitancy against SARS-CoV-2 increased across 28 European countries during the early stages of the vaccine rollout due to concerns over the AstraZeneca vaccine's potential link to rare blood clot cases [178]. In particular, countries suspending AstraZeneca's vaccine saw a notable increase in vaccine hesitancy, and overall trust in institutions was negatively associated with vaccine hesitancy. In this context, the Czech Republic was one of the countries with the least percentage of respondents receiving at least one vaccine dose [178].

Drawing on data from the Flash Eurobarometer 494, conducted in May 2021, the study by Dimiter Toshkov identified substantial regional disparities in COVID-19 vaccine hesitancy across Europe [179]. The survey, carried out on behalf of the European Commission, involved quota-based nationally representative samples from 27 EU member states, including the Czech Republic, categorised as Eastern Europe. The findings revealed elevated levels of vaccine hesitancy in Eastern Europe, driven by increased distrust in national governments and medical professionals. These results highlighted the importance of context-specific strategies to address vaccine hesitancy [179].

II.IV. Vaccine Hesitancy Literature in the Czech Republic

The technical term “vaccine hesitancy” was formally introduced into the scientific lexicon only a decade ago. Additionally, considering the unquestioned adherence to mandatory vaccination policies during the CSSR era (1948-1990) due to Soviet-imposed restrictions, the research into public attitudes and opinions on public health policies, including vaccinations, within the Czech Republic has only recently commenced.

Between November and December 2010, a cross-sectional survey-based study was conducted among medical students from two Czech universities (University of Ostrava and Masaryk University in Brno) to assess their attitudes towards seasonal influenza vaccination and the perceived risk of the H1N1 influenza pandemic [180]. The findings revealed a low proportion of students regularly vaccinated against seasonal flu (4%), and their interest in vaccination did not increase even during the pandemic, with only 5% expressing interest in vaccination. The study suggests that young people do not consider influenza vaccination as a significant anti-epidemic measure, and their opinions remained unchanged during the H1N1 pandemic in 2009 [180].

During the 2010/2011 northern hemisphere influenza season, a study was conducted to assess the acceptability of the intradermal influenza vaccine among adult vaccinees and vaccine prescribers in the Czech Republic and Turkey [181]. The results showed high satisfaction among vaccinees, with 96.1% expressing satisfaction with the vaccine and a preference for receiving it again in the future. Vaccine prescribers also expressed satisfaction with the intradermal vaccine and a preference for it over intramuscular vaccination, suggesting that the intradermal influenza vaccine could contribute to increasing seasonal influenza vaccination rates in adults [181].

In 2011, a large mumps outbreak primarily affecting high school and university students occurred in Pilsen despite over 90% of the population having been vaccinated with 2 doses. While waning vaccine immunity over time was likely the main driver, the analysis of Pazdiora *et al*. 2015 suggested that delayed childhood vaccination schedules, such as postponing the 1st dose past 24 months and extended intervals between doses, may have increased the susceptible population and contributed to the scale of the epidemic [182].

Between September 1, 2020, and August 31, 2021, a prospective observational study was conducted in a large maternity hospital in Prague to determine the influenza vaccination coverage (IVC) among pregnant women in the Czech Republic [169]. The analysis of completed questionnaires from 4,617 participants revealed a concerning low IVC, with less than 2% of women reporting influenza vaccination during pregnancy. To enhance vaccination coverage among pregnant women, raising awareness of recommendations and integrating vaccination into routine antenatal practice are crucial [169].

In April 2019, Šálek *et al.* 2020 conducted an analytical cross-sectional survey-based study to explore vaccination attitudes among undergraduate students in medical and pedagogical programs at Charles University, Prague [183]. Their findings, from 722 respondents, illustrated that pedagogical students displayed notably weaker vaccine confidence compared to medical students. The results also indicated the fear of infections as a significant factor in fostering positive vaccination perceptions. Notably, the impact of attitudes toward alternative medicine on vaccine confidence was substantial [183].

During the 2019 measles epidemic in the Czech Republic, Vochocová *et al.* 2022 analysed the online debates on vaccination [184]. They found that pro-vaccination comments in online discussion forums were often offensive and uncivil, undermining the potential for deliberation and contributing to polarisation. The study emphasised the importance of promoting more constructive communication strategies to facilitate productive discussions on vaccination [184].

Between 2020-2021, Liptaková *et al.* 2023 conducted an observational study in the Institute for Mother and Child Care in Prague to assess the pertussis vaccination coverage among pregnant women [185]. The study revealed a low vaccination coverage of 1.6% during pregnancy, with limited awareness of the possibility of vaccination. The study emphasised the need to increase awareness among the public and healthcare professionals about the recommendations and benefits of pertussis vaccination during pregnancy to improve vaccination coverage [185].

Over the past two decades, there has been an increasing number of students' theses in bachelor's and master's degree programs in Czech universities that have focused on exploring public attitudes towards vaccination, employing various quantitative and qualitative research methods. Table 9 provides a summary of these studies, which provide valuable insights into the factors influencing vaccine acceptance or refusal, the sociodemographic characteristics of individuals with critical perspectives, and the discourse surrounding immunisation.

Table 9. Summary of Students' Theses on Vaccination Attitudes in the Czech Republic, 2008 – 2022.

Author	Year	University	Title	Sample	Location	Ref.
Jitka Strachoňová	2008	University of South Bohemia	Současná právní úprava povinného očkování v České republice a důsledky vedoucí z jeho odmítnutí	Parents (n = 207)	České Budějovice and Liberec Regions	[186]
Monika Vokrouhlíková	2008	University of South Bohemia	Informovanost veřejnosti o onemocnění klíšťovou encefalitidou	High-risk groups (n = 141)	Příbram and České Budějovice Regions	[187]
Martina Sýkorová	2008	University of South Bohemia	Hodnocení prevence u cestovatelů do zahraničí	Travellers (n = 50)	České Budějovice Region	[188]
Irena Zemanová	2011	University of South Bohemia	Analýza zájmu zdravotnických pracovníků o očkován proti chřipce v Nemocnici Rudolfa a Stefanie Benešov	HCPs (n = 129)	Benešov (Central Bohemian Region)	[189]
Marie Maxová	2013	University of South Bohemia	Studie proočkovanosti a vakcinační disciplíny u povinného očkování	Children (n = 831)	České Budějovice Region	[190]
Ilona Palátová	2014	University of South Bohemia	Odmítání očkování v kraji Vysočina v období let 2010 - 2013	GPs of Children & Adolescents (n = 92)	Vysočina Region	[191]
Barbora Chocholová	2016	University of South Bohemia	Význam kontroly proočkovanosti u dětí	Parents (n = 590)	Příbram (Central Bohemian Region)	[192]
Petra Mejtská	2020	Charles University	Role otců při váhání o očkování	Fathers	Prague (Central Bohemian Region)	[193]
Martina Martinková	2022	Charles University	Postoje rodičů k očkování dětí	Parents (n = 11)	All over the CR	[194]
Klára Dziadková	2022	Charles University	Postoje rodičů k povinnému očkování dětí	Parents (n = 105)	All over the CR	[195]

In the context of COVID-19 vaccination, Štěpánek *et al.* 2021 conducted a cross-sectional survey of all employees (n = 4553) at the University Hospital Olomouc to investigate the demand for COVID-19 vaccination [196]. They found the vaccination coverage to be 70%

after several weeks of vaccine availability. The most common motive for vaccination was family protection (84%), patient protection (69.7%), self-protection (50.2%), and exemption from anti-epidemic measures (48%), while key reasons for vaccine hesitancy were concerns about vaccine safety and side effects (49.4%), doubts about vaccine efficacy (41.1%), and history of COVID-19 infection (33.4%). The study concluded that to increase vaccination coverage, it is crucial to target information campaigns towards these primary motives for vaccine acceptance and hesitancy, with a particular emphasis on improving awareness about the safety, efficacy, and protective ability of COVID-19 vaccines [196].

Kupsová *et al.* 2022 conducted a cross-sectional study among University of Defence members in Hradec Králové to investigate the determinants of COVID-19 vaccine acceptance. Their findings revealed that concern about COVID-19 and history of COVID-19 were significant predictors of vaccine acceptance, while concerns about vaccine safety and efficacy were the main reasons for vaccine refusal [197]. Moreover, Kosarková *et al.* 2021 explored the role of religiosity and spirituality on COVID-19 vaccine acceptance within a Czech adult population [198]. Their study indicated that spirituality, particularly among individuals identifying as spiritual without a religious affiliation, was significantly associated with belief in conspiracy theories about vaccination, thereby contributing to higher rates of vaccine refusal. These findings highlight the importance of incorporating an understanding of spiritual beliefs in vaccination campaigns to address and mitigate the development of conspiracy theories and vaccine hesitancy [198].

Using data from an anonymous self-reported online survey conducted in the Czech Republic during the COVID-19 vaccination campaign in April 2021, Žídková *et al.* 2023 investigated factors influencing vaccine refusal [199]. The findings revealed that sociodemographic factors, government trust, knowledge about COVID-19 vaccines, information sources, personal characteristics, and depression were associated with vaccine acceptance [199].

Šerek *et al.* 2023 assessed the effects of health worries and socio-political attitudes on COVID-19 vaccine uptake [200]. The findings revealed that individuals with higher health worries and lower distrust in politicians at the beginning of the vaccination campaign were more likely to receive the COVID-19 vaccine later on. Additionally, general trust in people was associated with a greater likelihood of vaccine uptake, while political submission did not significantly influence vaccine uptake [200].

In a study by Zapletal *et al.* 2022, a survey was conducted among pregnant women in November and December 2021 to assess their awareness and acceptance of COVID-19 vaccination [201]. The study found that 58% of respondents were vaccinated with at least one dose, and 51% were fully vaccinated. Also, a high percentage of respondents (77%) recognised the higher risk of severe COVID-19 infection in pregnant women compared to non-pregnant women, and 71% were aware of the risk of fetal death associated with COVID-19 [201].

In conclusion,

- The history of immunisation in the Czech Republic dates back to the 18th century, with the introduction of variolation and the subsequent implementation of compulsory vaccination programs.
- Anti-vaccination sentiments have emerged in recent decades, driven by concerns over disease incidence, post-vaccination complications, individual rights, and the influence of organisations like Paracelsus and Rozalio.
- Vaccination coverage in the Czech Republic has seen a decline in certain vaccines over the years, and there are disparities in coverage among different populations, such as Roma children.
- Within the European context, the Czech Republic has exhibited higher vaccine refusal rates, lower confidence in vaccine safety among healthcare professionals, and increased vaccine hesitancy during the COVID-19 vaccine rollout compared to other European countries.
- Limited evidence on vaccination attitudes in the Czech Republic due to historical adherence to mandatory vaccination policies during the CSSR era (1948-1990) and the recent introduction of the term "vaccine hesitancy".

COVID-19 Pandemic in the Czech and European Contexts

III.I. Epidemiology of COVID-19 in Europe

COVID-19 surveillance began in Europe on January 27th, 2020, following the identification of the disease in Wuhan, China in December 2019. Eurosurveillance, the official journal of the European Centre for Disease Prevention and Control (ECDC), published a report by Spiteri *et al.* 2020 documenting the first 47 confirmed COVID-19 cases across nine European countries as of February 21st, 2020 [202]. The report highlighted that 21 of these cases were linked to clusters in Germany and France, and 14 were contracted in China. The report acknowledged the delay in isolation efforts due to the late detection of initial cluster cases [202].

According to an investigation that utilised a phylodynamic model with geographic structure to analyse viral genome sequences, it was postulated that the inaugural SARS-CoV-2 outbreak in Europe was initiated in Italy, potentially following a transmission event in Hubei, China or Germany [203]. This study revealed that before the first European border closures, the rate of new cases from the within-country transmission was within or exceeded the estimated bounds of new cases from migration, shedding light on the early stage of the epidemic and migration patterns of the virus before border restrictions [203]. By March 5th, 2020, the case count had surged to 4,250. Notably, confirmation of all early cases was carried out using specific assays targeting separate genes, and although the majority of cases led to hospitalisations, these were mostly for isolation purposes rather than due to severe disease [202].

On March 11th, 2020, the WHO declared COVID-19 as a pandemic aiming to highlight the seriousness of the situation and mobilise global resources and efforts to combat the rapidly spreading virus [204]. Since then, COVID-19 epidemic waves in Europe had heterogeneous impacts across regions and over time. Western Europe has been the main driver of case rates, but the contributions from different regions have varied depending on population size and case rates [205]. The initial wave was broadly carried by all regions except Eastern Europe, but as the pandemic progressed, Eastern Europe became the main contributor to European mortality. The spread of the Delta and Omicron variants led to a significant increase in mortality, which has since decreased considerably post-spring 2022. The patterns of these waves and their impacts reveal a complex interplay of factors, including regional differences, variant spread, and public health responses [205].

As of July 5th, 2023, there have been a total of 767.73M COVID-19 confirmed cases globally, of which 248.96M (32.43%) were reported in Europe [206]. Figure 22 provides an overview of total cases and total deaths in Europe between January 8th, 2020 and July 5th, 2023.

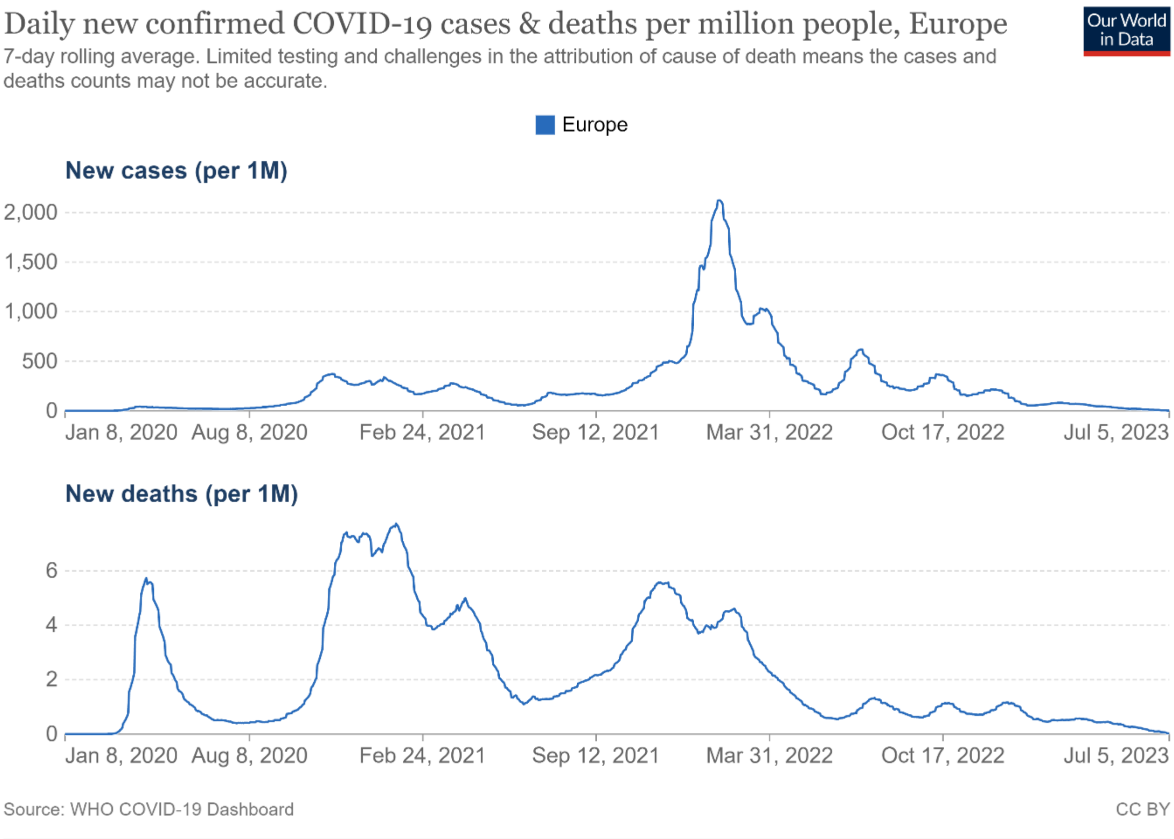
The ECDC provides a weekly overview of the COVID-19 situation in each country based on indicators, e.g., the 14-day notification rate, testing rate, positivity rate, hospitalisation rate and vaccination rate. As of July 2nd, 2023, COVID-19 trends across EU/EEA countries demonstrated either stability or decrease across all age groups. Of the 23 reporting countries, only one (Malta) exhibited a rise in overall case rates compared to the preceding week, while three (Lithuania, Malta, and Netherlands) showed increased test positivity. Notably, no escalation was recorded in hospitalisation or ICU metrics. Ensemble model forecasts suggest no uptick in COVID-19 cases, hospitalisations, or mortality through July 16th, 2023 [207].

The hospitalisation rate was the highest in Greece (1.7 per 100K population), followed by the Netherlands (0.2), Italy (0.2), and Slovakia (0.1). Also, the hospital occupancy rate was the highest in Bulgaria (2.5 per 100K population), followed by Lithuania (0.6), Austria (0.5), the Netherlands (0.2) and the Czech Republic (0.1). The ICU admission rate was almost (0) in all countries, while it was 0.3 per 100K population in Bulgaria and 0.1 in Austria [207].

As of July 5th, 2023, there have been a total of 6.95M COVID-19 mortality cases globally, of which 2.07M (29.78%) were reported in Europe [206]. Figure 22

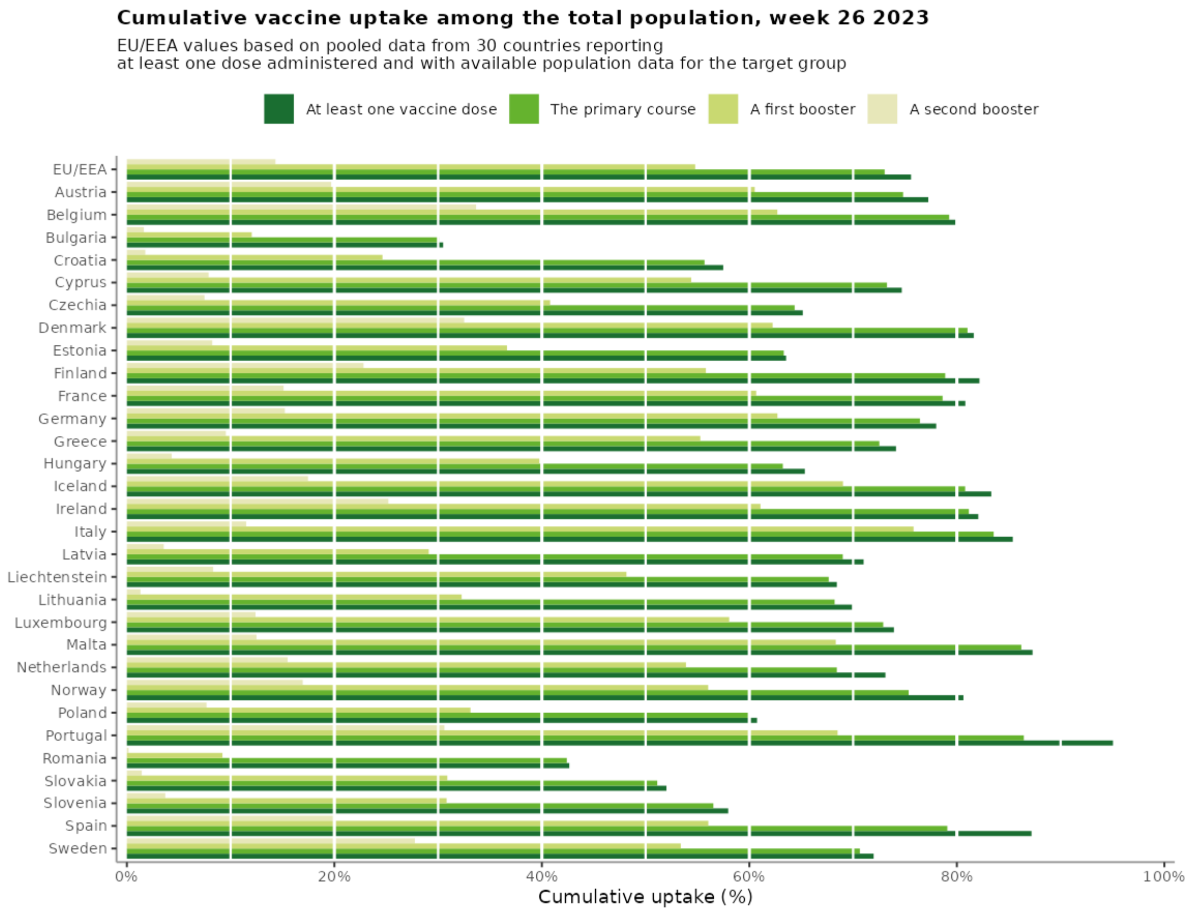
Only Malta exhibited a rise in the 14-day death rate per million (5.8), while Portugal (4.9) and Slovenia (3.8) exhibited a declining trend compared to the previous week [207]. Overall, Cyprus, Lichtenstein and Lithuania had almost (0) cases for death rate per million. On the other hand, Malta (5.8) was the highest, followed by Portugal (4.9), Slovenia (3.8), Croatia (3.4), Greece (3.2), Poland (2.8), Bulgaria (2.5), and Latvia (2.1). The average death rate of the EU/EEA was 1.3 [207].

Figure 22. Overview of total COVID-19 cases and total deaths in Europe, Our World in Data [208]



In terms of vaccination coverage, 75.6% of the total EU/EEA populations received at least one vaccine dose, 73% completed the primary course, 54.8% received the first booster, and only 14.3% received the second booster as of July 2nd, 2023 [207]. These percentages were significantly higher among the +60-year-old population: 92.4%, 91.2%, 84.9% and 35.6%, respectively. Likewise, these percentages were higher among HCPs except for the second booster; 95.3%, 90.4%, 67%, and 11.9%, respectively [207]. Figure 23

Figure 23. Cumulative COVID-19 Vaccine Uptake in Europe, July 2nd, 2023 [207].



III.II. Epidemiology of COVID-19 in the Czech Republic

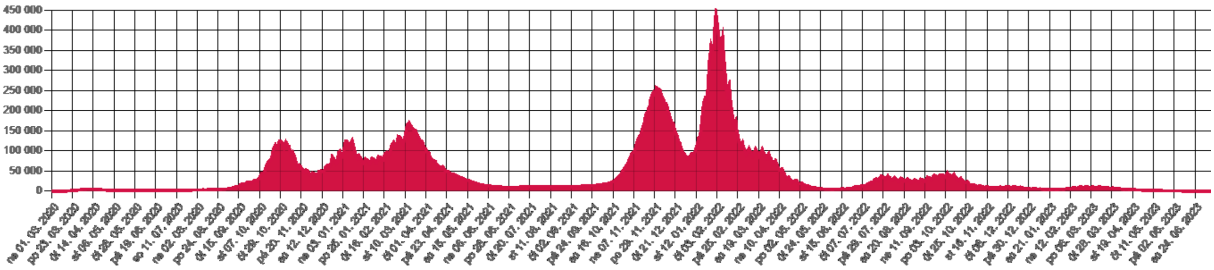
On March 1st, 2020, three cases of the novel coronavirus were reported in the Czech Republic, with two detected at a hospital in Prague and one in Ústí nad Labem, all with recent history of travel to Italy. The Czech Prime Minister, Andrej Babiš, proposed banning flights from Milan and Venice at the next Security Council meeting, to prevent further spread of the virus [209]. Ten days later, schools were closed and on March 11th, 2020, the state of emergency was declared nationwide (resolution no. 194) [210].

Since then, several epidemic waves were recorded by the Institute of Health Information and Statistics of the Czech Republic (IHIS-CR), leading to the development of a comprehensive portal to share open datasets detailing aspects of the COVID-19 epidemics, which have been widely used by the public, authorities, and scientists, garnering over 13 million API calls from its inception in March 2020 to December 2020, supporting transparency, decision-making, and research [211,212].

As of July 11th, 2023, a total of 4,642,836 confirmed COVID-19 cases were reported, of which 402,191 were re-infections (8.66%). Among the senior population (+65 years old), 624,589 confirmed cases were reported, of which 31,259 were reinfections (5%) [212]. The highest number of new cases per day was 67,064 (February 1st, 2022), while the highest number of active infections during a single day was 438,383 cases (February 2nd, 2022). Figure 24

Tuček *et al.* 2022, analysed data from March 2020 to December 2021, revealing that out of the 2,483,219 officially confirmed COVID-19 cases, 27% were work-related, with the occupations of clerks, machinists, craftsmen, agency workers, managers, and food workers seeing an increased risk in 2021 compared to 2020, while health professions and social workers experienced a decreased risk; thus highlighting the significance of workplace anti-epidemic measures and personal protective equipment in controlling the spread of the disease [213].

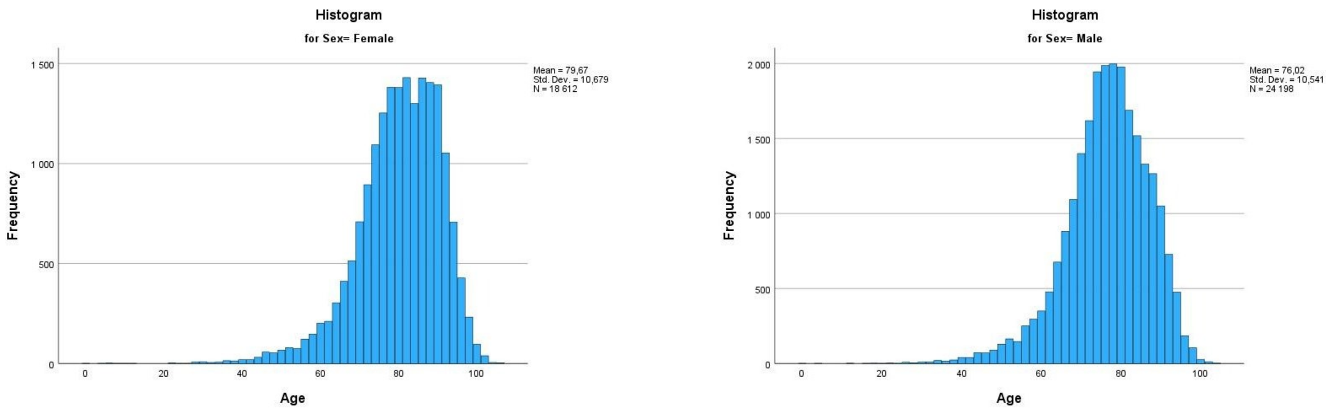
Figure 24. Overview of Daily COVID-19 Active Cases in the Czech Republic [212].



The total mortality cases due to COVID-19 in the Czech Republic reached 42,811 by July 11th, 2023. The demographic breakdown of these cases reveals that 56.5% were males with a mean age of 76 ± 10.5 years, while 43.5% were females with a higher mean age of 79.7 ± 10.7 years. This indicates a slightly higher vulnerability among the male population, and a longer life expectancy among females, which is consistent with general demographic trends.

Furthermore, age proved to be a significant factor in COVID-19 related deaths, with 93.7% of mortality cases occurring among individuals aged 60 years or above. This suggests that the virus has been particularly deadly for older age groups, which is likely due to a variety of factors, including the increased prevalence of comorbidities and a weakened immune response among the elderly. Figure 25

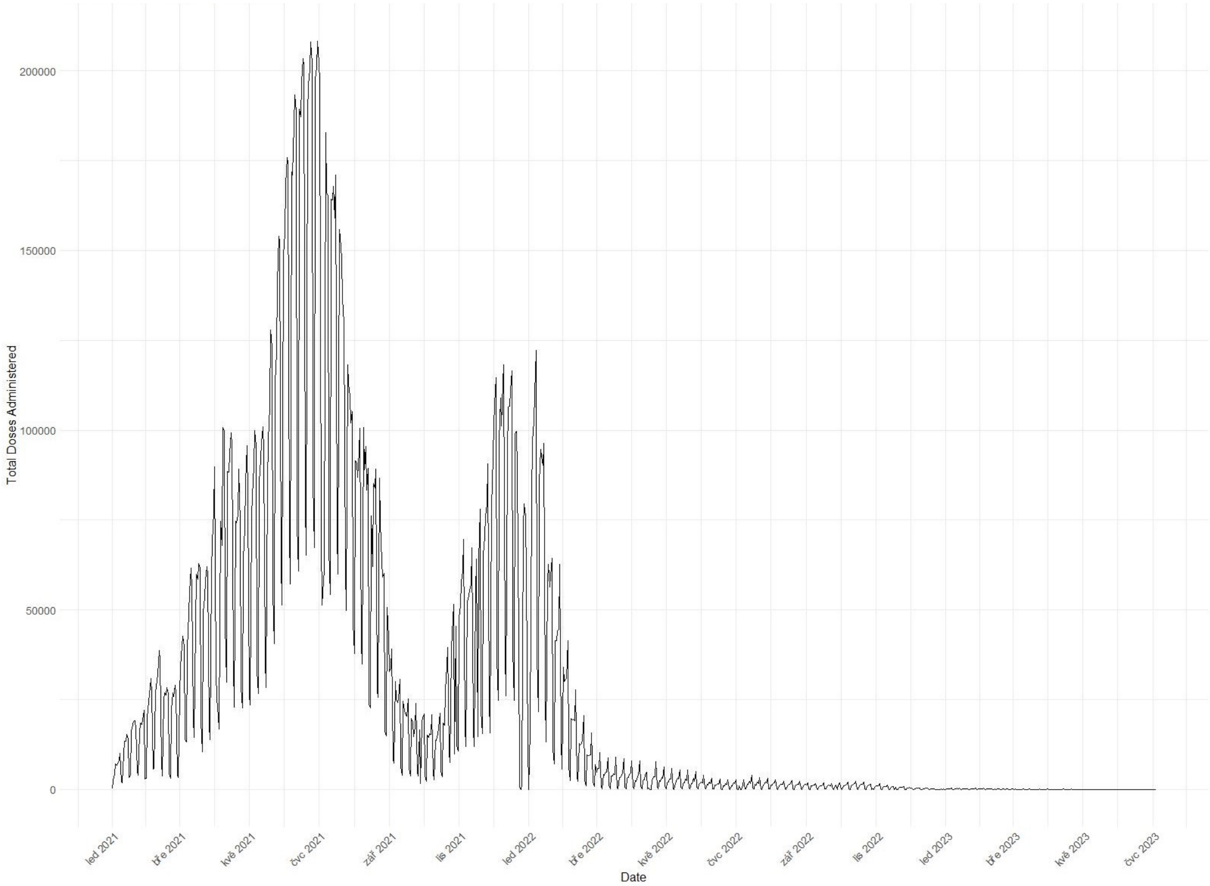
Figure 25. Overview of COVID-19 Mortality Age Structure, Stratified by Sex in the Czech Republic [212].



Overall, 18,625,801 vaccine doses were administered as of July 11th, 2023, of which 80.6% were Comirnaty (original), 8.8% Spikevax, 4.8% Vaxzevria, 2.3% Comirnaty (Bivalent BA.4/5), and 2.2% Janssen. While 6,893,442 received their primary vaccination doses, 4,364,054 received the first booster dose (monovalent), 800,610 received the second booster dose (bivalent), and only 2,418 received the third booster dose (bivalent).

Figure 26 displays a timeline for total doses administered per day from January 2021 to July 2023. The Czech Republic's vaccination progression, marked by considerable daily throughput and cyclic oscillations, was influenced by logistical constraints, public holidays, and booster shot deployment. The vaccination rate surged in mid-2021, and waned year-end but rebounded with the 2022 introduction of the first boosters, causing a subsequent decline in daily vaccinations due to extensive primary dose coverage.

Figure 26. Timeline of COVID-19 Vaccine Doses Administered Daily in the Czech Republic [212].



III.III. Government Responses and Public Health Measures

The European response to the COVID-19 pandemic was multifaceted and evolved over time as the situation developed. Table 10 provides a chronological summary of the key actions and strategies adopted at the European level between December 2019 and May 2022.

Table 10. Summary of the European Union's (EU) Actions Against COVID-19 Pandemic [214].

Date	EU Action
December 31st, 2019	Initiation of surveillance by the European Centre for Disease Prevention and Control
February 2020	Delivery of first aid worth €232 million to support global efforts
February 28th, 2020	Initiation of a joint procurement mechanism to secure masks and other equipment
April 24th, 2020	Pledge of €15.9 billion for the Coronavirus Global Response
June 16th, 2020	Adoption of the EU COVID-19 Vaccines Strategy
August 2020	Signing of contracts for vaccine supply with Johnson & Johnson, AstraZeneca, and BioNTech-Pfizer
August 31st, 2020	Joining the COVID-19 Vaccine Global Access Facility (COVAX)

October 19th, 2020	Adoption of the EU-wide system of contact tracing and warning apps
November 11th, 2020	Adoption of the European Health Union for coordinated preparedness and response
November 25th, 2020	Adoption of the Pharmaceutical Strategy for Europe
December 2020	Identification of the Alpha variant of COVID-19
December 27th, 2020	Commencement of vaccination in all EU Member States
January 2021	Signing of a second contract with BioNTech-Pfizer for additional vaccine doses
February 17th, 2021	Launch of the "HERA Incubator" as a European bio-defence preparedness plan
April 14th, 2021	Administration of 100 million vaccine doses in the EU
May 21st, 2021	Launch of a €1 billion Team Europe initiative in Africa
August 4th, 2021	Signing of a contract for vaccine supply with Novavax
August 31st, 2021	Achievement of full vaccination for 70% of the EU adult population
September 16th, 2021	Creation of the Health Emergency Preparedness and Response Authority (HERA)
September 22nd, 2021	Establishment of the EU-US Global Vaccination Partnership
October 18th, 2021	Export of 1 billion vaccine doses to over 150 countries worldwide
November 2021	Identification of the Omicron variant of COVID-19
December 1st, 2021	Adoption of a coordinated EU approach to address the resurgence of COVID-19
February 10th, 2022	Launch of a €1.3 billion work plan by HERA for response and preparedness

In parallel with EU actions, the ECDC has been instrumental in the fight against COVID-19. Their response was initiated on December 31st, 2019, when their Epidemic Intelligence team identified a cluster of pneumonia cases in Wuhan, China. This early detection led to the publication of their first risk assessment on January 9th, 2020 [215].

The ECDC's Emergency Operations Centre was activated on January 13th, 2020, to coordinate their response. They began publishing daily situation updates and weekly threat reports on January 29th and February 11th, 2020, respectively, providing crucial information to health authorities and the public. The ECDC also issued a series of guidelines and technical guidance documents on various topics, including health system preparedness, patient isolation management, surveillance, contact tracing, infection prevention and control, and physical distancing. These guidelines were vital in shaping the pandemic response across Europe [215].

Furthermore, the ECDC regularly published rapid risk assessments to provide timely information on the evolving situation, including the resurgence of reported cases and the situation in the EU/EEA and the UK. These assessments have been key in informing the public and health authorities about current risks and necessary mitigation measures. Overall, the ECDC's comprehensive and multifaceted response to the COVID-19 pandemic has significantly contributed to Europe's management of the ongoing situation [215].

Following the measures taken by the EU and the ECDC, the Czech government also implemented a comprehensive set of actions to combat the COVID-19 pandemic. A state of emergency was declared on March 12th, 2020, leading to the closure of educational institutions and the prohibition of large gatherings [216]. Retail operations were limited, with exceptions for essential services, and movement restrictions were imposed. The government mandated face coverings in public and designated specific shopping hours for seniors and disabled individuals over 50. These strategies aimed to mitigate virus spread and safeguard public health [216]. Table 11 provides a chronological summary of the anti-pandemic measures undertaken by the Czech government between March 2020 and February 2022.

Table 11. Summary of the Czech Government Measures Against COVID-19 Pandemic [216].

Month	Measure
March 2020	State of emergency declared, education halted, public gatherings of more than 30 people banned, retail sales limited, free movement restricted, mandatory face masks in public, 'smart quarantine' project initiated.
April 2020	Individual outdoor sports allowed, certain shops and services reopened, church services with up to 15 people permitted, social services operated online and via phone.
May 2020	Exemption for wearing masks approved, return to schools for final year students, masks mandatory in building interiors and public transport.
June 2020	Voluntary return to school for certain students, events with up to 500 people allowed, restaurant terraces could stay open past 11 pm.
July 2020	Czech Armed Forces deployed in rescue work to protect population and prevent virus spread.
September 2020	Restrictions on public events with more than 1,000 people (outdoors) and 500 people (indoors), mandatory masks in indoor spaces and public transport.
October 2020	State of emergency declared, mass-attendance events restricted, restrictions on school attendance, further limitations on services, masks mandatory at mass transit stops and in cars with non-household members, prohibition of free movement with exceptions.
November 2020	Extension of school operation restrictions.
December 2020	All shops and services allowed to open under certain conditions, remaining years of secondary school allowed to return to school under certain conditions.
January 2021	Exemption for shops selling remembrance goods, individual consultations for university students allowed, changes to visits to healthcare facilities and social care facilities.
February 2021	Visits to healthcare facilities in acute care wards banned again, state of emergency and valid crisis measures extended.
March 2021	New state of emergency applied, existing crisis measures re-confirmed.
April 2021	Activity of children’s groups permitted in certain regions, testing launched at higher education institutions, secondary school pupils able to attend practical training.
May 2021	Body care services and animal care services permitted under certain conditions, individual tours permitted in museums, galleries, castles, chateaux and other historical or cultural structures.
June 2021	Uniform entry conditions for service establishments, sports, and cultural institutions implemented, rules for wearing respiratory protection relaxed.
July 2021	Increase in the permitted capacity of establishments and the end of certain restrictions.
November 2021	Rules for visits to health and social care facilities tightened, state of emergency declared and additional restrictions implemented.
December 2021	Rule on the use of respiratory protection in cable cars and PCR testing in schools clarified.
January 2022	Amendments to the gathering restrictions in certain establishments and services made, changes in school policies for positive test cases, testing in schools on Mondays and Thursdays implemented.
February 2022	Temporary ban on visits to prisons and detention facilities with specified exceptions implemented, restrictions and conditions on trade, services, and leisure activities lifted.

In summary, the Czech government imposed significant restrictions during peaks of the pandemic including business and school closures, limits on gatherings and movement, mask mandates, curfews, and mandatory testing. There was a phased reopening as case levels declined.

III.IV. Impact of the COVID-19 Pandemic

The COVID-19 pandemic has had profound non-health impacts across Europe, and the Czech Republic has been no exception. It has disrupted economies, particularly hit the hospitality and tourism sectors and increased unemployment rates [217]. The pandemic has also changed social interactions, leading to increased stress and mental health disorders [218]. Education has been impacted by the shift to remote learning, affecting educational quality and access [219].

The task of managing inflation and scaling back fiscal support has emerged as a critical issue. The process of rolling back the emergency spending measures initiated to bolster economies during the pandemic is intricate and fraught with the risk of replicating the sluggish growth that ensued in the 2008 financial crisis. It is projected that fiscal deficits of major advanced European economies will shrink by approximately 4% of GDP in 2022, largely due to the phasing out of pandemic-related support. However, apprehensions persist that the growth rate in advanced economies could dwindle to a mere 1% by the end of 2022, as opposed to the anticipated 2-3%. This could pose significant hurdles in achieving full employment and reintegrating people into the workforce [220].

On October 19, 2021, the European Commission reignited the public consultation on the EU's economic governance framework, a process that had been put on hold in March 2020 due to the COVID-19 pandemic. The pandemic triggered a severe economic downturn, with the EU's real GDP plummeting by 6.1% in 2020, a steeper decline than during the global financial crisis. However, the EU's prompt and coordinated response, encompassing robust support for businesses and workers, substantial liquidity assistance for firms, and a wide range of monetary policy measures, helped to mitigate the economic fallout of the crisis [221].

The EU Recovery and Resilience Facility (RRF) is set to further bolster recovery by providing €338 billion in non-repayable support and up to €386 billion in loans by 2026. Despite the robust recovery, enduring structural challenges persist, including the impacts of an ageing population, sluggish productivity growth, accelerating climate change, and escalating inequality. The pandemic has intensified these challenges and introduced new ones, such as increased fiscal divergence between Member States and pressing investment needs [221]. Table 12 provides a summary of the EU's response to the economic fallout from COVID-19.

Table 12. Summary of the European Union's (EU) Response to Economic Fallout [217].

Initiative	Description	Amount (€)
Next Generation EU	A recovery effort designed to mitigate the pandemic's impact	750 billion
Long-term EU Budget (2021-2027)	A budget allocation to foster digital and green transitions and resilience	1,074.3 billion
Recovery and Resilience Facility (RRF)	Financial support to member states to address the socio-economic impact of the pandemic	672.5 billion
SURE (Support to mitigate Unemployment Risks in an Emergency)	Provision of loans to member states to subsidise costs related to national short-time work schemes	98.4 billion
European Investment Bank (EIB) Group Guarantee Fund	Provision of loans, with a focus on small and medium-sized enterprises (SMEs) across the EU	Up to 200 billion
European Stability Mechanism Pandemic Crisis Support	Provision of loans to all Euro area member states	Up to 240 billion
Redirection of EU Cohesion Funds	Redirection of cohesion funds to assist member states in tackling the pandemic	37 billion
European Institute of Innovation and Technology (EIT) Crisis Response Initiative	Additional funding to innovators to address social and economic challenges	60 million
Temporary State Aid Rules	Measures allowing member states to financially support struggling companies and citizens	Not specified
European Central Bank Pandemic Emergency Purchase Programme	Monetary policy measures to support the economy	Initial 750 billion, increased by 600 billion later

The COVID-19 pandemic has had significant social impacts across Europe, particularly among the older population [222]. The pandemic and the measures taken to control it have led to changes in social interactions, with people avoiding medical treatment for fear of infection and experiencing social shocks such as isolation or lack of help. The Survey of Health, Ageing and Retirement in Europe (SHARE) was used to investigate these impacts, revealing that older Europeans with pre-existing health conditions were more likely to adopt precautionary behaviours but also faced increased feelings of depression and loneliness due to reduced personal contact. The pandemic has also increased economic, social, and health inequality among the older population, with those still economically active facing the risk of job loss and subsequent economic hardship [222].

Furthermore, the pandemic has disproportionately affected women's employment and economic resources, raising fears that the crisis may intensify existing gender inequalities. Policies like short-time working schemes, implemented across Europe, carry inherent gender biases that potentially increase women's economic vulnerability. Continued research is crucial to ascertain whether these policies would ultimately exacerbate or alleviate gender disparities in areas such as employment rates, wage gaps, and job quality for women [223].

Kovacs *et al.* 2021 conducted a study revealing the substantial effects of the COVID-19 pandemic on children's physical activity and screen time in Europe, with only 19% meeting the WHO's physical activity recommendations and screen time exceeding two hours daily. The study advocated for structured routines, safe outdoor activities, and prioritising physical education during remote learning to help children maintain a healthy lifestyle during the pandemic [224]. In addition, Blaskó *et al.* 2022 argued that the pandemic has significantly exacerbated educational disparities worldwide. However, due to the lack of prompt educational outcome data, our understanding of the pandemic-induced learning losses at both national and international levels remained limited [225].

In conclusion,

- COVID-19 surveillance began in Europe in January 2020, with the first major outbreak possibly originating from Italy; as of July 2023, Europe accounts for 32.43% (248.96M) of the global 767.73M confirmed cases.
- As of July 2023, COVID-19 trends are stabilising or decreasing across EU/EEA countries, with 75.6% of the population receiving at least one vaccine dose and no predicted increases in cases, hospitalisations, or deaths through mid-July.
- Since its first cases in March 2020, the Czech Republic has reported 4,642,836 confirmed COVID-19 cases and 42,811 deaths by July 11, 2023, with a notably higher vulnerability among males and individuals aged 60 and above.
- As of July 2023, the country has administered 18,625,801 vaccine doses, with considerable daily throughput influenced by logistical constraints, public holidays, and booster shot deployment.
- The EU and the ECDC implemented comprehensive, evolving strategies from December 2019 to May 2022 to combat the COVID-19 pandemic, which informed the Czech government's own extensive measures, including a state of emergency, restrictions on movement, and retail operations.
- The COVID-19 pandemic has had significant non-health impacts across Europe and the Czech Republic, disrupting economies, exacerbating social and educational disparities, and increasing unemployment, stress, and mental health disorders; the EU has implemented numerous economic recovery initiatives, but concerns persist about enduring structural challenges and potential sluggish growth.

COVID-19 Vaccines: Types, Efficacy and Effectiveness, and Safety

The development of diverse COVID-19 vaccines has been a significant step in addressing the global health crisis caused by SARS-CoV-2. These vaccines, including inactivated or weakened virus vaccines, protein-based vaccines, viral vector vaccines, and RNA and DNA vaccines, have all received authorisation from the WHO and other regulatory bodies. The WHO's Emergency Use Listing (EUL) process, which guarantees rigorous standards of safety and efficacy, was crucial in the approval of these vaccines. However, as of May 2023, new COVID-19 vaccines are no longer eligible for EUL, reflecting a significant milestone in the trajectory of the pandemic, which is no longer deemed a Public Health Emergency of International Concern (PHEIC) [226].

IV.I. COVID-19 Vaccines Types

The WHO's COVID-19 Vaccine Tracker offers detailed updates on vaccine candidates' progress and characteristics, fostering transparency through regular, twice-weekly updates and inviting data contributions from various entities [227]. As of March 30th, 2023, there were 183 vaccine candidates in the clinical development phase and 199 vaccine candidates in pre-clinical development. Out of the 183 vaccines in the clinical phase, protein-subunit vaccines were the most common (32%), followed by RNA-based (24%) and viral vector-based vaccines (14%). The majority (90%) were injectable (82% intra-muscular, 9% intra-nasal, 5% intra-dermal, and 3% subcutaneous), and only 3% were orally administered. More than half (55%) of them consisted of 2 doses, 26% of one dose, and only 1% of three doses [227].

Heretofore, the EUL was granted to 11 vaccines representing four basic approaches of providing active immunisation, including the whole virus approach, the viral vector approach, the protein subunit approach, and the nucleic acid approach [228]. Table 13 provides an overview of COVID-19 vaccines mechanisms of action.

Table 13. Overview of COVID-19 Vaccines Types [228].

	Whole Virus	Viral Vector	Protein Subunit	Nucleic Acid
Mechanism of Action	Whole virus vaccines, either live attenuated or inactivated, trigger immunity by mimicking natural infection without causing disease, prompting a broad immune response. However, live attenuated vaccines may pose risks to individuals with compromised immune systems, while inactivated vaccines may stimulate weaker and less long-lasting responses.	Viral vector vaccines use harmless viruses to deliver the genetic code for a pathogen's antigens into host cells, triggering an immune response. However, pre-existing immunity to the viral vector can potentially reduce the vaccine's effectiveness.	Subunit vaccines containing fragments of the pathogen trigger immunity by inducing a targeted immune response, minimising side effects but potentially resulting in a weaker response. They are relatively cheap, easy to produce, and stable but may require adjuvants and booster doses.	Nucleic acid vaccines use DNA or RNA encoding the antigen to trigger an immune response. The key challenge for DNA vaccines is ensuring the DNA enters the cells, while RNA vaccines, due to their transitory nature, pose no risk of integrating with our genetic material.

Manufacturing	Whole virus vaccine production involves unique processes for different viruses, adding complexity. The subsequent steps of isolation, purification, and attenuation or inactivation require stringent procedures and specific resources, leading to increased costs.	Viral vector-based vaccine manufacturing faces scalability challenges. Despite advancements with suspension cell lines, the complex assembly process and the need for extensive testing after each step result in higher costs.	Subunit vaccine production, utilising living organisms, demands strict hygiene and specific growth conditions, making it costlier than chemically-synthesised vaccines like RNA ones. The process, varying by vaccine type, involves steps such as genetic code insertion, antigen harvesting, and component addition.	Nucleic acid vaccines, produced post-pathogen genome sequencing, offer a quick and simple production process, making them ideal for combating rapidly evolving pathogens. Their production, especially RNA vaccines synthesised chemically in labs, can occur in the same facilities, reducing costs.
Advantages	**Live-attenuated Vaccines:** • Well-established technology. • Strong immune response. • Immune response involves B cells and T cells. • Relatively simple to manufacture. **Inactivated Virus Vaccines:** • Well-established technology. • Suitable for people with compromised immune systems. • No live components, so there is no risk of the vaccine triggering the disease. • Relatively simple to manufacture. • Relatively stable.	• Well-established technology. • Strong immune response. • Immune response involves B cells and T cells.	• Well-established technology. • Suitable for people with compromised immune systems. • No live components, so there is no risk of the vaccine triggering the disease. • Relatively stable.	• Immune response involves B cells and T cells. • No live components, so there is no risk of the vaccine triggering the disease. • Relatively easy to manufacture.
Disadvantages	**Live-attenuated Vaccines:** • Unsuitable for people with compromised immune systems. • May trigger disease in very rare cases. • Relatively temperature sensitive, so careful storage is necessary. **Inactivated Virus Vaccines:** • Booster shots may be required.	• Previous exposure to the vector could reduce effectiveness. • Relatively complex to manufacture.	• Relatively complex to manufacture. • Adjuvants and booster shots may be required. • Determining the best antigen combination takes time.	• Some RNA vaccines require ultra-cold storage. • Never been licensed in humans. • Booster shots may be required.

In December 2020, the European Medicines Agency (EMA) issued an emergency authorisation for the first vaccine to be used for mass vaccination in the EU against SARS-CoV-2, Comirnaty (BNT162b2) [229]. One month later, Moderna (mRNA-1273) was the second vaccine to be approved by the EMA [230]. Both vaccines belonged to the nucleic acid-based vaccines category; therefore, this type remained the most prevalent in Europe till today. As of July 2023, there were eight COVID-19 vaccines authorised by the EMA, and they are summarised in Table 14.

Table 14. Overview of COVID-19 Vaccines Approved by the EMA [231].

Brand Name	Scientific Name	Manufacturer	First Approval Date	Platform
Comirnaty	BNT162b2	BioNTech Manufacturing GmbH	December 21st, 2020	Nucleic Acid
Spikevax	mRNA-1273	Moderna Biotech Spain S.L.	January 6th, 2021	Nucleic Acid
Vaxzevria	AZD1222	AstraZeneca AB	January 29th, 2021	Viral Vector
Jcovden	JNJ-78436735	Janssen-Cilag International NV	March 11th, 2021	Viral Vector
Nuvaxovid	NVX-CoV2373	Novavax CZ, a.s.	December 12th, 2021	Protein Subunit
Valneva	VLA2001	Valneva Austria GmbH	June 24th, 2022	Inactivated Virus
VidPrevtyn Beta	VAT00002	Sanofi Pasteur	November 10th, 2022	Protein Subunit
Bimervax		HIPRA Human Health S.L.U.	March 30th, 2023	Protein Subunit

With the emergence of new viral variants that caused massive epidemic waves, e.g., Delta and Omicron, and the waning immunity induced by primer doses, manufacturers were urged to develop updated versions of their vaccines to be used as boosters [232,233]. Given the flexibility and timeliness of mRNA technology, manufacturers of Comirnaty and Spikevax were able to acquire EMA approval for their adapted bivalent vaccines (Omicron BA.1 and Omicron BA.4-5) in September 2022 [230,234].

For primary vaccination, Comirnaty, Spikevax, Vaxzevria, Jcovden, Nuvaxovid, and Valneva are recommended. On the other hand, VidPrevtyn Beta and Bimervax are exclusively recommended for booster doses. Also, bivalent Comirnaty and Spikevax are recommended for booster doses.

While all EMA-approved vaccines are recommended for adults (≥ 18 years), only Comirnaty, Spikevax, Nuvaxovid and Bimervax are recommended for adolescents (≥ 12 years). Children aged 6 months or above are recommended to be vaccinated only by Comirnaty and Spikevax. Figure 27

Figure 27. COVID-19 Vaccines Authorised by the EMA [231].

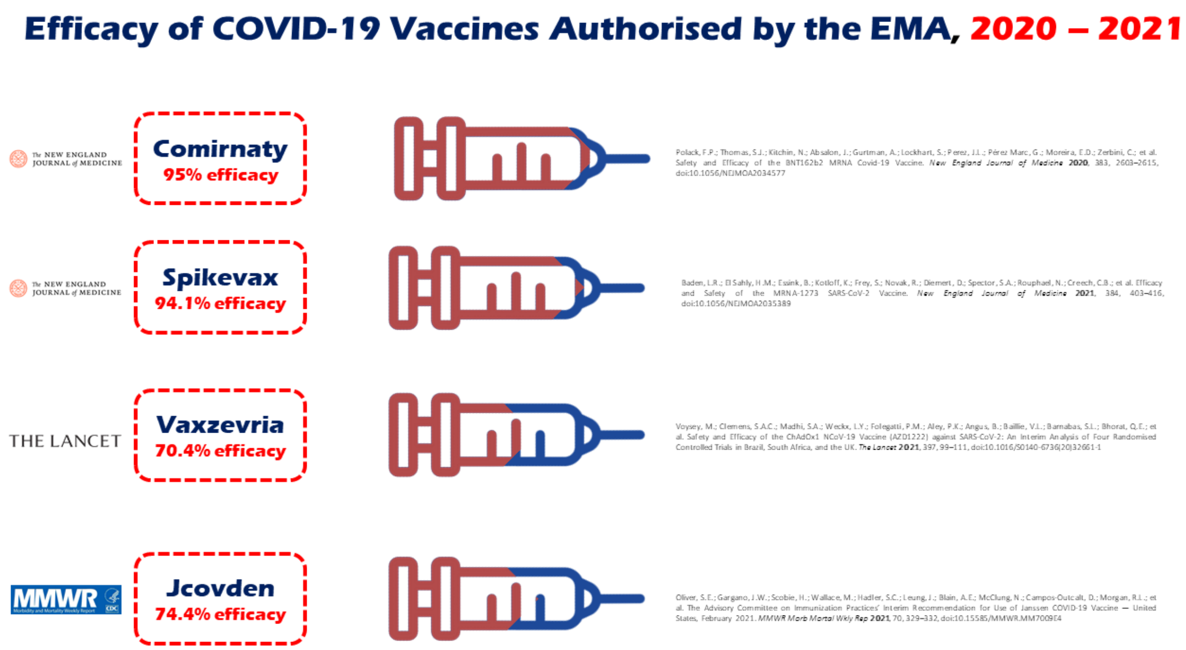
IV.II. COVID-19 Vaccines Efficacy and Effectiveness

Vaccine efficacy and vaccine effectiveness both measure the proportionate reduction in cases among vaccinated persons, but they are used in different contexts [235]. Vaccine efficacy, gauged in controlled clinical trials, is the relative reduction in disease cases among vaccinated individuals compared to those given a placebo. For instance, a vaccine with an efficacy of 80% means that vaccinated individuals in the trial had an 80% lower risk of developing the disease than the placebo group, but it does not imply that 20% of the vaccinated group will fall ill [235].

On the other hand, vaccine effectiveness measures how well vaccines work in real-world conditions. It is assessed by observing the vaccine's ability to protect entire communities. Effectiveness can differ from trial-measured efficacy due to the larger, more diverse population and varying conditions in the real world [235].

Polack *et al.* 2020 conducted a multinational, placebo-controlled, observer-blinded trial to evaluate the efficacy of the BNT162b2 vaccine in individuals aged 16 and older [236]. The study revealed a 95% efficacy of the vaccine in preventing COVID-19, with consistent results across various demographic and health-related subgroups. The safety profile of the vaccine was marked by short-term, mild-to-moderate side effects, with a low incidence of serious adverse events comparable to the placebo group [236]. Figure 28

Figure 28. Efficacy of COVID-19 Vaccines Approved by the EMA in 2020 – 2021 [236–239].



Baden *et al.* 2021 conducted a phase III clinical trial involving 30,420 participants to assess the efficacy of the mRNA-1273 vaccine. The study revealed that the vaccine had an efficacy of 94.1% in preventing COVID-19, including severe cases [237]. Apart from transient local and systemic reactions, no significant safety concerns were identified, with all severe COVID-19 cases occurring in the placebo group [237].

Voysey *et al.* 2021 evaluated the safety and efficacy of the AZD1222 vaccine through an interim analysis of four ongoing trials across the UK, Brazil, and South Africa [238]. The study found that the vaccine had an efficacy of 62.1% in participants who received two standard doses and 90.0% in those who received a low dose followed by a standard dose, with an overall efficacy of 70.4% across both groups. Despite ten cases of hospitalisation for COVID-19 in the control arm, including one death, the vaccine demonstrated an acceptable safety profile with 175 severe adverse events reported across 168 participants [238].

In February 2021, the Janssen COVID-19 vaccine, Jcovden, was granted emergency use authorisation by the US Food and Drug Administration (FDA). The Advisory Committee on Immunization Practices (ACIP) supported its use for individuals aged 18 and older to prevent COVID-

19 [239]. A phase III clinical trial with about 40,000 participants showed the vaccine had an efficacy of 66.3% against symptomatic, lab-confirmed COVID-19 ≥ 14 days post-vaccination and 65.5% ≥ 28 days post-vaccination. The vaccine's efficacy was consistent across age, sex, race, and ethnicity and among those with underlying medical conditions. Efficacy was highest in the US (74.4%), followed by Latin America (64.7%) and South Africa (52.0%). The vaccine also demonstrated high efficacy in preventing COVID-19-related hospitalisations (93.1% ≥ 14 days post-vaccination and 100% ≥ 28 days post-vaccination) and all-cause death (75.0%) [239].

The systematic review of Teerawattananon *et al.* 2022 aimed to consolidate the methodologies used in COVID-19 vaccine effectiveness studies, with a focus on their applicability in low- and middle-income countries [240]. The review, which analysed 42 studies, revealed that most research was conducted in high-income countries, primarily assessing mRNA vaccines. Major limitations identified across these studies included short follow-up time and inadequate assessment and mitigation of potential confounders. The study underscores the scarcity of such research in low- and middle-income countries, emphasising the need for context-specific vaccine effectiveness data in these regions [240].

Self *et al.* 2021 conducted a comparative investigation on 3,689 adults aged 18 years and above who were admitted to 21 hospitals across 18 states in the US from March 11th to August 15th, 2021. The study aimed to evaluate the effectiveness of the BNT162b2, mRNA-1273 and Jcovden vaccines in preventing COVID-19 hospitalisations [241]. The results revealed that the mRNA-1273 vaccine had the highest effectiveness at 93%, followed by the BNT162b2 vaccine at 88% and the Jcovden vaccine at 71%, with the BNT162b2 vaccine showing a decline in protection four months post-vaccination [241].

Recently, the rapid review of Wallace *et al.* 2022 on BNT162b2 effectiveness revealed the vaccine's remarkable effectiveness across all predetermined outcomes (symptomatic COVID-19, hospitalisation, mortality, and asymptomatic SARS-CoV-2 infection) [242]. Moreover, this groundbreaking study expanded our understanding of the vaccine's advantages, shedding light on outcomes and populations not previously studied in randomised controlled trials (RCTs). As the prospect of incorporating additional COVID-19 vaccines into standard recommendations endorsed by the ACIP looms, this innovative approach holds significant promise [242].

Andrews *et al.* 2022 assessed the effectiveness of the BNT162b2, AZD1222, and mRNA-1273 vaccines against the Omicron and Delta variants [243]. They discovered that the vaccines were more effective against the Delta variant than the Omicron variant across all time frames and combinations of primer and booster doses. After receiving two doses of AZD1222, there was no observable effect against the Omicron variant after 20 weeks, while BNT162b2 showed 65.5% effectiveness at 2 to 4 weeks, which declined to 8.8% at 25 weeks or more. A significant increase in protection was observed after BNT162b2 and mRNA-1273 booster following either the AZD1222 or BNT162b2 primer course, but this protection diminished over time [243].

Link-Gelles *et al.* 2023 conducted a case-control study, examining 82,229 emergency department encounters and 21,007 hospitalisations related to COVID-19-like illness and aiming to evaluate the effectiveness of first-generation COVID-19 mRNA vaccines during the prevalence of Omicron BA.4 and BA.5 sublineages [244]. The study revealed that the vaccine effectiveness was 68% for those who had their third dose 7 to 119 days before hospitalisation, but this effectiveness dwindled to 36% for those vaccinated 120 days or more prior to hospitalisation. This suggested that while the first-generation COVID-19 mRNA vaccines offered some defence against COVID-19 during the Omicron BA.4/BA.5 sublineage-dominant periods, this protection diminished over time [244].

IV.III. COVID-19 Vaccines Safety

Vaccine safety monitoring is an essential aspect of all clinical trial phases, including phase I, II, and III, which are conducted pre-authorisation. These stages rigorously evaluate the safety, immunogenicity, and efficacy of the vaccine in an increasingly larger group of volunteers [245,246]. Post-authorisation, phase IV studies, also known as post-marketing surveillance, continue to assess the safety and effectiveness of the vaccine in the wider population, identifying any uncommon or long-term adverse effects [245].

During phase IV, vaccine surveillance systems, categorised into active, passive, and hybrid types, are instrumental in monitoring vaccine safety [247]. Active surveillance involves systematic data collection on vaccine safety through regular follow-ups with vaccinated individuals, providing reliable but resource-intensive data. Passive surveillance, less resource-intensive, depends on self-reporting of adverse events by healthcare providers or vaccine recipients, potentially leading to underreporting. Hybrid systems amalgamate elements of both, actively monitoring a subset of the vaccinated population whilst accepting broader population reports, striking a balance between data comprehensiveness and resource use [247].

Passive surveillance systems, such as the Vaccine Adverse Event Reporting System (VAERS) in the US, the European Union Drug Regulating Authorities Pharmacovigilance (EudraVigilance) in the EU/EEA, the Yellow Cards in the UK, and the Database of Adverse Event Notifications (DAEN) in Australia are dependent on the active participation of healthcare professionals, vaccine manufacturers, and the public, who are tasked with reporting any adverse events post-immunisation [246–249]. The collected data is then scrutinised to identify any potential safety concerns associated with the vaccines, thereby enabling timely interventions to mitigate risks.

Gee *et al.* 2021 evaluated BNT162b2 and mRNA-1273 during the first month of mass vaccination in the US, utilising data from the VAERS database [250]. The findings of the study emphasised the reassuring safety profiles of these vaccines, characterised by typical local and systemic reactions, with severe allergic reactions being a rare anomaly. Crucially, no abnormal or unexpected reporting patterns were identified, thus instilling a sense of trust among healthcare professionals and vaccine recipients regarding the safety of these vaccines [250].

Shimabukuro *et al.* 2021 assessed the incidence of anaphylactic events during the first month of mass vaccination in the US. The initial estimated reporting rates for anaphylaxis were 11.1 cases per million doses for BNT162b2 and 2.5 cases per million doses for the mRNA-1273 [251]. Likewise, Boufidou *et al.* 2023 conducted a study to provide an updated evaluation of the incidence of anaphylaxis in the VAERS and EudraVigilance databases. The findings indicated a lower incidence of anaphylaxis associated with COVID-19 vaccination compared to previous estimates, with the majority of reported cases having a favourable outcome and extremely rare fatalities [252].

Regarding active surveillance of COVID-19 vaccines, numerous epidemiologic studies were designed and conducted at local and multi-national levels in order to collect data on post-vaccination side effects from the recently vaccinated individuals, e.g., COVID-19 Vaccines Safety Tracking (CoVaST) study [253].

In the Czech Republic, Riad *et al.* 2021 conducted a post-marketing (phase IV) survey-based study among HCPs to independently evaluate the side effects of BNT162b2. The most common side effects reported were injection site pain (89.8%), fatigue (62.2%), headache (45.6%), muscle pain (37.1%), and chills (33.9%) which were more prevalent in individuals aged 43 and under and typically lasted between one to three days. The study also found a higher frequency of side effects in individuals who received two doses of the vaccine, and while the distribution of side effects was largely consistent with the manufacturer's data, the overall prevalence of some local and systemic side effects was higher [254].

Another study in the Czech Republic evaluated the side effects of mRNA-based COVID-19 vaccines among university students [255]. A substantial majority (95.2%) of the 539 participants reported at least one side effect, with injection site pain (91.8%), fatigue (62.5%), headache (36.4%), and muscle pain (34.9%) being the most common. These side effects typically resolved within three days and were more likely to be reported by females and those who had received two doses of the vaccine [255].

In Slovakia, Riad *et al.* 2021 conducted a nationwide survey to assess the side effects of the BNT162b2 vaccine among HCPs [247]. The study, which included 522 participants, found that a significant 91.6% reported at least one side effect, with the most common being pain at the injection site (85.2%), fatigue (54.2%), headache (34.3%), muscle pain (28.4%), and chills (26.4%). These side effects were generally mild and resolved within three days and were more frequently reported by females and young adults [247].

In Poland, Dziedzic *et al*. 2021 conducted a survey among 317 healthcare professionals and medical students to evaluate the short-term adverse effects of BNT162b2, mRNA-1273, and AZD1222 [256]. The majority of participants reported at least one mild local or systemic adverse event, such as pain at the injection site (76.9%), fatigue (46.2%), headache (37.7%), and muscle pain (31.6%), which typically resolved within a day. The study confirmed the safety of these vaccines, although it noted that younger participants (under 29 years old) were generally more likely to experience side effects [256].

In conclusion,

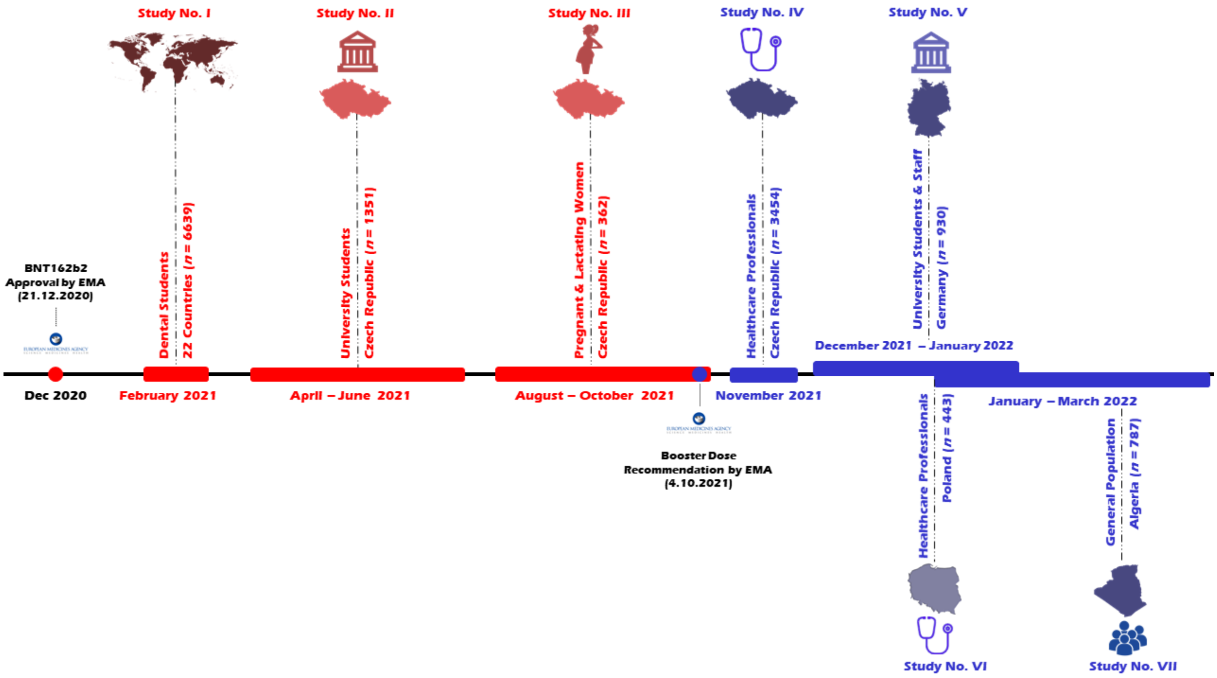
- As of March 2023, the landscape of vaccine development was marked by a significant number of candidates, with 183 in clinical development and 199 in pre-clinical stages. The most prevalent type was protein-subunit vaccines, closely followed by RNA-based and viral vector-based vaccines, reflecting the diverse strategies in the fight against COVID-19.
- Clinical trials have shown high efficacy rates for various COVID-19 vaccines, including BNT162b2 (95%), mRNA-1273 (94.1%), AZD1222 (70.4%), and Jcovden (66.3%).
- Real-world evidence demonstrated the high effectiveness of authorised COVID-19 vaccines in Europe and worldwide to the point that the pandemic status was relieved in May 2023.
- COVID-19 vaccines have shown reassuring safety profiles in various studies, with common mild side effects including injection site pain, fatigue, headache, and muscle pain, typically resolving within a few days.

Thesis Blueprint: Structure and Objectives

V.I. Structure

This thesis set out to evaluate COVID-19 vaccine hesitancy among specific population groups in the Czech Republic and globally during the mass vaccination campaigns for primer doses (winter – summer 2021) and booster doses (autumn 2021 – spring 2022). Comprising seven cross-sectional, survey-based studies, three were undertaken during the primer vaccination phase and four during the booster vaccination phase. Figure 29 presents a timeline of these studies, with those related to primer doses marked in red and those related to booster doses marked in blue.

Figure 29. Timeline of COVID-19 Vaccine Hesitancy Studies [121,257–264].



The findings of the thesis are organised into two sections. The first section comprises three nation-wide, cross-sectional, survey-based studies conducted in the Czech Republic among university students (spring 2021) [257], pregnant and lactating women (summer 2021) [258], and healthcare professionals (autumn 2021) [259]. The second section encompasses four cross-sectional, survey-based studies undertaken among dental students in 22 countries (winter 2021) [121,260,261], German university students and academics (winter 2022) [262], Polish healthcare professionals and students (spring 2022) [263], and the Algerian general adult population (winter 2022) [264]. Table 15

Table 15. Overview of COVID-19 Vaccine Hesitancy Studies [121,257–264].

Section	ID	Location	Data Collection	Campaign	Target Population	Sample (n)	Ref.
First	II	Czech Republic	April – June 2021	Primer	University Students	1,351	[257]
	III	Czech Republic	August – October 2021	Primer	Pregnant & Lactating Women	362	[258]
	IV	Czech Republic	November 2021	Booster	Healthcare Professionals	3,454	[259]

Second	I	22 Countries	February 2021	Primer	Dental Students	6,639	[121,260, 261]
	V	Germany	December 2021	Booster	University Students & Academics	930	[262]
	VI	Poland	December 2021 – January 2022	Booster	Healthcare Professionals & Students	443	[263]
	VII	Algeria	January – March 2022	Booster	General Adult Population	787	[264]

A variety of theoretical models informed the studies included in this thesis. The WHO-SAGE matrix model was applied in studies I and II, while the socio-ecological model (SEM) was employed to analyse the data from study I via machine-learning techniques. Studies IV, V, VI, and VII - the vaccine behaviour hesitancy (VBH) studies - utilised a custom instrument inspired by aspects of the health belief model (HBM), such as perceived susceptibility and benefit. Study III applied a custom instrument adapted from pre-existing tools used for pregnant and lactating women.

Table 16 presents a diverse set of instruments employed in the studies, characterised by varying numbers of multiple-choice questions (MCQs) that focused on demographics, COVID-19 and/or vaccine anamnesis, medical anamnesis, and psychological drivers.

In the first section, the instrument for study II consisted of 21 MCQs, achieving validation of Cohen's κ value of 0.83 ± 0.17. Study III incorporated a more extensive 32 MCQ instrument, validated through a panel of seven experts. A 19 MCQ instrument was utilised in study IV, yielding a Cohen's κ value of 0.8 ± 0.19 for validation.

In the second section, study I's instrument comprised 21 MCQs, validated with a Cohen's κ of 0.81 ± 0.16. Studies V and VI implemented instruments with 19 and 17 MCQs, respectively, both obtaining validation of Cohen's κ of 0.8 ± 0.19. Lastly, study VII utilised a more comprehensive instrument of 27 MCQs, also validated with a Cohen's κ of 0.8 ± 0.19.

Table 16. Theoretical Models and Instruments of COVID-19 Vaccine Hesitancy Studies [121,257–264].

Section	ID	Theoretical Model	Instrument	Validation	Language	Ref.
First	II	WHO-SAGE Matrix Model	21 MCQ (demographics, COVID-19 anamnesis, psychological drivers)	Cohen's κ = 0.83 ± 0.17 (0.52–1)	Czech	[257]
	III	Adapted from literature	32 MCQ (demographics, medical anamnesis, COVID-19 anamnesis, psychological drivers)	Expert panel (n = 7)	Czech	[258]
	IV	Health Belief Model (HBM)	19 MCQ (demographics, COVID-19 anamnesis, COVID-19 vaccine-anamnesis, psychological drivers)	Cohen's κ = 0.8 ± 0.19 (0.6–1)	Czech	[259]
Second	I	WHO-SAGE Matrix Model & Socio-Ecological Model (SEM)	21 MCQ (demographics, COVID-19 anamnesis, psychological drivers)	Cohen's κ = 0.81 ± 0.16 (0.55–1)	English	[121,260, 261]
	V	Health Belief Model (HBM)	19 MCQ (demographics, COVID-19 anamnesis, COVID-19 vaccine-anamnesis, psychological drivers)	Cohen's κ = 0.8 ± 0.19 (0.6–1)	German	[262]

VI	Health Belief Model (HBM)	17 MCQ (demographics, COVID-19 anamnesis, COVID-19 vaccine-anamnesis, psychological drivers)	Cohen's κ = 0.8 ± 0.19 (0.6–1)	Polish	[263]
VII	Health Belief Model (HBM)	27 MCQ (demographics, medical anamnesis, COVID-19 anamnesis, psychological drivers)	Cohen's κ = 0.8 ± 0.19 (0.6–1)	Arabic / French	[264]

All studies collected data using digital forms through KoboToolBox (Harvard Humanitarian Initiative, Cambridge, MA, USA), with the exception of study II [265]. This study adopted a hybrid approach, using both digital and paper forms to accumulate data from pregnant and lactating women attending outpatient clinics [258]. All studies were designed and reported according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for cross-sectional studies [266].

In accordance with the Declaration of Helsinki for research involving human subjects, all studies were conducted with rigorous adherence to ethical standards [267]. Prior to initiation, ethical approval was procured from the respective institutional review boards. All participants (n = 13,966) provided informed consent prior to their involvement, and it was explicitly communicated that they retained the freedom to withdraw from the study at any time without repercussions. Neither incentives were offered, nor threats were imposed to enhance the response rate.

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) and the R-based open software, Jamovi [268,269]. An array of statistical methods was deployed, incorporating both descriptive and inferential statistics. Descriptive statistics were employed to summarise qualitative variables through frequencies (n) and percentages (%) and quantitative variables using central tendency values, namely mean and median, along with dispersion values such as range, inter-quartile range (IQR), and standard deviation (SD). Inferential statistics were utilised at a significance level of < 0.05, incorporating chi-squared test (χ^2), Fisher's exact test, correlation tests (parametric and non-parametric), Student's t-test, analysis of variance (ANOVA), Mann-Whitney (U) test, Kruskal-Wallis (H) test, and regression tests (logistic, multiple, and linear).

The findings from the seven studies constituting this thesis were disseminated in nine original articles. All these articles were published in scholarly journals, which are indexed in both the Clarivate Analytics' Web of Science (WoS) and Elsevier's Scopus databases. The thesis author (Abanoub RIAD) emerged as the first author of 4/9 (44.4%), the last author of 4/9 (44.4%), and the corresponding author of 6/9 (66.7%) of the published articles. The cumulative Impact Factor (IF) of the journals that published these articles is 47.61, as determined by the IF values corresponding to the respective years of publication. Table 17

Table 17. Overview of the Published Articles [121,257–264].

Section	ID	Title	Authors	Journal	Ref.
First	II	Prevalence and Drivers of COVID-19 Vaccine Hesitancy among Czech University Students: National Cross-Sectional Study	**Abanoub RIAD*;** Andrea POKORNÁ; Natália ANTALOVÁ; Martin KROBOT; Nutsa ZVIADADZE; Iryna SERDIUK; Michal KOŠČÍK; Miloslav KLUGAR	*Vaccines* (2021 WoS Q2; IF = 4.96)	[257]

	III	COVID-19 Vaccine Acceptance of Pregnant and Lactating Women (PLW) in Czechia: An Analytical Cross-Sectional Study	**Abanoub RIAD*;** Anna JOUZOVÁ; Batuhan ÜSTÜN; Eliška LAGOVÁ; Lukáš HRUBAN; Petr JANKŮ; Andrea POKORNÁ; Jitka KLUGAROVÁ; Michal KOŠČÍK; Miloslav KLUGAR*	*IJERPH* (2021 WoS Q1; IF = 4.61)	[258]
	IV	COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Workers in Czechia: National Cross-Sectional Study	Miloslav KLUGAR; **Abanoub RIAD*;** Lekshmi MOHANAN; Andrea POKORNÁ	*Vaccines* (2021 WoS Q2; IF = 4.96)	[259]
Second	I	Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy	**Abanoub RIAD***; Huthaifa ABDULQADER; Mariana MORGADO; Silvi DOMNORI; Michal KOŠČÍK; José João MENDES; Miloslav KLUGAR; Elham KATEEB; IADS-SCORE	*Vaccines* (2021 WoS Q2; IF = 4.96)	[260]
	I	Universal Predictors of Dental Students' Attitudes towards COVID-19 Vaccination: Machine Learning-Based Approach	**Abanoub RIAD*;** Yi HUANG; Huthaifa ABDULQADER; Mariana MORGADO; Silvi DOMNORI; Michal KOŠČÍK; José João MENDES; Miloslav KLUGAR; Elham KATEEB; IADS-SCORE	*Vaccines* (2021 WoS Q2; IF = 4.96)	[121]
	I	Predictors of Willingness to Receive COVID-19 Vaccine: Cross-Sectional Study of Palestinian Dental Students	Elham KATEEB; Mayar DANADNEH; Andrea POKORNÁ; Jitka KLUGAROVÁ; Huthaifa ABDULQADER; Miloslav KLUGAR*; **Abanoub RIAD**	*Vaccines* (2021 WoS Q2; IF = 4.96)	[261]
	V	Prevalence and Drivers of COVID-19 Vaccine Booster Hesitancy Among German University Students and Employees	Sameh ATTIA*; Katharina MAUSBACH; Miloslav KLUGAR; Hans-Peter HOWALDT; **Abanoub RIAD**	*Frontiers in Public Health* (2022 WoS Q2; IF = 5.20)	[262]
	VI	COVID-19 vaccine booster Hesitancy (VBH) of healthcare professionals and students in Poland: Cross-sectional survey-based study	Arkadiusz DZIEDZIC; Julien ISSA; Salman HUSSAIN; Marta TANASIEWICZ; Robert WOJTYCZKA; Robert KUBINA; Marta DYSZKIEWICZ KONWINSKA; **Abanoub RIAD***	*Frontiers in Public Health* (2022 WoS Q2; IF = 5.20)	[263]
	VII	COVID-19 Vaccine Booster Hesitancy (VBH) and Its Drivers in Algeria: National Cross-Sectional Survey-Based Study	Mohamed LOUNIS*; Djihad BENCHERIT; Mohammed Amir RAIS; **Abanoub RIAD**	*Vaccines* (2022 WoS Q1; IF = 7.80)	[264]

The asterisk (*) denotes the corresponding authors.

As of July 16th, 2023, the collective citation count for the thesis articles stands at 350 according to WoS, 377 according to Scopus, and 508 according to Google Scholar. Bibliometric analysis revealed that among the documents citing these studies were policy documents from the OECD [270].

V.II. Objectives

The overarching goal of this thesis was to evaluate the current status of COVID-19 vaccine hesitancy among population groups in the Czech Republic and worldwide during the mass-vaccination campaigns in 2021 – 2022, in order to provide policymakers with timely evidence to better navigate the ongoing pandemic.

The **primary** objectives included:

1) To measure the prevalence of COVID-19 vaccine hesitancy among target population groups in the Czech Republic and worldwide during primer vaccination campaigns (winter–summer 2021) and booster vaccination campaigns (winter–spring 2022).
2) To explore the demographic and anamnestic risk factors of COVID-19 vaccine hesitancy among the target population groups during primer and booster vaccination campaigns.
3) To explore the psychological correlates of COVID-19 vaccine hesitancy among the target population groups during primer and booster vaccination campaigns.

The **secondary** objectives included:

1) To explore the systemic determinants of COVID-19 vaccine hesitancy utilising the SEM in a multi-country context.
2) To develop a validated psychometric instrument for assessing COVID-19 VBH.
3) To compare the psychological correlates of COVID-19 VBH among the Czech, German, Polish and Algerian populations.

COVID-19 Vaccine Hesitancy in the Czech Republic

This section presents three studies conducted among various Czech population groups in spring 2021 (study II), summer 2021 (study III), and autumn 2021 (study IV). Studies II and III aimed to investigate vaccine hesitancy during the primer vaccination campaigns among university students and pregnant or lactating women, respectively. Conversely, study IV was designed to explore vaccine hesitancy during booster vaccination campaigns specifically targeting healthcare professionals.

VI.I. COVID-19 Vaccine Hesitancy among Czech University Students (Study II)

University students, often perceived as prospective opinion leaders possessing elevated levels of health literacy, epitomised a vital demographic group in the struggle against COVID-19. Their attitudes towards vaccination could significantly mould broader societal trends, making the comprehension of the factors propelling vaccine hesitancy within this group paramount.

The primary objective of this study was to estimate the prevalence of COVID-19 vaccine hesitancy among Czech university students. While the secondary objective was to identify demographic risk factors and drivers of vaccine hesitancy within this population.

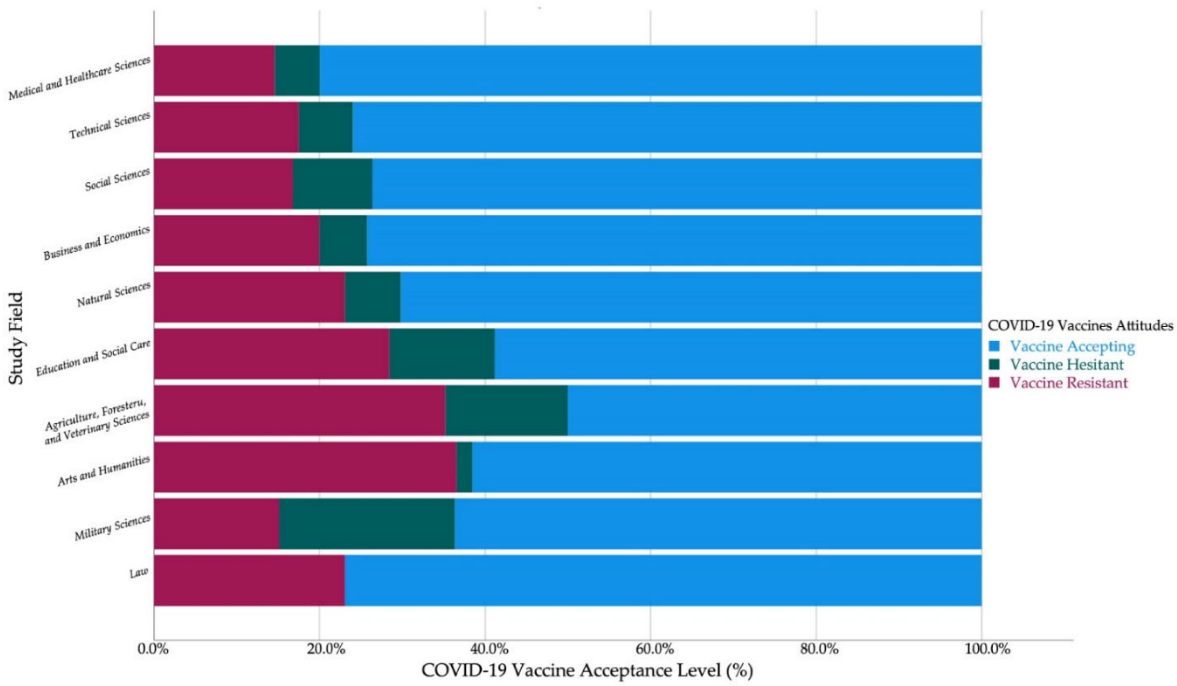
This cross-sectional, survey-based study employed a digital self-administered questionnaire (SAQ) inspired by the WHO-SAGE matrix model of vaccine hesitancy. The questionnaire, disseminated to a sample of 1169 students from all Czech universities between April and June 2021, incorporated demographic information, COVID-19-related anamnesis, influenza vaccine-related anamnesis, level of acceptance for the COVID-19 vaccine, and potential drivers of vaccine hesitancy.

Among the 1351 students incorporated into the final analysis, 73.3% accepted the COVID-19 vaccine, 19.3% demonstrated vaccine resistance, and 7.4% exhibited vaccine hesitancy. A temporal analysis of attitudes towards the COVID-19 vaccine indicated a rise in vaccine resistance, from 18.7% in the initial week to 29.5% by the fifth week.

There was no significant difference in acceptance levels between males and females, but a slightly elevated vaccine hesitancy was noted amongst females (8.3%) compared to males (5.2%). Non-healthcare students (non-HCS) displayed higher vaccine resistance (22.6% vs. 14.6%) and hesitancy (8.7% vs. 5.5%), and lower vaccine acceptance (68.7% vs. 80%) than healthcare students (HCS). Among non-HCS, students of law, technical sciences, business and economics, social sciences, and natural sciences indicated comparatively high vaccine acceptance, whilst students of military sciences, agriculture, forestry, veterinary sciences, and education and social care exhibited greater vaccine hesitancy. Figure 30

Factors which predicted higher odds of vaccine acceptance encompassed trust in the pharmaceutical industry, trust in healthcare providers, and the perceived sufficiency of knowledge. Contrarily, factors that predicted higher odds of vaccine hesitancy included influence from media and social media, personal beliefs, misconceptions about immunity, previous COVID-19 infection, and suspicions about novel vaccines and their local availability.

Figure 30. Czech university students' COVID-19 vaccine acceptance by study field (April–June 2021, *n* = 1337*); Riad *et al.* 2021 [257].



* Out of 1351 participants, fourteen did not specify their study program. Therefore, the diagram represents 1137 students only.

These findings advocated for promotional interventions and educational programmes on vaccines in Czech universities, specifically targeting non-HCS students due to their lower vaccine acceptance and awareness levels. Future prevention strategies ought to be culturally inclusive, ensuring international students are not overlooked. This study, the first of its kind in the Czech Republic, highlighted critical disparities across gender, academic fields, and years of study in vaccine hesitancy, providing necessary evidence for informed policy recommendations.

The study's limitations included its reliance on self-reported data, which might have been subject to bias. Additionally, the snowballing technique used for participant recruitment might have resulted in a disproportionately higher number of participants from healthcare-related study programmes.

ATTACHMENT NO. 1

Riad A, Pokorná A, Antalová N, Krobot M, Zviadadze N, Serdiuk I, Koščík M, Klugar M. Prevalence and Drivers of COVID-19 Vaccine Hesitancy among Czech University Students: National Cross-Sectional Study. *Vaccines*. **2021**; 9(9):948. https://doi.org/10.3390/vaccines9090948

VI.II. COVID-19 Vaccine Hesitancy among Czech Pregnant and Lactating Women (Study III)

Pregnant and lactating women (PLW), due to their increased vulnerability to severe outcomes from COVID-19 and the potential implications for neonatal health, had been the target group of this study. Moreover, their initial exclusion from vaccine trials had led to a delay in providing evidence on the safety and efficacy of COVID-19 vaccines for them, contributing to vaccine hesitancy among PLW. Therefore, understanding their attitudes towards vaccination and the factors influencing vaccine acceptance had been deemed vital to optimising vaccine coverage in this group.

The primary objective had been to gauge the level of COVID-19 vaccine hesitancy among PLW in the Czech Republic, whilst the secondary objective had been to determine the potential factors that might influence COVID-19 vaccine hesitancy among PLW.

This cross-sectional study, conducted from August to October 2021, assessed COVID-19 vaccine attitudes among unvaccinated Czech PLW. The participants, sourced from the outpatient gynaecologic clinic of the University Hospital Brno, had completed a SAQ designed with KoBoToolbox. The questionnaire, comprising 32 closed-ended items, included demographic data, medical and COVID-19-related anamneses, and attitudes towards COVID-19 vaccination. Out of 401 responses, 362 (278 PW and 84 LW) had been deemed eligible and were included in the final analysis.

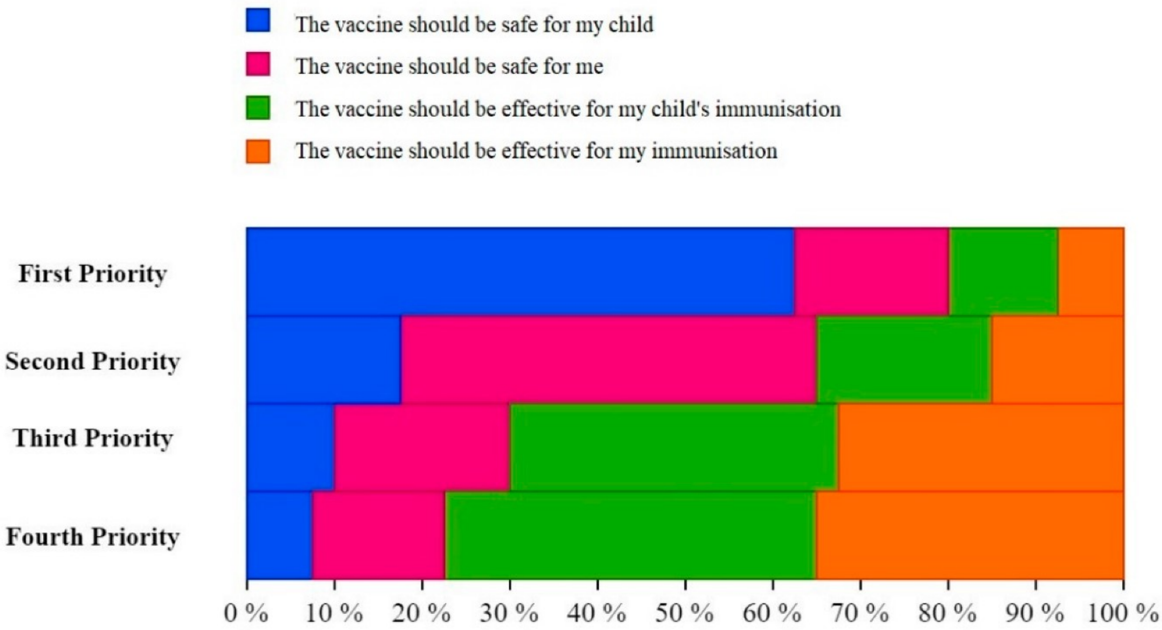
Two-thirds of the participants (66.6%) were willing to receive the COVID-19 vaccine but preferred to delay it until after pregnancy or the weaning of their children. A small fraction (3.6%) had been ready for immediate vaccination, whilst a considerable proportion (29.8%) had rejected the vaccine outright. PW in their third trimester had shown a significantly higher acceptance level of the vaccine (80.7%) compared to those in their first trimester (41.7%).

Education level and employment status emerged as significant factors in vaccine acceptance among PLW. Those holding a master’s degree or higher had shown an acceptance level of 85.3%, significantly higher than those with basic education at 42.9%. Employed PLW had also shown a higher acceptance level. However, pregnant healthcare workers had a slightly lower acceptance level (74%) compared to non-healthcare workers (80.7%).

Both PW and LW had prioritised the safety of children (58.4% and 71.1%, respectively) and the mother (46.2% and 49.4%, respectively), followed by the effectiveness of children's immunisation (33.6% and 38.3% for PW, 39.8% and 50.6% for LW). The order of these priorities had been largely similar for both groups. Figure 31

Trust in the pharmaceutical industry and healthcare professionals had significantly increased the odds of vaccine acceptance by 15.590 times and 4.355 times, respectively. PLW with a favourable risk-benefit ratio had an acceptance odds ratio of 15.518 times more than their counterparts. Interestingly, perceived knowledge had been associated with a decreased odds ratio of acceptance at 0.911.

Figure 31. Top priorities of pregnant and lactating women (PLW) regarding COVID-19 vaccines, University Hospital Brno, August–October 2021 (*n* = 362); Riad *et al.* 2021 [258].



The findings highlighted the importance of promotional interventions targeting PLW, emphasising the benefits of COVID-19 vaccines and the potential risks of infection during pregnancy. Web-based interventions were recommended to increase PLW's knowledge of COVID-19 vaccine safety. Furthermore, the study evaluated the immediate impact of preliminary evidence on vaccine safety and explored several determinants of vaccine acceptance among PLW, helping to minimise bias due to the questionnaire's anonymous nature. The study called for further research to distinguish between perceived and factual knowledge to identify knowledge gaps and to include ethnic minorities and immigrant communities in public health planning.

This study was limited by the absence of ethnic minorities, making its findings most relevant to the Czech-speaking population in the Czech Republic and a low number of LW that might have influenced the effect size of some risk factors. Additionally, vaccine-related knowledge assessment was based solely on perceived knowledge, precluding verification of knowledge gaps, and the cross-sectional design prevented causality determination, while self-reported outcomes risked misreporting and bias.

ATTACHMENT NO. 2

Riad A, Jouzová A, Üstün B, Lagová E, Hruban L, Janků P, Pokorná A, Klugarová J, Koščík M, Klugar M. COVID-19 Vaccine Acceptance of Pregnant and Lactating Women (PLW) in Czechia: An Analytical Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. **2021**; 18(24):13373. https://doi.org/10.3390/ijerph182413373

VI.III. COVID-19 Vaccine Booster Hesitancy (VBH) among Czech Healthcare Professionals (Study IV)

The emergence of novel SARS-CoV-2 variants that led to massive epidemic waves, such as Delta and Omicron, coupled with the waning effectiveness of primer vaccine doses, underlined the importance of investigating attitudes towards booster doses prior and amid the booster vaccination campaigns [271]. Healthcare professionals (HCPs) have been disproportionately affected by COVID-19 experiencing high levels of morbidity and mortality. Also, they play a pivotal societal role in promoting and recommending vaccines to the public. Therefore, their attitudes towards booster doses can significantly influence public perception and uptake of these doses.

Conducted from November 3rd to 11th, 2021, this nationwide, cross-sectional study aimed to understand the attitudes of Czech HCPs towards receiving COVID-19 vaccine booster doses. An SAQ, inspired by the health belief model (HBM) and validated by a panel of public health, health policy, and healthcare management experts, was used to collect data from target participants online. The study aimed to reach a nationally representative sample of HCPs. While the sample size was calculated to be 2379, the study included 3454 participants in the final analysis after excluding those who did not consent and those with incomplete responses.

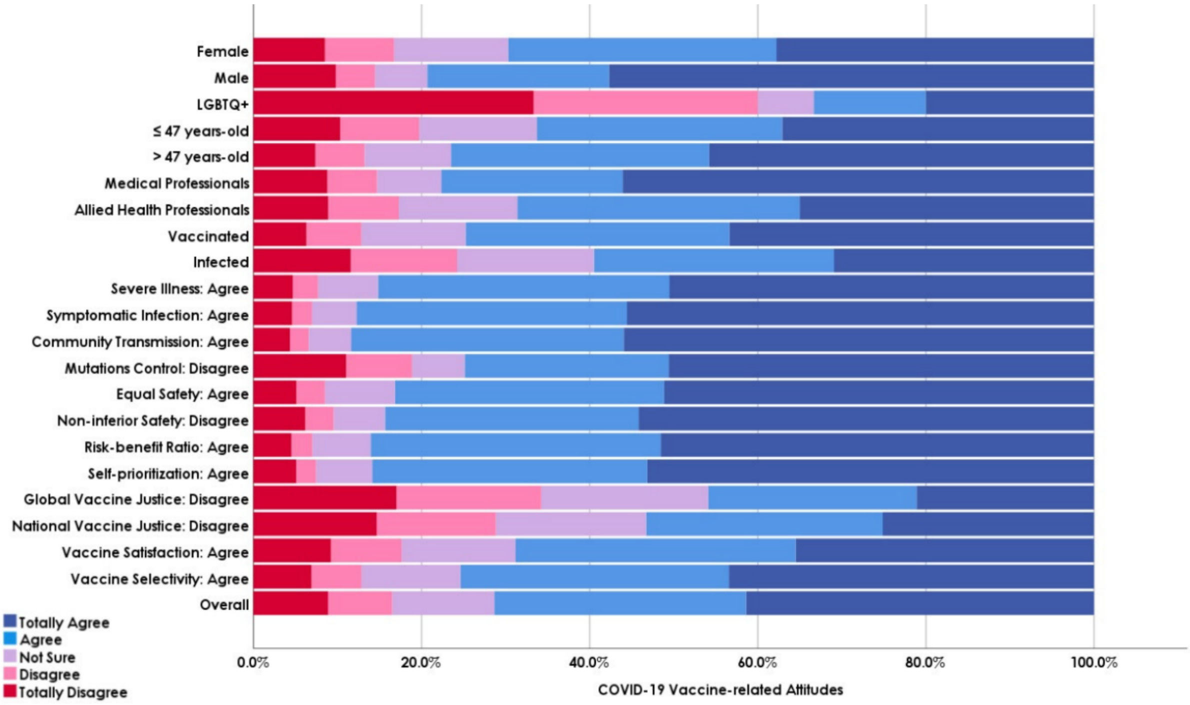
Most participants were females (80.9%), and the study sample represented all fourteen administrative regions of the Czech Republic, with the most contributions coming from Prague (29.2%). The study found that 32% of participants had previously been infected with COVID-19, with the most common clinical manifestation being fatigue (77.1%). The study also noted that there was no significant difference in COVID-19 onset or severity across professions, gender, or age groups.

In terms of vaccination anamnesis, 95.2% of the sample had received primer doses of COVID-19 vaccines, with the most commonly administered vaccine being BTN162b2 (90.7%). Less than half of the sample (48.5%) had received a third dose at the time of the survey. The study found that male participants and those in medical professions were significantly more likely to have received three doses than their counterparts.

When asked about their attitudes towards receiving COVID-19 vaccine booster doses, 71.3% indicated acceptance, 12.2% were hesitant, and 16.5% rejected the idea. Notably, acceptance was higher among males, those in medical professions, and participants over 47 years old, compared to their counterparts. The primary motivator for accepting the booster dose was the desire to protect their families, cited by 83.0% of participants, suggesting a strong sense of familial responsibility in healthcare decisions. Figure 32

The study also explored the psychosocial drivers of attitudes towards booster doses. It found that 80.3% of participants agreed that the current booster dose could protect them from severe illness, while only 57.8% agreed that booster doses could prevent symptomatic infection. The study also found that 76.5% agreed that the current booster doses are as safe as the primer doses, while only 12.5% believe that the booster dose may impose more severe side effects compared to the primer ones. The study found that demographic variables, previous infection status, and previous vaccination status all had an impact on booster dose acceptance.

Figure 32. COVID-19 Vaccine Booster Dose-related Attitudes of Czech HCPs, November 2021 (*n* = 3454); Klugar *et al.* 2021 [259].



The findings indicated that future COVID-19 vaccine booster hesitancy (VBH) research should have considered demographic factors like age and gender among general population groups. They also recommended that public health communication about COVID-19 booster doses should emphasise their effectiveness against severe illness, symptomatic infection, and community transmission, as well as their safety. The study also highlighted the need to address ethical conflicts related to vaccine justice and to adjust individual risk-benefit ratios of booster doses, particularly among frontline HCPs. Altruistic motivators for vaccine uptake should be prioritised over mandates. The study, the first to evaluate Czechs' attitudes towards COVID-19 booster doses, used an anonymous questionnaire to minimise bias and ensure a representative sample. It also provided insights into the COVID-19 infection rate, clinical severity, and vaccination rate among Czech HCPs.

The study faced limitations such as missing data on the type of vaccine administered for each dose, participants' general medical history and BMI, underrepresentation of pregnant women, LGBTQ+ and other minority groups, and lack of detailed information on post-vaccination side effects.

ATTACHMENT NO. 3

Klugar M, **Riad A**, Mohanan L, Pokorná A. COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Workers in Czechia: National Cross-Sectional Study. *Vaccines*. **2021**; 9(12):1437. https://doi.org/10.3390/vaccines9121437

COVID-19 Vaccine Hesitancy Worldwide

This section presents four studies conducted among various international population groups in winter 2021 (study I), winter 2022 (studies V and VI), and spring 2022 (study VII). Study I aimed to investigate vaccine hesitancy among an international sample of dental students representing 22 countries during the primer vaccination campaigns. On the other hand, studies V, VI and VII were designed to explore vaccine hesitancy during booster vaccination campaigns among German university students and staff, Polish healthcare professionals and students and the Algerian general adult population, respectively.

VII.I. COVID-19 Vaccine Hesitancy among Dental Students Globally (Study I)

The study targeted dental students due to their role as future healthcare providers, who can influence their patients' health behaviours, including attitudes towards vaccinations. Given that healthcare students, including dental students, often retain high levels of health-related knowledge and attitudes, they are perceived as opinion leaders of public health issues. Moreover, dental students are required to receive certain vaccines as part of their clinical training due to their increased risk of contracting infectious diseases, thus providing a unique perspective on vaccine acceptance or hesitancy.

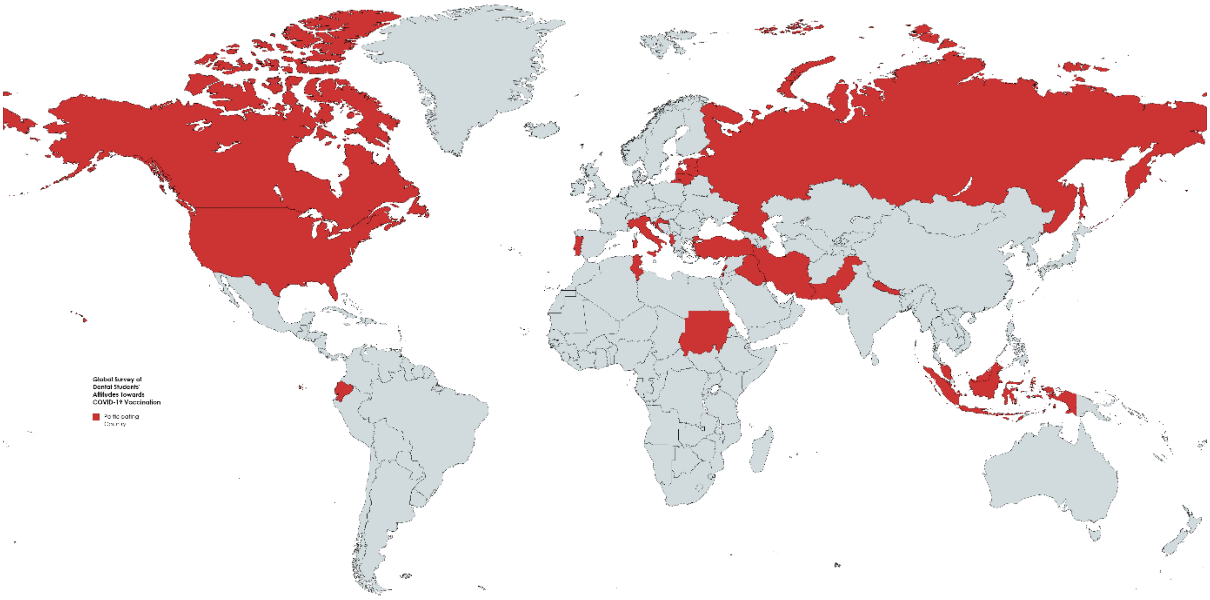
This global study was organised by the International Association of Dental Students (IADS), with the thesis author, Abanoub Riad, playing a key role in its design and coordination from his position as an advisory board member of the IADS. His role would have encompassed conceptualisation, development of the study's objectives and methodology, and coordinating efforts among national and local member organisations of the IADS.

The study employed a cross-sectional design and was conducted between February 6th and 28th, 2021. The survey targeted undergraduate dental students in 22 participating countries, including recent graduates and those undergoing their compulsory training year. A digital SAQ, composed of 20 multiple-choice items and inspired by the WHO-SAGE matrix model, was used as the primary data collection tool. The SAQ focused on demographic data, COVID-19-related anamnesis, willingness to receive the COVID-19 vaccine, and the potential drivers of vaccination willingness. Figure 33 presents the 22 participating countries.

Out of 6639 included participants, 70.5% were females, 27.7% males, 0.8% non-binary, and 1% undisclosed, with an average age of 22.06 years; 7% were from low-income economies, 18.6% from lower-middle-income, 45.7% from upper-middle-income, and 28.7% from high-income economies, while regionally, 11.3% hailed from Africa, 11.1% from the Americas, 19.6% from Asia-Pacific, 19.1% from the Eastern Mediterranean, and 39% from Europe.

About 16.6% reported prior SARS-CoV-2 infection, with more infections in low and lower-middle-income economies (19.5%) versus upper-middle and high-income economies (15.6%), males (19.8%) compared to females (14.9%), and clinical students (17.6%) versus pre-clinical students (14.7%), with Albania and Iran recording the highest infection rates at 43.9% and 34.3% respectively.

Figure 33. Participating Countries in the IADS Survey of Dental Students' Attitudes Towards COVID-19 Vaccination, February 2021 (n = 22); Riad *et al.* 2021 [260].



When asked about their position on COVID-19 vaccination, 13.9% disagreed, 22.5% were hesitant, and 63.6% were willing to get vaccinated. Students from low and lower-middle-income economies were significantly more hesitant to take the COVID-19 vaccine at 30.4% compared to their peers from upper-middle and high-income economies at 19.8%, with the greatest hesitancy in low-income economies at 37.5%, resistance in low-income economies at 18.6%, and the highest acceptance found in high-income economies at 81.6%. Figure 34

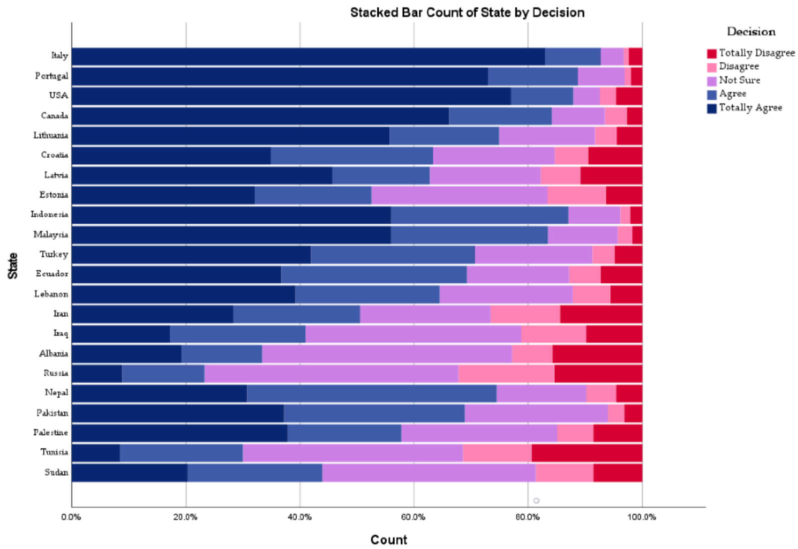


Figure 34. Dental students' COVID-19 vaccine acceptance level by state, February 2021 (n = 6,639); Riad *et al.* 2021 [260].

Low and lower-middle-income students, influenced more by media (42%) and leaders (21.3%), had less confidence in government (27.1%) and pharmaceuticals (37%); vaccine acceptance varied among years (3.93 for fifth-year students, 3.59 for interns) and countries (4.7 in Italy, 3.62 in Estonia), with lower acceptance among the previously infected (3.57) and caregivers (3.68).

ATTACHMENT NO. 4

Riad A, Abdulqader H, Morgado M, Domnori S, Koščík M, Mendes JJ, Klugar M, Kateeb E, on behalf of IADS-SCORE. Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy. *Vaccines*. **2021**; 9(6):566. https://doi.org/10.3390/vaccines9060566

The sheer volume of responses collected in this global survey-based study warranted deeper examination to uncover underlying trends and associations. This led us to publish a companion paper, where we harnessed machine learning techniques to analyse the extensive dataset more thoroughly. This paper uncovered critical predictors influencing dental students' vaccine acceptance worldwide. Our comprehensive approach adopted the socio-ecological model (SEM) to analyse demographic and psychological variables.

Initially, our study utilised a regression decision tree analysis to confirm variables associated with vaccination willingness. Using the R package 'rpart', we divided the sample into training and testing datasets, employing stringent rules to avoid overfitting. Following this, a multi-level regression model based on the socio-ecological theory was used to predict individuals' vaccination willingness. Considering the socio-ecological theory's guidelines, all significant predictors were categorised into individual or contextual levels, aiding us in constructing an accurate, slope-fixed linear multi-level model.

The decision tree analysis identified five key predictors of individuals' willingness to be vaccinated: 1) the economic level of the country, 2) the individual's trust in the pharmaceutical industry, 3) the individual's misconceptions about natural immunity, 4) the individual's attitudes towards novel vaccines, and 5) the individual's views on the risk-benefit ratio of COVID-19 vaccines. This model could explain 27% of the variance of the dependent variable. Figure 35

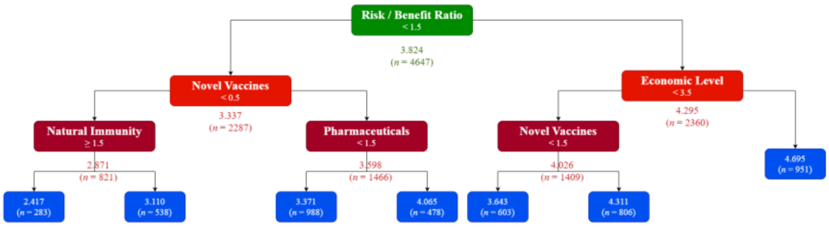


Figure 35. Decision tree for prediction of dental students' willingness to receive COVID-19 vaccines, February 2021 (*n* = 6639); Riad *et al.* 2021 [121].

A bivariate correlation analysis was run using Pearson's correlation coefficient (ρ), showing significant associations (Sig. < 0.001) between vaccination willingness and the five important predictors. In the multi-level regression analysis, it was found that the trust in the pharmaceutical industry (β = 0.304; Sig. < 0.001), belief in the risk-benefit ratio (β = 0.285; Sig. < 0.001), and attitudes towards novel vaccines (β = 0.382; Sig. < 0.001) had a significant and positive effect on vaccination willingness. However, misconceptions about natural immunity showed a negative influence on vaccination willingness (β = -0.270; Sig. < 0.001). Based on the socio-ecological theory, the economic level of the country was seen as a contextual factor, and it was found that higher economic level predicted higher vaccination willingness. The final regression model explained 30% of the variance. Figure 36

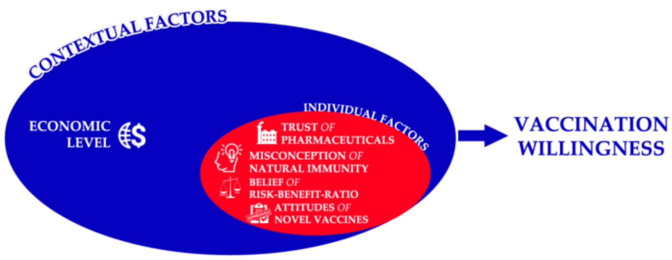


Figure 36. Conceptual map of vaccination willingness predictors according to the socio-ecological theory, February 2021 (*n* = 6639); Riad *et al.* 2021 [121].

ATTACHMENT NO. 5

Riad A, Huang Y, Abdulqader H, Morgado M, Domnori S, Koščík M, Mendes JJ, Klugar M, Kateeb E, IADS-SCORE. Universal Predictors of Dental Students' Attitudes towards COVID-19 Vaccination: Machine Learning-Based Approach. *Vaccines*. **2021**; 9(10):1158. https://doi.org/10.3390/vaccines9101158

Given the diverse local contexts and the vast quantity of data gathered in this global study, there was a clear necessity for more detailed, granular analyses. This led to the development of a further research paper, focusing specifically on the data from Palestinian dental students. The aim was to identify specific predictors affecting their willingness to receive the COVID-19 vaccine, providing more focused insights that could potentially inform tailored health interventions in similar contexts.

The analysis included 417 Palestinian dental students, with 86.1% of them aged 22 or below. The vaccination habits of these students were varied, with 53% (n=220) having never taken an influenza vaccine before and 14.9% (n=62) not willing to take the COVID-19 vaccine. The decision to receive the COVID-19 vaccine was influenced by social media for 47% (n=195) of the students and by celebrities and leaders for 31% (n=128). Trust issues were also evident, with 30% (n=123) not trusting government's vaccine decision-making and 21% (n=88) distrusting pharmaceutical companies' data on vaccine safety.

Inferential analyses revealed significant associations between willingness to vaccinate and several factors. These included the influence of social media ($H=11.97$, $p=0.003$) and trust in both government's vaccine decisions ($H=82.32$, $p<0.001$) and pharmaceutical companies' data ($H=106.6$, $p<0.001$). Females were less willing to vaccinate (U-test=13,289, $p<0.001$) and a prior influenza vaccination significantly influenced the decision ($U=13{,}684$, $p<0.001$). The final model, explaining 46% of the variance, showed that attitudes towards new vaccines ($\beta=6.23$, $p<0.001$), favourable risk–benefit ratio belief ($\beta=5.64$, $p<0.001$), trust in the pharmaceutical industry ($\beta=5.92$, $p=0.001$), natural immunity preference ($\beta=-4.24$, $p<0.001$), and having enough vaccine information ($\beta=4.12$, $p<0.001$) influenced the willingness to vaccinate. Table 18

Table 18. Model of Palestinian dental students' attitudes towards COVID-19 vaccine, February 2021 (*n* = 417); Kateeb *et al.* 2021 [261].

Model	**Beta**	***t***	***Sig.***
(Constant)		9.736	<0.001
In general, when a new vaccine is introduced, are you inclined to consent on your vaccination?	0.479	6.426	<0.001
If "Yes", do you agree with these people?	−0.333	−4.450	<0.001
Never	−0.287	−3.751	<0.001
Do you trust pharmaceutical companies to provide credible data on COVID-19 vaccine safety and effectiveness vaccines?	0.190	2.519	0.014
Do you feel you have enough information about COVID-19 vaccines and their safety?	0.248	3.219	0.002
Do you trust that your government is making decisions in your best interest with respect to what vaccines are provided (e.g., your government purchases the highest quality vaccines available)?	−0.182	−2.267	0.026
Do you think that there are better ways to prevent diseases than using COVID-19 vaccines (e.g., developing immunity by getting sick and recovered)?	−0.175	−2.193	0.031

ATTACHMENT NO. 6

Kateeb E, Danadneh M, Pokorná A, Klugarová J, Abdulqader H, Klugar M, **Riad A**. Predictors of Willingness to Receive COVID-19 Vaccine: Cross-Sectional Study of Palestinian Dental Students. *Vaccines*. **2021**; 9(9):954. https://doi.org/10.3390/vaccines9090954

VII.II. COVID-19 Vaccine Booster Hesitancy (VBH) among German University Students and Academics (Study V)

University settings, characterised by close social interactions and international mobility, may be particularly susceptible to the transmission of infectious diseases such as COVID-19. Given their advanced educational attainment, university students and academics are likely to demonstrate distinctive perceptions and attitudes towards immunisation, thus constituting an interesting group for investigating vaccine hesitancy. As such, gaining insight into vaccine booster hesitancy (VBH) among this demographic can provide valuable information, assisting in the formulation of strategies to promote vaccine uptake in comparable cohorts.

The study was designed as an analytical cross-sectional survey-based study, conducted between December 7th and 19th, 2021. A SAQ was developed and digitally circulated using KoBoToolbox to collect data from the target population, and it was adapted and translated from the one used in study IV among Czech healthcare professionals. The SAQ comprised of 19 multiple-choice items divided into five sections. These sections covered demographic characteristics, COVID-19-related anamnesis, COVID-19 vaccine-related anamnesis, intentions to receive COVID-19 vaccine boosters, and psychosocial drivers of vaccine booster acceptance. The sample size was calculated to be 923 participants, and after exclusions, 930 participants were included in the analyses.

Most participants came from the German state of Hessen, with a mean age of 29.08 years. Predominantly females participated in the study (73.3%), and a minor percentage (1.5%) were expecting. Only 5.9% of the participants had previously contracted SARS-CoV-2, with the most common clinical feature being headache (62.3%). In terms of immunisation, 95.7% of the participants had received at least one dose of a COVID-19 vaccine, with the BNT162b2 vaccine being most commonly administered.

The majority (87.8%) expressed their willingness to receive a COVID-19 vaccine booster (VB), with protection of personal health (95.6%) cited as the primary reason. Students were more inclined to decline the VB (9.9%) compared to employees (3.7%). Regarding perceived efficacy, 90.1% of participants agreed that VBs could mitigate severe illness, while only 63.4% and 60.3% concurred that VBs could prevent symptomatic infection and community transmission, respectively. Over one third of the participants expressed hesitancy in receiving VBs due to ethical considerations regarding global and national vaccine equity.

The binary logistic regression confirmed the role of previous COVID-19 infection, receiving only one dose, hospital admission, and seeking medical care/treatment in decreasing the odds of accepting a VB. Agreement with the notion that VBs could prevent severe illness had an adjusted odds ratio (AOR) of 47.65 for VB acceptance. Similarly, agreement with the notion that VBs could prevent symptomatic infection and community transmission had AORs of 9.87 and 5.34 for VB acceptance, respectively. Agreement with equal safety and disagreement with severe side effects of VBs had AORs of 24.27 and 6.68 for VB acceptance, respectively. Table 19

The highest AOR for VB acceptance was found in case of agreement with the risk-benefit ratio notion, which was 104.55. Agreement with the self-prioritisation notion also had an AOR of 15.43 for VB acceptance. Ignoring the ethical dilemmas of vaccine justice globally and nationally had AORs of 6.65 and 8.65 for VB acceptance, respectively. Vaccine satisfaction and vaccine selectivity did not have a significant impact on VB acceptance.

Table 19. Regression analysis of COVID-19 vaccine-related acceptance among German university students and staff, December 2021 (n = 930); Attia *et al.* 2022 [262].

Predictor	B (SE)	Wald	OR (CI 95%)	*Sig.*
Severe illness: agree	3.86 (0.36)	115.25	47.65 (23.65–96.49)	**<0.001**
Symptomatic infection: agree	2.29 (0.33)	49.17	9.87 (5.20–18.71)	**<0.001**
Community transmission: agree	1.68 (0.29)	32.56	5.34 (3.00–9.49)	**<0.001**
Mutations control: disagree	2.95 (0.30)	95.41	19.12 (10.57–34.55)	**<0.001**
Equal safety: agree	3.19 (0.32)	98.53	24.27 (12.93–45.56)	**<0.001**
Non-inferior safety: disagree	1.90 (0.29)	44.05	6.68 (3.81–11.71)	**<0.001**
Risk-benefit ratio: agree	4.65 (0.39)	143.04	104.55 (48.80–224.01)	**<0.001**
Self-prioritization: agree	2.74 (0.38)	53.13	15.43 (7.39–32.21)	**<0.001**
Global vaccine justice: agree	1.89 (0.53)	12.95	6.65 (2.37–18.65)	**<0.001**
National vaccine justice: agree	2.16 (0.60)	12.91	8.65 (2.67–28.07)	**<0.001**
Vaccine satisfaction: disagree	0.11 (0.26)	0.17	1.11 (0.67–1.86)	0.680
Vaccine selectivity: disagree	−0.06 (0.26)	0.05	0.95 (0.57–1.57)	0.831

Binary logistic regression had been used with a significance level (Sig.) ≤ 0.05. The bold values indicate the significant values.

The results of this study emphasise the crucial role of clear and effective communication regarding the benefits of COVID-19 vaccination, not only for personal health but also for safeguarding family members and the wider community. It further highlighted a research gap, suggesting future studies ought to actively include underrepresented demographics such as immigrants and other minority populations in Germany. Interestingly, the study suggested that enforcing mandatory vaccination might not be necessary in the German context. This conclusion was drawn from the observation that employer endorsement played a minimal role in influencing vaccine acceptance among study participants, indicating that personal health beliefs and community responsibility were more influential factors.

This study, a pioneer of its kind, evaluated COVID-19 VBH among the German populace, mirroring key characteristics such as infection rate and vaccine type distribution. The study identified catalysts for vaccine acceptance and psychosocial predictors, with participant anonymity preserved to mitigate Hawthorne's effect and minimise information bias.

The study's limitations include its cross-sectional design, which prevents longitudinal tracking of vaccination intentions. Moreover, the focus on a highly educated subset of the German populace, specifically university students and employees, might skew results regarding health literacy and vaccine intention. Also, the sample's imbalance in terms of gender and pregnancy status, absence of racial information, and overrepresentation of respondents from Hessen state may limit the applicability of the findings on a broader demographic and national scale.

ATTACHMENT NO. 7

Attia S, Mausbach K, Klugar M, Howaldt H-P, **Riad A**. Prevalence and Drivers of COVID-19 Vaccine Booster Hesitancy Among German University Students and Employees. *Frontiers in Public Health*. **2022**; 10:846861. https://doi.org/10.3389/fpubh.2022.846861

VII.III. COVID-19 Vaccine Booster Hesitancy (VBH) among Polish Healthcare Professionals and Students (Study VI)

Healthcare professionals (HCPs) and medical university students (MUSs) are influential in shaping societal attitudes towards vaccination due to their role as trusted health information sources. As they are at elevated risk of COVID-19 exposure, understanding their vaccine hesitancy is important to improving vaccine uptake. Their perspectives can inform targeted interventions to build public confidence and accelerate progress towards achieving herd immunity.

The study primarily aimed to measure COVID-19 VBH among Polish HCPs and MUSs, and secondarily to investigate the factors driving vaccine booster acceptance and examine the relationship between acceptance and actual uptake.

This study, carried out between December 2021 and January 2022, used an analytical cross-sectional survey design with a digital SAQ created on KoBoToolbox. The target participants were HCPs and MUSs in Poland, excluding those not in these categories or providing inadequate information. Participants were recruited through a non-random convenience approach across various channels in two leading academic centres (Katowice and Poznan), with participation being voluntary and anonymous. The SAQ was adapted from study IV and made up of 17 items split into four sections, capturing demographic data, COVID-19-related anamnesis, willingness to receive the COVID-19 vaccine booster dose, and psychosocial influencers of vaccine booster hesitancy.

Out of 443 participants, 52.6% were HCPs and 47.4% were MUSs. Females constituted 76.3% of the population, males 22.8%, with diverse-gender individuals making up 0.9%. The average age was 31.1, with HCPs being significantly older than MUSs (38.8 vs. 22.6). Approximately one-third (31.8%) had experienced a COVID-19 infection, and 93.7% had received at least one dose of a COVID-19 vaccine. The Pfizer-BioNTech vaccine was the most common, received by 78.3% of participants, more so by HCPs (89.3%) than MUSs (66.7%). The AstraZeneca-Oxford vaccine was more prevalent among MUSs (22.9%) than HCPs (3.7%). Most participants had received three doses of vaccine (74%), with HCPs again showing higher rates (79%) than MUSs (68.7%).

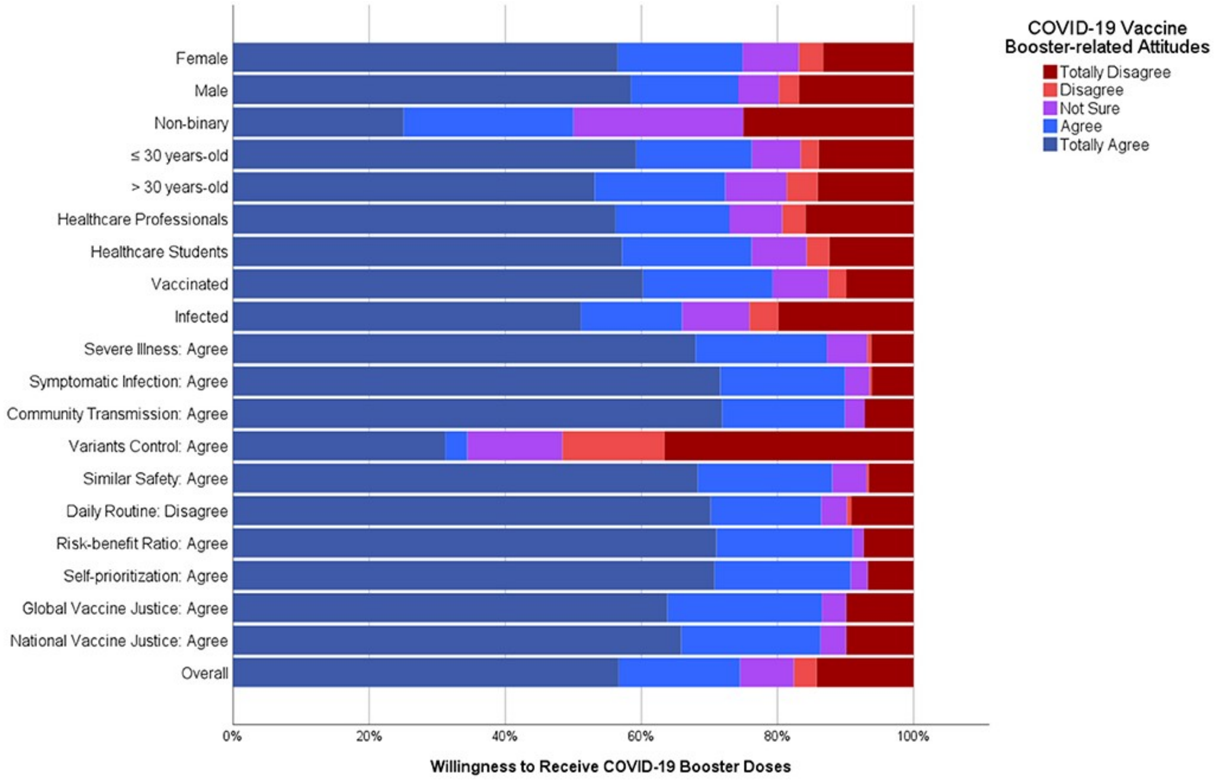
When exploring attitudes towards the COVID-19 vaccine booster dose (VBD), 74.5% of participants indicated acceptance, with 17.6% rejecting it and 7.9% expressing hesitancy. The rate of acceptance was significantly higher among those who were triple vaccinated (87.9%) compared to those who were not (44.1%). The primary reasons for accepting the booster included personal health protection (96.3%), family health protection (82.5%), and community health protection (65%). Figure 37

The study found that 76.1% of participants believed the vaccine booster dose (VBD) could prevent severe infection, particularly among the triple vaccinated (87.9%). 73.6% of this group also thought the VBD could prevent symptomatic infection. A significant majority (68.4%) rejected delaying their VBD for more evidence on emerging variants, and 75% believed it was as safe as primer doses, while 66.6% expected no severe side effects.

Regarding the safety of the VBD, 75.4% believed it was as safe as the primary doses, with this figure rising to 86.3% amongst those triple vaccinated. Meanwhile, 66.6% disagreed that the VBD would cause severe side effects. Most participants agreed that the benefits of the

VBD outweighed the risks (70.9%) and felt they should be prioritised for the VBD due to occupational risk (73.5%). However, views on the ethical implications of vaccine distribution were evenly divided.

Figure 37. Determinants of COVID-VBH among Polish HCPs and MUSs, December 2021–January 2022 (n = 443); Dziedzic *et al.* 2022 [263].



The study's strengths include being the first of its kind targeting this demographic in Poland and ensuring participant anonymity. However, limitations arise from a non-random sampling technique that may limit representativeness and result in selection bias. Additionally, the results might not be universally applicable as HCPs and MUSs generally have a better understanding of vaccines than the general public. Moreover, the study faced potential measurement bias due to its online format and disproportionate representation of certain professional groups.

ATTACHMENT NO. 8

Dziedzic A, Issa J, Hussain S, Tanasiewicz M, Wojtyczka R, Kubina R, Konwinska MD, **Riad A**. COVID-19 vaccine booster hesitancy (VBH) of healthcare professionals and students in Poland: Cross-sectional survey-based study. *Frontiers in Public Health*. **2022**; 10:938067. https://doi.org/10.3389/fpubh.2022.938067

VII.IV. COVID-19 Vaccine Booster Hesitancy (VBH) among Algerian Adult Population (Study VII)

This study primarily targeted the vaccinated adult population of Algeria, to assess their attitudes towards vaccine boosters. Through understanding demographic, anamnestic, and psychosocial factors associated with vaccine booster acceptance or hesitancy, this study aimed to help devise strategies to increase vaccination rates in Algeria and similar developing contexts where vaccine uptake remained inadequate.

Utilising a cross-sectional design, data was collected via a SAQ circulated online between January and March 2022. The target population groups comprised Algerian adults, with the recruitment process utilising non-random snowballing methods; prerequisites for participation included Algerian nationality, a minimum age of 18 years, fluency in either Arabic or French and prior vaccination against SARS-CoV-2. The survey instrument incorporated a 27-item questionnaire divided into sections encompassing demographic information, medical anamnesis, COVID-19-related anamnesis, and attitudes towards COVID-19 vaccine booster doses. Out of an initial 790 responses, 787 were deemed suitable for evaluation after excluding entries deficient in data pertaining to attitudes towards vaccine booster doses.

Most participants were female (61.6%), non-healthcare professionals (61.2%), aged between 31-40 (31.3%), married (61.1%), and urban residents (91.2%), with 48.2% holding postgraduate degrees. Medical history revealed that 27.8% reported having at least one chronic illness, while 24.3% had recently received the influenza vaccine, and 65.3% reported previous SARS-CoV-2 infection. Among COVID-19 vaccine-related anamnesis, the most commonly administered vaccines were Sinovac (66.1%), AstraZeneca-Oxford (12.6%), and Sputnik V (10.2%), with 58.2% feeling relieved after vaccination, 11.4% expressing regret, and 13.2% having received a booster dose at the time of the survey.

A majority of the participants (51.6%) expressed willingness to receive COVID-19 vaccine booster doses, while a quarter rejected them (25%), and 23.4% were hesitant. Healthcare professionals were less inclined (45.9%) to accept boosters than non-healthcare professionals (55.2%), with the primary reasons for acceptance being expert recommendations (24.6%) and the perceived necessity and efficiency of boosters (23.4%). The most preferred vaccine type was Sinovac (33.3%), and the leading reason for rejection was the belief that the primary doses were sufficient (15.5%).

COVID-19 vaccine booster acceptance was found to be significantly higher among males (59.9%) compared to females (46.4%), and also higher in older age groups (>60 years at 71.8% and 51–60 years at 66.3%) than in the 18–30 age group (43.9%). Individuals with lower education levels (college or school) exhibited the highest acceptance level (71.9%) compared to bachelor’s and postgraduate degree holders (47.1% and 52.2%, respectively). There were, however, no significant differences in booster acceptance between single and married participants, or between urban and rural residents.

In the binary logistic regression, males (OR: 1.729), those over 60 years old (OR: 3.257), and individuals with chronic illnesses (OR: 1.394) showed higher odds for accepting COVID-19 booster doses, while healthcare professionals (OR: 0.689) and those with postgraduate degrees (OR: 0.428) were less likely to accept. Multivariable logistic regression revealed that the belief in the necessity and efficiency of booster doses had the highest adjusted odds ratio (AOR: 28.112), followed by disagreement with the notion that primer doses were not sufficient

(AOR: 23.641), and having no breakthrough infections (AOR: 6.870). Expert recommendations (AOR: 4.801) and the desire to travel abroad (AOR: 1.804) were significant promoters of booster acceptance. Table 20

Table 20. Regression Analysis of Demographic and Anamnestic Factors for COVID-19 VB Acceptance among Algerian Adults, January – March 2022 (*n* = 787); Lounis *et al.* 2022 [264].

Predictor	B (SE)	Wald	OR	CI 95%	*Sig.*
Sex: Male (vs. Female)	0.547 (0.149)	13.565	1.729	1.292–2.313	**<0.001**
Age Group: 31–40 yo (vs. 18–30 yo)	0.263 (0.188)	1.950	1.301	0.899–1.881	0.163
Age Group: 41–50 yo (vs. 18–30 yo)	0.247 (0.200)	1.520	1.280	0.865–1.894	0.218
Age Group: 51–60 yo (vs. 18–30 yo)	0.924 (0.255)	13.178	2.520	1.530–4.152	**<0.001**
Age Group: >60 yo (vs. 18–30 yo)	1.181 (0.382)	9.565	3.257	1.541–6.884	**0.002**
Education: BA./BSc. (vs. College/School)	−1.055 (0.298)	12.504	0.348	0.194–0.625	**<0.001**
Education: MSc. or above (vs. College/School)	−0.848 (0.296)	8.193	0.428	0.239–0.765	**0.004**
Profession: Healthcare (vs. Non-healthcare)	−0.373 (0.147)	6.427	0.689	0.517–0.919	**0.011**
Chronic Illness: Yes (vs. No)	0.332 (0.160)	4.280	1.394	1.018–1.908	**0.039**
COVID-19 Infection: No (vs. Yes)	0.297 (0.151)	3.882	1.345	1.002–1.807	**0.049**
Post-vaccination Relief: Agree (vs. Disagree)	2.094 (0.259)	65.601	8.120	4.892–13.479	**<0.001**
Post-vaccination Regret: Disagree (vs. Agree)	2.089 (0.302)	47.785	8.077	4.467–14.605	**<0.001**

Binary logistic regression was used with a significance level Sig. < 0.05. Statistically significant differences are indicated with bold character.

This study, the first to have assessed attitudes towards COVID-19 vaccine booster acceptance in Algeria, had limitations, including a non-random snowball sampling technique, potential exclusion of individuals without internet access, and reliance on self-reporting without a standard measure for acceptance or hesitancy. Furthermore, the cross-sectional nature could only provide a snapshot in time, and the lack of side effect data from primer doses also limited the findings. However, the strengths of this study lay in the use of an online survey reducing social and interviewer biases and its broad coverage across Algerian demographic sectors. These findings offered valuable insights for health authorities, particularly in developing nations with high vaccine hesitancy, to guide strategies promoting booster awareness and uptake.

ATTACHMENT NO. 9

Lounis M, Bencherit D, Rais MA, **Riad A**. COVID-19 Vaccine Booster Hesitancy (VBH) and Its Drivers in Algeria: National Cross-Sectional Survey-Based Study. *Vaccines*. **2022**; 10(4):621. https://doi.org/10.3390/vaccines10040621

Discussion

The present thesis attempts to portray the superimposing nature of the two pandemics, "vaccine hesitancy" and "COVID-19". Vaccine hesitancy, a phenomenon with historical roots, dating back to the late 18th century with the invention of the first-ever vaccine in human history, the "smallpox vaccine", by the English physician Dr. Edward Jenner. This phenomenon has grown steadily over centuries, especially in western societies, contributing to sporadic outbreaks of vaccine-preventable diseases (VPDs) in both high- and low-income countries. The emergence of the COVID-19 pandemic has created a vicious cycle with vaccine hesitancy. Characterised by high levels of stress, uncertainty, and infodemic, the COVID-19 pandemic has provided the perfect environment to exacerbate vaccine hesitancy. On the other hand, the increased levels of vaccine hesitancy had complicated efforts to control the spread of COVID-19, as achieving herd immunity requires widespread acceptance of the vaccine. The complex interplay between these two pandemics presents unique challenges for health systems; therefore, the title "COVID-19 Vaccine Hesitancy: A Tale of Two Pandemics" was used to capture this complex relationship. The following discussion will further explore this narrative, placing my findings within the broader context of existing literature and implications for public health.

VIII.I. Age as a Social Determinant of COVID-19 Vaccine Hesitancy

Since the first epidemic wave of COVID-19 in the winter of 2020, it became clearly evident that age constitutes a risk factor for severe clinical outcomes and mortality [272]. Therefore, older adults have been prioritised in all public health strategies, including the rollout of vaccinations, with the aim of affording them the utmost protection [273].

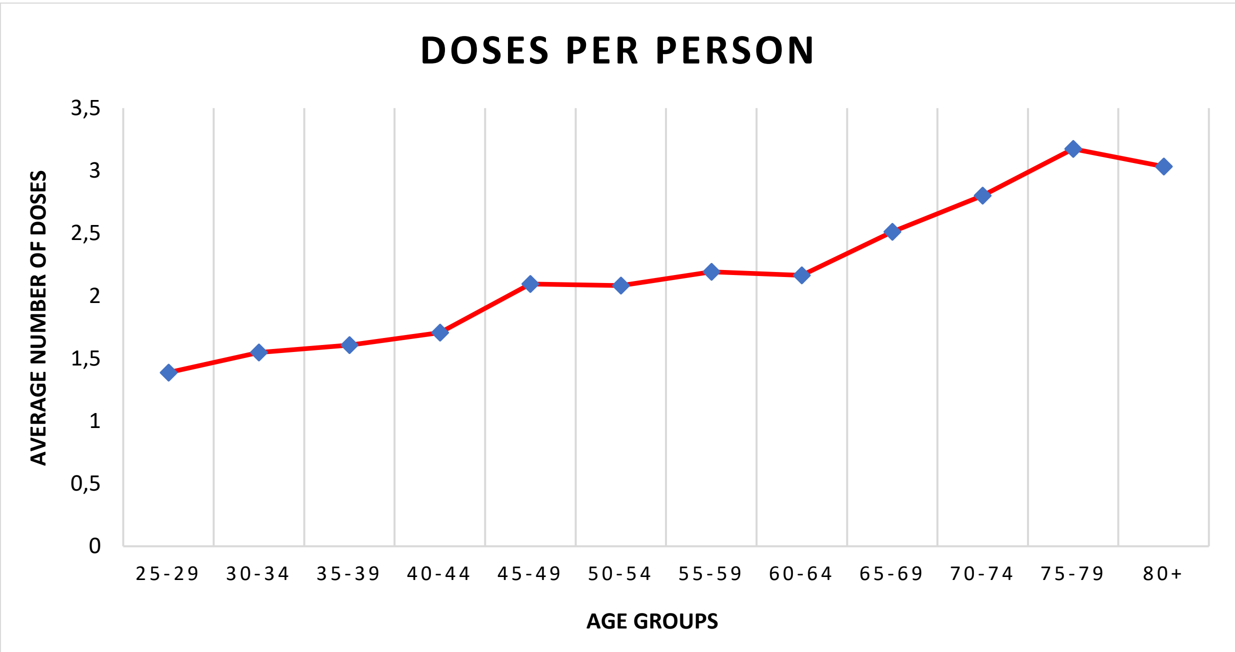
Numerous studies have demonstrated that older adults had higher risk perceptions during the COVID-19 pandemic. For instance, a study conducted in the US in March 2020 found that older adults perceived a higher risk of dying if they contracted COVID-19, but they perceived less risk of contracting the virus, being quarantined, or running out of money [274]. Another study from the US revealed that factors such as female gender, older age, poorer health, city residency, personal acquaintance with someone who had COVID-19, and correct knowledge of vaccine/treatment were significant predictors of higher risk perception among older adults. This higher risk perception was associated with increased preventive behaviour and/or avoidance of medical care, with knowledge having the strongest correlation with risk perception [275]. In Italy, Rosi *et al*. 2021 found that while older adults perceived a lower vulnerability to contracting COVID-19, they perceived a higher severity if they were to get infected, with self-reported anxiety over the pandemic being a key predictor of risk perceptions across all age groups [276].

In the Czech Republic, study II (of university students) found that the younger group of students (≤ 22 years old) had an odds ratio (OR) of 1.82 times (*CI* 95%: 1.19–2.81; *Sig*. = 0.006) of COVID-19 vaccine hesitancy compared to the older group (> 22 years old) [257]. Likewise, study IV (of healthcare professionals) demonstrated that younger participants (≤ 47 years old) had an OR of 1.42 times (*CI* 95%: 1.15–1.74; *Sig*. < 0.001) of COVID-19 vaccine booster hesitancy (VBH) compared to older participants (> 47 years old) [259]. Contrarily, study III (of pregnant and lactating women) revealed that age had no significant association with COVID-19 vaccination attitudes among pregnant and lactating women [258].

Kosarková *et al.* 2021, carried out a survey on a sample of Czech adults (n = 459) to explore the associations between religiosity, spirituality, and religious conspiracy theories about COVID-19 vaccination, as well as the connections of these factors with vaccine refusal and hesitancy. Vaccine refusal was notably higher amongst adults aged 65 and over (10.66%) compared to those aged between 18 and 34 (27.16%). Similarly, vaccine hesitancy was significantly more prevalent amongst adults aged 65 and over (12.30%) compared to those aged between 18 and 34 (28.40%) [198]. In another Czech study by Štěpánek *et al.* 2021, age was identified as a significant predictor of COVID-19 vaccine acceptance among employees of University Hospital Olomouc, with older employees more likely to accept the vaccine [196].

As of July 2023, vaccination rates among adults in the Czech Republic showed a direct correlation with age. The age group 25-29 years had the lowest average number of doses received per person (1.39), followed by the 30-34 years group (1.55 doses/person) and the 35-39 years group (1.61 doses/person). On the other side, the 75-79 years group had the highest average number of doses received per person (3.17), followed by those aged above 80 (3.03 doses/person). Figure 38 presents the average number of COVID-19 vaccine doses administered per person in the Czech Republic; data was driven from the Czech Statistics Office (CZSO) and the Institute of Health Information and Statistics (IHIS-CR) [212].

Figure 38. COVID-19 Vaccine Doses Administered Per Person in the Czech Republic [212].



The phenomenon of higher COVID-19 vaccine uptake in older age groups compared to younger ones was not unique to the Czech Republic. A similar pattern was evident in several European countries. For instance, in Slovakia, the vaccine uptake was 69.8% and 62.5% for the age groups 60+ years and 50-59 years, respectively, compared to 54.2% and 55.6% for the 25-49 years and 18-24 years age groups. Similarly, in Poland, the uptake was 76.1% and 69.5% for the 60+ years and 50-59 years age groups, respectively, compared to 61.2% and 58.6% for the younger age groups. In Hungary, the figures were 81.9% and 74.8% for the older age groups compared to 66% and 54.8% for the younger ones [277]. Table 21

Table 21. Cumulative COVID-19 Vaccine Coverage in the EU/EEA Stratified by Age Groups [277].

Country	< 18 years	18-24 years	25-49 years	50-59 years	≥ 60 years
Austria	31.5%	78.6%	78.7%	83.9%	92.0%
Belgium	36.0%	82.9%	84.9%	91.5%	98.2%
Bulgaria	2.3%	28.7%	33.6%	39.1%	38.5%
Croatia	4.7%	46.8%	58.8%	71.7%	77.3%
Cyprus	20.9%	74.7%	83.7%	86.7%	92.8%
Czech Republic	20.3%	69.8%	66.4%	77.2%	86.0%
Denmark	36.7%	84.0%	86.4%	93.9%	100.0%
Estonia	16.8%	72.8%	68.2%	75.4%	81.6%
Finland	35.7%	81.3%	84.0%	90.9%	95.4%
France	28.1%	90.2%	89.2%	91.8%	91.1%
Germany	30.6%	-	-	-	91.4%
Greece	25.3%	72.7%	78.2%	83.0%	89.8%
Hungary	24.4%	54.8%	66.0%	74.8%	81.9%
Iceland	43.4%	88.0%	86.4%	93.3%	100.0%
Ireland	32.3%	88.7%	90.1%	100.0%	100.0%
Italy	50.8%	90.5%	85.5%	90.0%	94.0%
Latvia	21.4%	83.2%	80.9%	82.5%	77.4%
Liechtenstein	22.7%	72.8%	71.0%	76.8%	86.6%
Lithuania	16.7%	77.7%	80.1%	80.9%	78.2%
Luxembourg	33.7%	74.8%	77.7%	84.8%	91.2%
Malta	45.1%	92.8%	93.0%	90.4%	97.3%
Netherlands	23.0%	66.1%	71.3%	83.4%	90.3%
Norway	13.4%	87.9%	87.0%	94.3%	97.5%
Poland	24.6%	58.6%	61.2%	69.5%	76.1%
Portugal	48.6%	88.1%	91.3%	94.9%	99.0%
Romania	6.9%	49.9%	51.4%	56.0%	46.8%
Slovakia	12.1%	55.6%	54.2%	62.5%	69.8%
Slovenia	10.9%	58.9%	57.2%	70.2%	77.3%
Spain	47.2%	73.4%	79.2%	88.4%	96.7%
Sweden	12.1%	79.6%	81.4%	90.5%	92.5%

Looking at a different socioeconomic context, study VII (of the Algerian adult population) found that older age groups (over 60 years and 51-60 years) had significantly higher vaccine acceptance levels at 71.8% and 66.3%, respectively, compared to the 43.9% in the 18-30 years age group (*Sig*. < 0.001 and = 0.002, respectively) [264]. Similarly, a study in Ethiopia by Erega *et al.* 2023 found that age played a significant role in vaccine hesitancy, with individuals aged over 49 years showing a higher likelihood of hesitancy towards COVID-19 vaccination, alongside factors such as rural residency, fear of adverse effects, and myths about vaccine ineffectiveness [278].

Considering the lower risk of severe clinical outcomes in younger adults, it is conceivable that communication interventions focusing solely on an individual's perceived susceptibility, severity, and benefits may not be enough to motivate this demographic. Hence, the fifth C of the 5-C model, "Collective Responsibility", could play a crucial role in enhancing vaccination uptake among these groups. Living with elderly individuals was identified as a risk factor for occupational stress among critical care nurses. This living situation was significantly associated with deterioration in their general health. The concern of potentially exposing vulnerable family members to the virus likely contributed to the increased stress and subsequent negative health impacts [279]. In a study of nurses in Saudi Arabia, living with an individual older than 60 years was found to have statistically significant relationships with increased levels of depression, anxiety, and the impact of events during the COVID-19 pandemic [280].

Building on this, a study conducted among nurses in Hong Kong emphasised the role of collective responsibility in shaping vaccination intentions. The study found that an increased sense of collective responsibility was positively associated with the intention to receive the COVID-19 vaccine [281]. In Italy, Barello *et al.* 2021 identified collective responsibility as a significant predictor of COVID-19 vaccine acceptance. The researchers advocated for public health communications that emphasise the altruistic aspects of immunisation, highlighting its role in communal protection to promote this sense of collective responsibility [282]. In the US, Rancher *et al.* 2023 found that in conjunction with demographic characteristics, collective responsibility played a significant role in influencing vaccine trust and intentions, emphasising the need to foster a sense of communal duty in vaccine uptake strategies [283].

VIII.II. Gender as a Social Determinant of COVID-19 Vaccine Hesitancy

The role of gender as a social determinant of health-related behaviours has been widely recognised across a spectrum of behaviours; these range from preventive behaviours such as screening uptake and vaccination, to psychological coping mechanisms in response to illness, adherence to medical advice and treatment regimes, and even health-seeking behaviours [284].

In the Czech Republic, study II (of university students) revealed that despite similar mean acceptance levels for the COVID-19 vaccine among males and females, female students exhibited a statistically significant higher vaccine hesitancy (8.3%) compared to males (5.2%). Approximately one-third of female students (32%) acknowledged their lack of sufficient information about vaccine safety, compared to 26.2% of male students. Moreover, female students (27.7%) showed a significantly higher dependency on safety surveillance data to inform their vaccination decision than male students (20.7%) [257]. In line with these findings, study IV (of healthcare professionals) found that males had higher acceptance level of COVID-19 vaccine booster doses (79.3%) compared with females (69.7%). More males (81.5%) believed in booster doses effectiveness against severe illness compared to females (73.9%). In terms of risk-benefit perception, more males (85.1%) viewed the boosters favourably than females (74.3%). Additionally, a smaller fraction of males (14.5%) hesitated due to vaccine justice dilemmas, in contrast to 23.7% of females. Females were 2.36 times more likely to exhibit booster dose hesitancy [259].

Recently, Žídková *et al.* 2023 found that female gender was one of the predictors for COVID-19 vaccine refusal among a nationally representative sample of Czech adults (n = 1,401) [199]. Likewise, the study of Šerek *et al.* 2023 indicated that Czech males were more likely to get vaccinated than females [200]. In the study of Štěpánek *et al.* 2021 female healthcare professionals were more likely to be hesitant about getting vaccinated compared with their male peers [196]. On the other hand, the study of Kosarková *et al.* 2021, found no significant difference between Czech participants based on gender [198].

From a global perspective, numerous studies showed males' tendency to accept COVID-19 vaccination, including study I (of dental students worldwide) which found that female students were significantly less willing to get vaccinated compared with their male peers in Palestine [261]. Similarly, study VII (of Algerian adults) revealed that male participants had a significantly higher level of booster dose acceptance (59.9%) than females (46.4%) [264]. Contrarily, study V (of German university students and staff) demonstrated no significant difference between females and males in terms of booster dose acceptance [262]. Likewise, in Poland, study VI (of healthcare professionals and students) found no significant difference between gender groups in terms of booster dose attitudes or actual uptake [263].

Green *et al.* 2021 conducted a study investigating the differences in attitudes toward COVID-19 vaccines based on ethnicity, gender, and education in Israel. Their findings suggested that, regardless of ethnicity, male respondents were generally more willing to receive the vaccine than female respondents [285]. Specifically, 27.3% of Jewish men and 23.1% of Arab men expressed a desire to be immediately vaccinated, as opposed to only 13.6% of Jewish women and 12.0% of Arab women. Similarly, a higher proportion of females, across both ethnic groups, stated they would never want the vaccine compared to males. These findings persisted even after adjusting for age and educational differences [285].

In Japan, Horiuchi *et al.* 2021 assessed the factors that contribute to parental COVID-19 vaccine hesitancy. The study found that mothers were more likely to exhibit vaccine hesitancy compared to fathers (adjusted odds ratio of 2.43) [286]. Additionally, the study noted an interaction between parental gender and level of satisfaction with social relationships; mothers with lower satisfaction in their social relationships were more hesitant to vaccinate their children compared to fathers, who showed consistent intention to vaccinate regardless of their level of satisfaction with their social relationships [286].

A recent systematic review of 519 studies with a total population of 7,990,117 analyzed global acceptance and uptake of COVID-19 vaccination, revealing gender-specific disparities. The review found that the COVID-19 vaccination acceptance rate among males (68.3%) was higher than females (64.7%), indicating that women were less likely than men to accept the vaccine [287]. Additionally, a systematic review by Yasmin *et al.* 2021, comprising 65 studies, investigated predictors of COVID-19 vaccine hesitancy and acceptance across various groups in the United States. The review revealed that vaccine hesitancy is particularly high among Black/African Americans and pregnant or breastfeeding women, but is relatively low among the male population, indicating a significant difference in vaccine uptake between men and women [288].

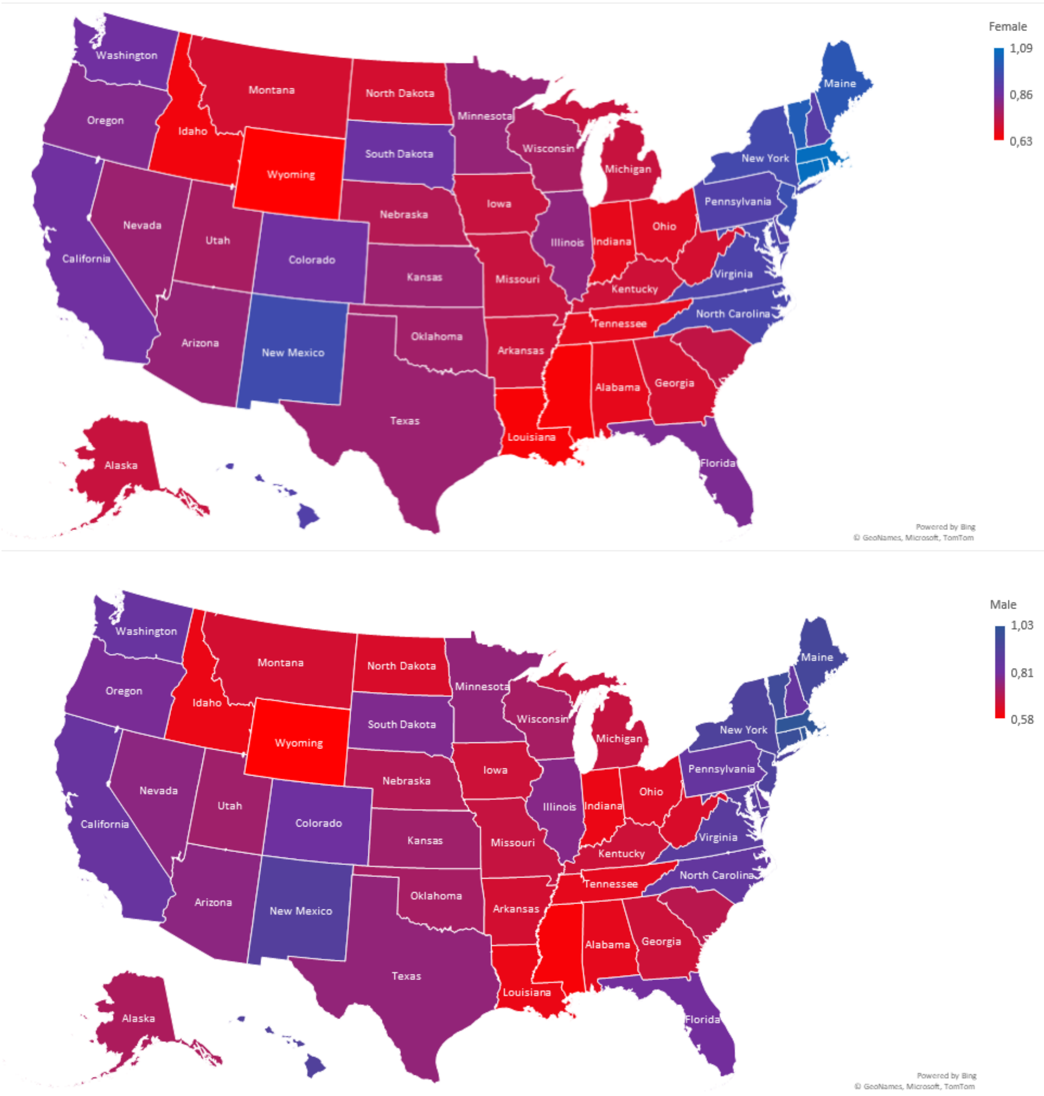
In a cross-sectional study of healthcare professionals (n = 2953) from 12 countries in Africa, Asia, Latin America, and Middle East, females had lower odds of COVID-19 vaccine acceptance compared with males [289]. Another global survey of adult populations (n = 10,491) from 83 low- and middle-income countries revealed that female gender was associated with lower odds of COVID-19 vaccine acceptance [290].

Based on two surveys conducted in 27 European countries in 2021, Toshkov attempted to explore the gender gap in COVID-19 vaccination attitudes [291]. The findings suggest that the gender gap is not due to concerns about pregnancy, fertility, breastfeeding, trust in internet and social networks for medical information, trust in health authorities, or perceived risks of

COVID-19 infection. Rather, women are more likely to view COVID-19 vaccines as unsafe and ineffective, leading them to perceive the risks of vaccination as outweighing the benefits. Despite these findings, the gender gap in vaccine hesitancy remains, indicating a need for further research [291]. In a US-based study, it was found that American women exhibited higher COVID-19 vaccine hesitancy than men, with this hesitancy [292]. The study also revealed that lack of a college education contributed to vaccine hesitancy in both genders, with women's hesitancy largely driven by safety concerns, while men's hesitancy was more linked to lower perceptions of COVID-19 dangers and belief in conspiracy theories [292].

Despite the scepticism towards COVID-19 vaccination found among females in various studies, real-world data from 2023 shows a contrasting trend, with women receiving more doses than men. As of July 2023, in the Czech Republic, the average number of doses administered per person was 1.74, with a slightly higher rate in females (1.76) compared to males (1.71) [212]. A similar disparity was observed in the US as of May 2023, with females receiving an average of 0.82 doses per person, compared to 0.78 in males [293]. It is important to note that these data are not adjusted for age and medical contradictions that may eliminate or enhance these gender disparities in vaccine uptake. Figure 39

Figure 39. COVID-19 Vaccine Doses Administered Per Person in the US [293].



Regarding sexual and gender minorities, the systematic review of Garg *et al.* 2021 demonstrated that COVID-19 vaccine hesitancy in the LGBTQ+ community was largely driven by concerns about vaccine safety, effectiveness, and past negative healthcare experiences. The review emphasised the need for targeted efforts to build trust, address systemic discrimination, and include LGBTQ+ individuals in public health policies [294]. Recently, the scoping review of Balaji *et al.* 2023, highlighted the under-studied issue of COVID-19 vaccine uptake and refusal within the LGBTQIA+ community [295]. The review found that factors such as social stigma, discrimination, lack of access, and non-prioritisation in vaccine drives contributed to vaccine hesitancy, while HIV-affected individuals within this community showed a higher willingness to get vaccinated [295].

In New York, a cross-sectional survey-based study conducted from June to December 2021 found that vaccination uptake among 1,032 LGBTQ+ participants was comparable to the general population [296]. However, socioeconomic factors, such as lower income and lack of health insurance, were significantly associated with vaccine hesitancy in this economically vulnerable group [296]. Similarly, in Australia, a national online survey conducted from April to June 2021 among 1,280 gay and bisexual men found that 28.0% of the respondents had been partially or fully vaccinated against COVID-19, and 80.0% of the unvaccinated were willing to be vaccinated [297]. The study identified that vaccination was associated with older age, university education, and HIV-positive status, while willingness to be vaccinated was linked to living in a capital city and being university educated, with those who had lost income or their job due to COVID-19 being less willing to be vaccinated. These Australian data confirmed that vaccine uptake and willingness were similar between gay and bisexual men and general population [297].

In the research carried out for this thesis, representation of sexual and gender minorities varied across studies. For instance, in study II (of Czech university students), 0.7% of the total participants identified as LGBTQ+. Interestingly, their level of acceptance of the COVID-19 vaccine was on par with that of the female and male participants [257]. Contrarily, study I (of dental students worldwide) found out that vaccine acceptance was significantly lower among the LGBTQ+ participants compared to their female and male peers [260]. Study V (of German university students and staff) revealed that LGBTQ+ participants who constituted 1.7% of the sample had a significantly higher level of booster dose refusal [262]. In Poland, study VI (of healthcare professionals and students), booster dose hesitancy was higher among the LGBTQ+ participants [263].

VIII.III. Safety Evidence: Promoter of Vaccine Hesitancy

Clear and convincing evidence on COVID-19 vaccine safety is fundamental in shaping public attitudes towards vaccination, dispelling myths and fears that contribute to vaccine hesitancy. The majority of adverse events post-vaccination are mild and understanding this can build trust. However, cognitive biases can influence decisions, emphasising the necessity to consider and address these in health communication strategies [298].

In the Czech Republic, study II (of university students) found that students with insufficient knowledge about vaccine safety were 6.061 times more likely to be hesitant about getting vaccinated. Additionally, students who based their vaccination decisions on safety surveillance data were 2.965 times more likely to be hesitant. Despite 74.7% of students expressing confidence in the pharmaceutical industry's ability to provide safe vaccines, 30% felt they did not have enough safety information. These findings highlight the critical role of accessible and clear vaccine safety information in shaping students' attitudes towards COVID-19 vaccines [257].

The vaccine safety evidence was more critical for pregnant and lactating women (PLW) in the Czech Republic when considering COVID-19 vaccination as demonstrated by study III [258]. Safety for their children was the top priority for 61.5% of PLW, followed by their own safety (47%). However, trust in the transparency of pharmaceutical companies regarding safety data for pregnant women was low (15%), and only a minority of women (32.5%) felt they had sufficient knowledge about COVID-19 vaccines, further emphasising the importance of clear and reliable vaccine safety information for this population group [258]

Study VI (of Czech healthcare professionals) revealed that perceptions regarding the safety of COVID-19 booster doses significantly influenced attitudes towards receiving these doses. The majority (76.5%) believed that the safety profile of booster doses was equivalent to that of the primary doses, and this belief was positively associated with acceptance of booster doses. Contrarily, a minority of respondents, only 12.5%, held concerns that booster doses might yield more severe side effects than primary doses. The perception of safety, whether positive or negative, thus proved pivotal in shaping attitudes towards booster dose acceptance among these healthcare professionals [259].

In Štěpánek *et al.* 2021's study on healthcare professionals in Olomouc, concerns about vaccine safety significantly influenced attitudes towards COVID-19 vaccination. Almost half of the respondents, 49.4%, expressed hesitancy towards getting vaccinated due to fears about the vaccine's safety and potential side effects. These fears were especially pronounced among younger respondents, non-physicians, and individuals without a history of COVID-19 [196].

Globally, study I (of dental students worldwide) demonstrated that vaccine safety concerns greatly influenced dental students' acceptance of COVID-19 vaccines. These concerns were prominent among students from lower-middle-income countries, where only 27% felt they had enough information about vaccine safety compared to 33.1% from upper-middle-income countries students. Also, students who felt they lacked information about vaccine safety had significantly lower vaccine acceptance [260]. In Germany, study V (of university students and staff) exhibited a high acceptance rate (87.8%) for COVID-19 vaccine boosters, significantly influenced by their perception of vaccine safety and effectiveness. Participants who believed that the booster doses were as safe as the primary doses (89.1%) and those who disagreed that boosters would cause more severe side effects (70.2%) were significantly more likely to accept the booster, highlighting the crucial role of perceived safety in vaccine acceptance [262]. In Poland, study VI (of healthcare professionals and students) revealed that approximately 75.4% of participants believed the COVID-19 vaccine booster doses to be as safe as the primer doses, and 66.6% disagreed with the notion that booster doses would cause severe side effects. This perceived safety was a significant factor in vaccine booster acceptance, with those agreeing on equal safety showing an adjusted odds ratio (aOR) of 3.733 (95% CI: 1.622–8.592) for acceptance and an aOR of 2.323 (95% CI: 1.024–5.273) for actual uptake of the booster doses [263].

In Portugal, Soares *et al.* 2021 discovered high levels of COVID-19 vaccine hesitancy, with 56% of respondents wanting to wait and 9% refusing vaccination, and this was linked to a lack of trust in the vaccine's safety [299]. The study found that those with little trust in the vaccines were much more likely to delay (aOR: 9.94, 95% CI: 7.48–13.20) or refuse (aOR: 109.69, 95% CI: 57.38–206.69) vaccination, and respondents who answered before the release of vaccine safety and efficacy information also showed higher odds of delay (aOR: 2.05, 95% CI: 1.68–2.50) and refusal (aOR: 4.69, 95% CI: 3.21–6.86) [299]. Likewise in Italy, Reno *et al.* 2021 found that 31.1% of the sample reported hesitancy towards COVID-19 vaccination, with 54% voicing safety concerns [300]. Among hesitant respondents, the primary motivation to increase vaccine confidence was assurance that the vaccine could not cause immediate or long-term injury (54.1%), and that its fast production did not compromise its safety (26.1%) [300].

A multi-country study of healthcare professionals in 23 countries, with a sample size of 3,295, revealed that 15% of participants reported vaccine hesitancy, with safety and risk concerns acting as significant factors (OR: 9.07, 95% CI: 7.30–11.29). Particularly, among physicians, community health workers, and other healthcare providers, doubts about the science behind the vaccines and safety concerns were the most potent contributors to hesitancy [301]. Similarly, another multi-center study of 10 low- and middle-income countries including 44,260 individuals from general populations demonstrated that concerns about vaccine side effects remained the primary cause for hesitancy, indicating the need for effective messaging about vaccine safety and efficacy, particularly delivered by trusted healthcare professionals [302].

Recently, Zhao *et al.* 2023 carried out a systematic review, identifying misinformation about COVID-19 vaccines as a significant factor contributing to vaccine hesitancy worldwide. Key sources of misinformation revolved around conspiracy theories and unfounded concerns about vaccine safety and effectiveness, noted in 77 and 63 studies, respectively, and this misinformation was more prevalent among younger, less educated, economically disadvantaged individuals, and those with right-wing or conservative ideologies [303]. The spread of such misinformation was found to foster fears about the safety profile of vaccines and even reducing the uptake of preventive behaviors like mask wearing and social distancing [303].

VIII.IV. Effectiveness Evidence: Promoter of Vaccine Hesitancy

The compelling evidence of COVID-19 vaccine effectiveness has been a critical factor in shaping public attitudes, providing reassurance about the vaccines' ability to reduce virus transmission and severe illness. Despite this, surveys illustrate ongoing public concerns about the duration of immunity and potential side effects, and the rapid development of vaccines may intensify these apprehensions [143]

In the Czech Republic, study II (of university students) exhibited that a majority (74.7%) expressed confidence in the pharmaceutical industry's ability to provide effective COVID-19 vaccines, with significantly higher confidence levels among healthcare students (83.2%) and non-Czech students (84.7%), suggesting the crucial role of perceived vaccine efficacy in shaping attitudes towards vaccination [257]. Among pregnant and lactating women, safety for children (61.5%) was the first priority, followed by safety for the mother (47%), vaccine effectiveness for children's immunisation (35.2%), and effectiveness for mother's immunisation (41.4%), thus reflecting the impact of perceived vaccine safety and efficacy on their vaccination decisions [258]. Figure 31

Regarding booster doses acceptance, study V (of Czech healthcare professionals) showed that most participants believed in the booster doses' effectiveness against severe illness and community transmission, with 80.3% and 60.8% agreement respectively, leading to high booster dose acceptance [259]. However, the efficacy against circulating variants was less crucial to this group, indicating that while evidence of effectiveness in preventing severe illness and transmission is crucial in shaping attitudes, the vaccines' performance against specific variants is not as influential in their decision-making [259].

Štěpánek *et al.* 2021 found that distrust in the vaccine's efficacy (41.1%) was one of the main reasons for vaccine hesitancy among healthcare professionals in Olomouc, particularly amongst younger, non-physician staff and those without a history of COVID-19. The study emphasised that to improve vaccine uptake among healthcare professionals, increasing awareness around the safety and effectiveness of COVID-19 vaccines was pivotal [196].

Globally, study V (of German university students and staff) exhibited a strong belief in COVID-19 vaccine booster effectiveness and safety, with 90.1% of participants agreeing that booster doses could prevent severe illness, and 89.1% affirming that booster doses were as safe as the primer doses. Nevertheless, the study also revealed a significant contingent of respondents (7.6%) would not take booster doses until reliable evidence confirmed their effectiveness against emerging variants, highlighting the crucial role of scientific evidence in shaping vaccine attitudes [262]. In Poland, study VI (of healthcare professionals and students) demonstrated that majority (76.1%) acknowledged the effectiveness of COVID-19 vaccine booster doses in preventing severe infection, notably higher among triple-vaccinated participants (87.9%). This belief, along with acceptance of the vaccine's ability to prevent symptomatic infection (AOR: 5.502) and community transmission (AOR: 5.898), contributed to a 17.4 times greater likelihood (AOR: 17.407) of vaccine acceptance, underscoring the role of efficacy evidence in vaccination attitudes [263]. Study VII (of Algerian adults) found that belief in the effectiveness of COVID-19 booster doses played a vital role in shaping public attitudes towards vaccination, with an AOR of 28.112 for booster acceptance among those who believed in their necessity and efficiency [264].

In Soares *et al.* 2021's study of Portuguese adults, the report highlighted that individuals with little to no trust in the efficacy of COVID-19 vaccines were nearly 10 times more likely to delay and over 100 times more likely to refuse vaccination, while those who were surveyed before the release of efficacy information were twice as likely to delay and approximately 4.7 times more likely to refuse the vaccine [299]. In France, Schwarzinger *et al.* 2021 demonstrated that the efficacy of COVID-19 vaccines influenced vaccine hesitancy, with acceptance rates dropping from 61.3% for a vaccine with 90% efficacy to 27.4% for one with 50% efficacy, the latter also being more hesitant if the vaccine was manufactured in China [304].

In the US, Shih *et al.* 2021 revealed that the efficacy of COVID-19 vaccines plays a significant role in vaccine acceptance, with 33% of respondents rejecting a hypothetical vaccine with 50% efficacy compared to only 12.8% rejecting a vaccine with 95% efficacy [305]. While general vaccine hesitancy and COVID-19 vaccine rejection show similar patterns across demographic factors, COVID-19 vaccine rejection rates are specifically influenced by the vaccine's effectiveness, thus indicating that vaccine efficacy evidence significantly shapes public attitudes towards COVID-19 vaccination [305]. Another hypothetical vaccine study conducted in low- and middle-income countries across Asia, Africa, and South America among 1,337 respondents demonstrated that COVID-19 vaccine acceptance varied notably with vaccine efficacy and safety; vaccines with 75% efficacy and 5% side effects received the highest acceptance rate of 80.1%, followed by a 95% efficacy vaccine with 20% side effects at 74.0%, while vaccines with lower efficacy or higher side effects received lower acceptance rates (58.3% for a 50% efficacy, 5% side effects vaccine and 55.6% for a 75% efficacy, 20% side effects vaccine), underscoring the role of efficacy evidence in influencing public vaccination attitudes [306].

Multi-centre studies confirmed the role of effectiveness evidence in shaping the public's attitudes towards COVID-19 vaccines, for instance, the study by Lazarus *et al.* 2021 surveyed 23,000 participants from 23 countries and found a 3.7% increase in vaccine acceptance from the previous year, reaching 75.2% [307]. The study also identified trust in vaccine efficacy as a key factor in acceptance, with the statements "I trust the science behind the COVID-19 vaccines," "The COVID-19 vaccines available to me are safe," and "COVID-19 can be prevented by vaccination" being significant negative correlates of vaccine hesitancy across all surveyed countries, demonstrating the impact of vaccine effectiveness communication in reducing vaccine hesitancy [307].

Khatatbeh *et al.* 2022 conducted a Middle Eastern multi-country study involving 3,744 parents from eight countries, revealing that a parent's own vaccination status and their beliefs regarding the efficacy and safety of vaccines significantly impacted their willingness to vaccinate their children against COVID-19, as parents who had received the COVID-19 vaccine were about five times more likely to vaccinate their children, indicating the importance of effectively communicating vaccine efficacy to the public [308].

In Southeast Asia, a cross-sectional study involving 5,260 participants from six countries showed that 81.2% of participants believed vaccines could effectively prevent and control COVID-19, with 84.0% expressing willingness to accept a vaccine when available [309]. Despite this, around 50% of participants expressed hesitancy towards receiving a COVID-19 vaccine, revealing that factors such as age, residential area, education level, employment status, family economic status, and country of residence significantly influenced this hesitancy, thus illustrating the need for tailored approaches in communication about vaccine efficacy [309].

The recent systematic review of Zhao *et al.* 2023 revealed that misinformation surrounding COVID-19 vaccine safety and efficacy, present in 2.78% to 55.4% of the general population and 12.2% to 96.7% within anti-vaccine/vaccine hesitant groups, substantially contributes to vaccine hesitancy. It emphasised the need for debunking these misconceptions as an effective means of positively shaping public attitudes towards vaccination [303].

VIII.V. Are COVID-19 Vaccine Mandates Needed?

Implementing mandates for COVID-19 vaccines could significantly increase vaccine uptake by making them an integral part of participation in certain societal activities, thereby indirectly addressing vaccine hesitancy. Nevertheless, these mandates might intensify resistance, especially among those who perceive them as an infringement of personal freedoms or among individuals with deep-seated vaccine hesitancy stemming from misinformation or mistrust [310]. Despite these potential challenges, the data indicates a compelling case for vaccine mandates for healthcare professionals due to the increased morbidity and mortality rates of COVID-19 compared to influenza and the marked disruption it causes to healthcare services and workforce continuity [311].

In the Czech Republic, study IV (of healthcare professionals) suggested that rather than enforcing COVID-19 vaccination mandates, focusing on altruistic motivations such as the protection of family, patients, and community health might foster more acceptance and enthusiasm towards booster doses among healthcare workers [259]. Likewise in Germany, study V (of university students and staff) showed that acceptance of the COVID-19 vaccine booster was primarily driven by altruistic motives such as protection of personal health, family, and community health, rather than vaccine mandates, as only a small percentage of participants endorsed employer mandates as a reason for vaccination [262]. Study VI (of Polish healthcare professionals and students) revealed that COVID-19 vaccine booster doses acceptance was largely driven by factors such as protection from severe infection and community transmission, and the perception of a good safety profile and favourable risk-benefit ratio, with no significant impact of COVID-19 vaccine mandates on their willingness to get vaccinated [263].

Mayan *et al.* 2021 conducted a cross-sectional study involving 1,899 US medical students from 151 medical schools, revealing that 57.82% of these students approved of making the COVID-19 vaccine mandatory for healthcare professionals, while only 16.27% approved of the same for patients [312]. It was also noted that students who tested more knowledgeable about the vaccine (those answering all 5 questions correctly constituted 71% of the respondents) were less likely to approve making the vaccine mandatory for patients (66.67% vs 72.70%) and more likely to personally receive the vaccine (72.35% vs 62.99%), as opposed to less knowledgeable students who were less inclined to get the vaccine (4.12% vs 14.17%) [312].

In Australia, Smith *et al.* 2021 found that 66% of 1,200 surveyed Australians indicated willingness to take a COVID-19 vaccine, compared to 88% in 2017 who believed vaccines were safe and necessary [313]. It was observed that 70% of hesitant respondents were worried about the vaccine's safety if developed too swiftly, and 73% supported government mandates for COVID-19 vaccination for work, travel, and study, lower than the 85% support for the 2017 childhood vaccine mandate but higher than those willing to personally take the vaccine [313].

The multi-country study of Lazarus *et al.* 2022 found that the vaccine-hesitant were highly resistant to vaccination requirements, with only 31.7%, 20%, 15%, and 14.8% approving mandates for international travel, indoor activities, employment, and public schools respectively, demonstrating the need to address these concerns to improve vaccination coverage [307]. In the following year, Lazarus *et al.* 2023 identified a downward shift in public attitudes towards COVID-19 vaccination mandates, with a decrease of 2.6% in support for employer vaccination requirements and a more significant drop of 6.9% in support for international travel vaccination proof. Despite the decline, the endorsement for vaccination proof for international travel remained high at 69.2%, thus indicating the persistent challenge in achieving broad public support for vaccination mandates [314].

Shah *et al.* 2023 conducted a systematic review and discovered that mandatory COVID-19 vaccinations and potential booster requirements led to increased vaccination rates, especially in lower pre-mandate nations like France and Israel, with the most significant response from younger age groups, under 20 and 20-29 years [315]. Despite an observed surge, uncertainties around mandates, varying compliance among different age groups, and concerns about long-term safety data fostered a level of hesitancy, indicating that the success of any mandatory vaccination policy would depend on factors such as clear communication, evidence-based decisions, and the ethical implications of restricting personal autonomy [315].

Another systematic review by Peterson *et al.* 2022 which was concerned with healthcare professionals and vaccine hesitancy identified longstanding concerns surrounding vaccination safety, efficacy, and personal rights infringement, with these hesitations further increased during the COVID-19 pandemic [316]. Despite vaccination rates being as low as 31% during the H1N1 pandemic, the implementation of COVID-19 vaccination mandates increased compliance to 76% overall, and even higher for physicians (91%) and nurses (90%), but also sparked opposition, with up to 57% of healthcare professionals in certain surveys being against such mandates, indicating the powerful influence of COVID-19 mandates in shaping attitudes towards vaccination among healthcare professionals [316].

In conclusion, vaccine mandates can significantly boost vaccination rates, yet they encounter resistance over personal autonomy and safety concerns. Success lies in clear, evidence-based communication and respect for personal freedoms, striking a balance that could effectively lead us towards public health objectives.

VIII.VI. Implications for Addressing COVID-19 Vaccine Hesitancy

Table 22 presents a set of recommendations to address COVID-19 vaccine hesitancy among healthcare professionals, pregnant and lactating women, and young adults, including university students, based on the findings of this thesis studies.

Table 22. Implications for Addressing COVID-19 Vaccine Hesitancy among Various Population Groups

Group	Implications / Recommendations
Healthcare Professionals	1. Emphasise altruistic motivations like protecting family, patients, and community health rather than enforcing mandates. This can increase enthusiasm and acceptance.
	2. Ensure safety evidence is clearly communicated as concerns over side effects are a major driver of hesitancy. Emphasise that boosters are as safe as primary doses.
	3. Communicate efficacy evidence effectively, focusing on prevention of severe illness and community transmission rather than performance against specific variants.
	4. Leverage their role as opinion leaders by having healthcare professionals share their positive vaccination experiences with colleagues and patients.
	5. Provide convenient access to vaccination, as situational barriers like lack of time contribute to hesitancy amongst busy healthcare professionals.
Pregnant & Lactating Women	6. Prioritise clear communication about safety evidence, as this is the top concern for pregnant and lactating women regarding vaccination. Address transparency issues.
	7. Emphasise benefits of vaccination for mothers and babies versus risks of COVID-19 infection during pregnancy and lactation.
	8. Increase accessibility to web-based interventions that provide reliable information on vaccine safety for pregnant and lactating women.
	9. Tailor messaging for different trimesters, as vaccine acceptance varies across pregnancy timeline.
	10. Partner with obstetricians and paediatricians to leverage pregnant and lactating women's high trust in healthcare providers for vaccine recommendations.
	11. Leverage sense of collective responsibility, emphasising vaccination's role in protecting vulnerable family and community members.

Young Adults (incl. University Students)	12. Address misconceptions and knowledge gaps through social media campaigns and campus events led by student leaders.
	13. Highlight safety evidence from clinical trials and real-world data to alleviate concerns over novel vaccines.
	14. Share positive experiences of vaccination from influential young icons and peers over traditional health authorities.
	15. Increase access through convenient on-campus vaccination clinics and incentives like extra-curricular credits or prize draws.

Regarding COVID-19 vaccine booster doses, the studies included in this thesis highlight several key implications. Firstly, the perceived safety and efficacy of booster doses play a pivotal role in shaping acceptance, indicating a need for clear communication of emerging evidence on booster effectiveness and side effects. Trusted healthcare providers should take the lead in addressing misconceptions. Secondly, acceptance is driven more by altruistic motivations like protecting family and community rather than mandates or restrictions. Communication campaigns could leverage these motivators over coercion. Thirdly, those previously infected show more hesitancy, suggesting a need to communicate better that natural immunity wanes and boosters augment protection. As Šimánek *et al.* 2021 demonstrated, while antibodies from mild COVID-19 may persist around 18 months, vaccination remains vital to reducing transmission and severe outcomes [317]. Fourthly, hesitancy persists over ethical concerns regarding global vaccine equity, emphasising that authorities should transparently address justice arguments. Lastly, tailored strategies for hesitant groups like females, youth, and racial minorities are needed, taking into account cultural factors and knowledge gaps. Overall, addressing knowledge deficits and misconceptions with compassion could foster greater booster uptake.

Additionally, the thesis findings suggest several key implications regarding COVID-19 vaccine mandating. Firstly, vaccine mandates appear capable of driving substantial increases in uptake but still face resistance stemming from safety worries and infringement of autonomy. Thus, mandates should be judiciously implemented based on transparent risk-benefit analysis and ethical considerations. Secondly, healthcare professionals exhibit high booster acceptance without mandates, driven by altruism and occupational risk perception. Mandating vaccination for them should be carefully weighed, given existing goodwill. Thirdly, general populations show lower support for mandates compared to personally getting vaccinated, indicating mandates could harden hesitancy. Fourthly, high-risk groups like the elderly demonstrate greater acceptance, suggesting targeted rather than blanket mandating. Finally, success lies in clear communication of evidence, respect for diverse viewpoints, and shared responsibility appeals over coercion. Overall, vaccine mandates require nuanced implementation as one strategy among many to increase uptake.

VIII.VII. Strengths and Limitations

The strengths of the present thesis lie in its individual studies, their conceptualisation, design, and findings. They can be summarised in the following points:

1. **Diverse Population Groups:** The thesis comprises seven cross-sectional, survey-based studies, facilitating the collection of data from diverse population groups across different national and international contexts. The large sample sizes, that ranged from 362 to 6,639 participants with a collective sample of 13,966, also

augment the studies' comprehensive nature and statistical power. This enhances the generalisability of the findings.

2. **Timeliness and Phased Approach:** The studies were conducted during the mass vaccination campaigns for primer doses (winter – summer 2021) and booster doses (autumn 2021 – spring 2022), a critical period in the global fight against the COVID-19 pandemic.
3. **Use of Validated Instruments and Theoretical Models:** The studies employed a variety of validated instruments and theoretical models, including the WHO-SAGE matrix model, the socio-ecological model (SEM), and the health belief model (HBM). These models and instruments have been widely used and validated in previous research, enhancing the reliability and validity of the findings.
4. **Advanced Statistical Techniques:** Advanced statistical techniques were employed, including machine-learning techniques that were utilised in study I. These methods allowed for a robust examination of intricate relationships between predictors and vaccine hesitancy, providing deeper insights into the factors influencing vaccine acceptance and refusal.
5. **Alignment with Reporting Guidelines and Ethical Principles:** The studies were conducted in strict alignment with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines and the Declaration of Helsinki for research involving human subjects. Ethical approval was procured prior to the initiation of the studies, enhancing the methodological strength of the research.

The limitations also stemmed from the individual studies and can be summarised in the following points:

1. **Lack of Qualitative Data:** The studies primarily utilised quantitative methods, and the absence of qualitative data restricted a deeper understanding of the determinants of vaccine hesitancy.
2. **Cross-Sectional Design:** The cross-sectional design of the studies provided a snapshot of the situation at a specific point in time but did not permit the examination of changes over time. Cohort studies would have been needed to assess how vaccine hesitancy evolved as the pandemic progressed and as new information about the vaccines became available.
3. **Digital Data Collection:** The use of digital forms for data collection, whilst efficient, might have excluded individuals without access to the necessary technology or those who were not comfortable using it. Also, the anonymous format precluded verification of data and introduced chance of duplicates.
4. **Cognitive and Selection Biases:** The studies' use of self-reported data and voluntary participation might have introduced biases. Social desirability bias could have skewed results if participants responded in socially acceptable ways rather than reflecting their true beliefs. Also, self-selection bias, where the individuals who chose to participate differed significantly from those who did not, could have limited generalisability of the findings.

Conclusion

In conclusion, this thesis explored the complex interplay between COVID-19 and vaccine hesitancy—two converging pandemics with profound public health impacts. Through seven timely cross-sectional studies spanning diverse demographics in the Czech Republic and abroad, the findings reveal valuable insights into the multi-level factors shaping vaccine acceptance, hesitancy, and refusal during the mass-vaccination campaigns in 2021 and 2022.

The studies in this thesis highlighted the critical role of altruistic motivations, clear communication of safety and effectiveness evidence, and respect for diverse viewpoints in fostering vaccine acceptance. They also noted that mandates could potentially harden hesitancy if not judiciously implemented based on transparent risk-benefit analysis and ethical considerations.

Certain sociodemographic characteristics, like younger age and female gender, emerged as recurring risk factors for vaccine hesitancy. The research emphasised the importance of compassionately addressing knowledge deficits and misconceptions to foster greater vaccine uptake. It advocated for tailored strategies for hesitant groups such as females, youth and racial minorities, considering cultural factors and knowledge gaps. Promoting public health communications that emphasise the altruistic aspects of immunisation was also suggested, highlighting its role in community protection to promote a sense of collective responsibility.

These multi-country insights can inform policies worldwide; with COVID-19 transitioning to an endemic disease, maintaining vaccine acceptance is critical and requires enduring vigilance—waning immunity and new variants could rekindle hesitancy. Moreover, the legacy of this pandemic may have permanently altered vaccination attitudes, necessitating rebuilding public confidence in routine immunisation. As vaccine hesitancy and infectious diseases persist, these lessons remain ever relevant in safeguarding public health.

LIST OF FIGURES

LIST OF TABLES

LIST OF ATTACHMENTS

No.	Description
Attachment 1	**Riad A,** Pokorná A, Antalová N, Krobot M, Zviadadze N, Serdiuk I, Koščík M, Klugar M. Prevalence and Drivers of COVID-19 Vaccine Hesitancy among Czech University Students: National Cross-Sectional Study. *Vaccines*. **2021**; 9(9):948. https://doi.org/10.3390/vaccines9090948
Attachment 2	**Riad A,** Jouzová A, Üstün B, Lagová E, Hruban L, Janků P, Pokorná A, Klugarová J, Koščík M, Klugar M. COVID-19 Vaccine Acceptance of Pregnant and Lactating Women (PLW) in Czechia: An Analytical Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. **2021**; 18(24):13373. https://doi.org/10.3390/ijerph182413373
Attachment 3	Klugar M, **Riad A**, Mohanan L, Pokorná A. COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Workers in Czechia: National Cross-Sectional Study. *Vaccines*. **2021**; 9(12):1437. https://doi.org/10.3390/vaccines9121437
Attachment 4	**Riad A**, Abdulqader H, Morgado M, Domnori S, Koščík M, Mendes JJ, Klugar M, Kateeb E, on behalf of IADS-SCORE. Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy. *Vaccines*. **2021**; 9(6):566. https://doi.org/10.3390/vaccines9060566
Attachment 5	**Riad A,** Huang Y, Abdulqader H, Morgado M, Domnori S, Koščík M, Mendes JJ, Klugar M, Kateeb E, IADS-SCORE. Universal Predictors of Dental Students' Attitudes towards COVID-19 Vaccination: Machine Learning-Based Approach. *Vaccines*. **2021**; 9(10):1158. https://doi.org/10.3390/vaccines9101158
Attachment 6	Kateeb E, Danadneh M, Pokorná A, Klugarová J, Abdulqader H, Klugar M, **Riad A**. Predictors of Willingness to Receive COVID-19 Vaccine: Cross-Sectional Study of Palestinian Dental Students. *Vaccines*. **2021**; 9(9):954. https://doi.org/10.3390/vaccines9090954
Attachment 7	Attia S, Mausbach K, Klugar M, Howaldt H-P, **Riad A**. Prevalence and Drivers of COVID-19 Vaccine Booster Hesitancy Among German University Students and Employees. *Frontiers in Public Health*. **2022**; 10:846861. https://doi.org/10.3389/fpubh.2022.846861
Attachment 8	Dziedzic A, Issa J, Hussain S, Tanasiewicz M, Wojtyczka R, Kubina R, Konwinska MD, **Riad A**. COVID-19 vaccine booster hesitancy (VBH) of healthcare professionals and students in Poland: Cross-sectional survey-based study. *Frontiers in Public Health*. **2022**; 10:938067. https://doi.org/10.3389/fpubh.2022.938067
Attachment 9	Lounis M, Bencherit D, Rais MA, **Riad A**. COVID-19 Vaccine Booster Hesitancy (VBH) and Its Drivers in Algeria: National Cross-Sectional Survey-Based Study. *Vaccines*. **2022**; 10(4):621. https://doi.org/10.3390/vaccines10040621

BIBLIOGRAPHY

1. World Health Organisation (WHO) Thirteenth General Programme of Work 2019-2023 Available online: https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019---2023 (accessed on 24 June 2023).
2. World Health Organisation (WHO) Ten Threats to Global Health in 2019 Available online: https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019 (accessed on 7 May 2021).
3. MacDonald, N.E.; Eskola, J.; Liang, X.; Chaudhuri, M.; Dube, E.; Gellin, B.; Goldstein, S.; Larson, H.; Manzo, M.L.; Reingold, A.; et al. Vaccine Hesitancy: Definition, Scope and Determinants. *Vaccine* **2015**, *33*, 4161–4164, doi:10.1016/j.vaccine.2015.04.036.
4. World Health Organisation (WHO) Vaccine Hesitancy: A Growing Challenge for Immunization Programmes Available online: https://www.who.int/news/item/18-08-2015-vaccine-hesitancy-a-growing-challenge-for-immunization-programmes (accessed on 25 June 2023).
5. Callender, D. Vaccine Hesitancy: More than a Movement. *Hum Vaccin Immunother* **2016**, *12*, 2464–2468, doi:10.1080/21645515.2016.1178434.
6. Riedel, S. Edward Jenner and the History of Smallpox and Vaccination. *Baylor University Medical Center Proceedings* **2005**, *18*, 21–25, doi:10.1080/08998280.2005.11928028.
7. Jenner, E. *An Inquiry into the Causes and Effects of the Variolae Vaccinae: A Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire, and Known by the Name of the Cow Pox*; Springfield: Massachusetts, 1802;
8. Lantos, J.D.; Jackson, M.A.; Opel, D.J.; Marcuse, E.K.; Myers, A.L.; Connelly, B.L. Controversies in Vaccine Mandates. *Curr Probl Pediatr Adolesc Health Care* **2010**, *40*, 38–58, doi:10.1016/j.cppeds.2010.01.003.
9. Erica X Eisen "The Mark of the Beast": Georgian Britain's Anti-Vaxxer Movement Available online: https://publicdomainreview.org/essay/the-mark-of-the-beast-georgian-britains-anti-vaxxer-movement (accessed on 25 June 2023).
10. William Rowley *Cow-Pox Inoculation No Security against Small-Pox Infection*; London, 1805;
11. Wolfe, R.M.; Sharp, L.K. Anti-Vaccinationists Past and Present. *BMJ* **2002**, *325*, 430–432, doi:10.1136/BMJ.325.7361.430.
12. University of Glasgow Vaccination Available online: https://www.gla.ac.uk/schools/socialpolitical/research/economicsocialhistory/projects/scottishwayofbirthanddeath/vaccination/ (accessed on 25 June 2023).
13. Durbach, N. *Bodily Matters: The Anti-Vaccination Movement in England, 1853–1907*; Duke University Press, 2005; ISBN 0822334232.
14. UK Government Victorian Health Reform - How Did the Victorians View Compulsory Vaccination? Available online: https://www.nationalarchives.gov.uk/education/resources/victorian-health-reform/ (accessed on 25 June 2023).
15. KAUFMAN, M. THE AMERICAN ANTI-VACCINATIONISTS AND THEIR ARGUMENTS. *Bull Hist Med* **1967**, *41*, 463–478.
16. The College of Physicians of Philadelphia History of Anti-Vaccination Movements Available online: https://historyofvaccines.org/vaccines-101/misconceptions-about-vaccines/history-anti-vaccination-movements (accessed on 25 June 2023).

17. Grignolio, A. A Brief History of Anti-Vaccination Movements. In *Vaccines: Are they Worth a Shot?*; Grignolio, A., Ed.; Springer International Publishing: Cham, 2018; pp. 25–40 ISBN 978-3-319-68106-1.
18. Parodi, A.; Martini, M. History of Vaccine and Immunization: Vaccine-Hesitancy Discussion in Germany in XIX Century. *Vaccine* **2023**, *41*, 1989–1993, doi:10.1016/j.vaccine.2023.02.029.
19. Siani, A. Vaccine Hesitancy and Refusal: History, Causes, Mitigation Strategies. In *Integrated Science of Global Epidemics*; Rezaei, N., Ed.; Springer International Publishing: Cham, 2023; pp. 503–517 ISBN 978-3-031-17778-1.
20. US Centers for Disease Control and Prevention (CDC) Historical Safety Concerns Available online: https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html (accessed on 26 June 2023).
21. US Centers for Disease Control and Prevention (CDC) GBS (Guillain-Barré Syndrome) and Vaccines Available online: https://www.cdc.gov/vaccinesafety/concerns/guillain-barre-syndrome.html (accessed on 26 June 2023).
22. Kulenkampff, M.; Schwartzman, J.S.; Wilson, J. Neurological Complications of Pertussis Inoculation. *Arch Dis Child* **1974**, *49*, 46, doi:10.1136/adc.49.1.46.
23. Gareth Millward The Pertussis Crisis. In *Vaccinating Britain: Mass vaccination and the public since the Second World War*; Manchester University Press: Manchester, 2019.
24. Wakefield, A.J.; Murch, S.H.; Anthony, A.; Linnell, J.; Casson, D.M.; Malik, M.; Berelowitz, M.; Dhillon, A.P.; Thomson, M.A.; Harvey, P.; et al. RETRACTED: Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children. *The Lancet* **1998**, *351*, 637–641, doi:10.1016/S0140-6736(97)11096-0.
25. Nuwarda, R.F.; Ramzan, I.; Weekes, L.; Kayser, V. Vaccine Hesitancy: Contemporary Issues and Historical Background. *Vaccines (Basel)* **2022**, *10*, 1595, doi:10.3390/VACCINES10101595.
26. Gangarosa, E.J.; Galazka, A.M.; Wolfe, C.R.; Phillips, L.M.; Gangarosa, R.E.; Miller, E.; Chen, R.T. Impact of Anti-Vaccine Movements on Pertussis Control: The Untold Story. *The Lancet* **1998**, *351*, 356–361, doi:10.1016/S0140-6736(97)04334-1.
27. World Health Organisation (WHO) Vaccine-Preventable Diseases Available online: https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases (accessed on 27 June 2023).
28. World Health Organisation (WHO) Immunization Coverage Estimates Available online: https://www.who.int/data/gho/data/themes/topics/immunization-coverage (accessed on 27 June 2023).
29. Park, J.J.; Narayanan, S.; Tiefenbach, J.; Lukšić, I.; Ale, B.M.; Adeloye, D.; Rudan, I. Estimating the Global and Regional Burden of Meningitis in Children Caused by Haemophilus Influenzae Type b: A Systematic Review and Meta-Analysis. *J Glob Health* **2022**, *12*, 04014, doi:10.7189/jogh.12.04014.
30. Hsu, Y.C.; Huang, D.Q.; Nguyen, M.H. Global Burden of Hepatitis B Virus: Current Status, Missed Opportunities and a Call for Action. *Nature Reviews Gastroenterology & Hepatology 2023* **2023**, *20*, 524–537, doi:10.1038/s41575-023-00760-9.
31. Serrano, B.; Brotons, M.; Bosch, F.X.; Bruni, L. Epidemiology and Burden of HPV-Related Disease. *Best Pract Res Clin Obstet Gynaecol* **2018**, *47*, 14–26, doi:https://doi.org/10.1016/j.bpobgyn.2017.08.006.
32. Zunt, J.R.; Kassebaum, N.J.; Blake, N.; Glennie, L.; Wright, C.; Nichols, E.; Abd-Allah, F.; Abdela, J.; Abdelalim, A.; Adamu, A.A.; et al. Global, Regional, and National Burden of Meningitis, 1990–2016: A Systematic Analysis for the Global

Burden of Disease Study 2016. *Lancet Neurol* **2018**, *17*, 1061–1082, doi:10.1016/S1474-4422(18)30387-9.
33. World Health Organisation (WHO) Meningitis Available online: https://www.who.int/news-room/fact-sheets/detail/meningitis (accessed on 27 June 2023).
34. World Health Organisation (WHO) Measles Available online: https://www.who.int/news-room/fact-sheets/detail/measles (accessed on 27 June 2023).
35. Knoema Mumps Reported Cases Available online: https://knoema.com/atlas/topics/Health/Communicable-Diseases/Mumps-cases?type=maps (accessed on 27 June 2023).
36. US Centers for Disease Control and Prevention (CDC) Global Pneumococcal Disease and Vaccination Available online: https://www.cdc.gov/pneumococcal/global.html (accessed on 27 June 2023).
37. Global Change Data Lab Pneumonia Available online: https://ourworldindata.org/pneumonia (accessed on 27 June 2023).
38. Kalkowska, D.A.; Voorman, A.; Pallansch, M.A.; Wassilak, S.G.F.; Cochi, S.L.; Badizadegan, K.; Thompson, K.M. The Impact of Disruptions Caused by the COVID-19 Pandemic on Global Polio Eradication. *Vaccine* **2023**, *41*, A12–A18, doi:10.1016/j.vaccine.2021.04.026.
39. World Health Organisation (WHO) Poliomyelitis (Polio) Available online: https://www.who.int/health-topics/poliomyelitis#tab=tab_1 (accessed on 27 June 2023).
40. World Health Organisation (WHO) Rotavirus Available online: https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/vaccines-quality/rotavirus (accessed on 27 June 2023).
41. Du, Y.; Chen, C.; Zhang, X.; Yan, D.; Jiang, D.; Liu, X.; Yang, M.; Ding, C.; Lan, L.; Hecht, R.; et al. Global Burden and Trends of Rotavirus Infection-Associated Deaths from 1990 to 2019: An Observational Trend Study. *Virol J* **2022**, *19*, 1–10, doi:10.1186/S12985-022-01898-9/TABLES/2.
42. Vynnycky, E.; Knapp, J.K.; Papadopoulos, T.; Cutts, F.T.; Hachiya, M.; Miyano, S.; Reef, S.E. Estimates of the Global Burden of Congenital Rubella Syndrome, 1996-2019. *medRxiv* **2023**, 2023.04.19.23288818, doi:10.1101/2023.04.19.23288818.
43. Garske, T.; Van Kerkhove, M.D.; Yactayo, S.; Ronveaux, O.; Lewis, R.F.; Staples, J.E.; Perea, W.; Ferguson, N.M.; Burke, D.; De La Hoz, F.; et al. Yellow Fever in Africa: Estimating the Burden of Disease and Impact of Mass Vaccination from Outbreak and Serological Data. *PLoS Med* **2014**, *11*, e1001638, doi:10.1371/JOURNAL.PMED.1001638.
44. Omer, S.B.; Orenstein, W.A.; Koplan, J.P. Go Big and Go Fast — Vaccine Refusal and Disease Eradication. *New England Journal of Medicine* **2013**, *368*, 1374–1376, doi:10.1056/nejmp1300765.
45. Yahya, M. *Polio Vaccines : Difficult to Swallow : The Story of a Controversy in Northern Nigeria*; Working paper series; IDS: Brighton, 2006;
46. Mesa, D.O.; Winskill, P.; Ghani, A.C.; Hauck, K. The Societal Cost of Vaccine Refusal: A Modelling Study Using Measles Vaccination as a Case Study. *Vaccine* **2023**, *41*, 4129–4137, doi:10.1016/J.VACCINE.2023.05.039.
47. Mesa, D.O.; Hogan, A.B.; Watson, O.J.; Charles, G.D.; Hauck, K.; Ghani, A.C.; Winskill, P. Modelling the Impact of Vaccine Hesitancy in Prolonging the Need for Non-Pharmaceutical Interventions to Control the COVID-19 Pandemic. *Communications Medicine* **2022**, *2*, doi:10.1038/S43856-022-00075-X.

48. Ozawa, S.; Portnoy, A.; Getaneh, H.; Clark, S.; Knoll, M.; Bishai, D.; Yang, H.K.; Patwardhan, P.D. Modeling the Economic Burden of Adult Vaccine-Preventable Diseases in the United States. *Health Aff* **2016**, *35*, 2124–2132, doi:10.1377/hlthaff.2016.0462.
49. Simms, K.T.; Hanley, S.J.B.; Smith, M.A.; Keane, A.; Canfell, K. Impact of HPV Vaccine Hesitancy on Cervical Cancer in Japan: A Modelling Study. *Lancet Public Health* **2020**, *5*, e223–e234, doi:10.1016/S2468-2667(20)30010-4.
50. Bussink-Voorend, D.; Hautvast, J.L.A.; Vandeberg, L.; Visser, O.; Hulscher, M.E.J.L. A Systematic Literature Review to Clarify the Concept of Vaccine Hesitancy. *Nat Hum Behav* **2022**, *6*, 1634–1648, doi:10.1038/s41562-022-01431-6.
51. Betsch, C.; Böhm, R.; Chapman, G.B. Using Behavioral Insights to Increase Vaccination Policy Effectiveness. *Policy Insights Behav Brain Sci* **2015**, *2*, 61–73, doi:10.1177/2372732215600716.
52. US Department of Health and Human Services (DHHS) *Theory at a Glance: A Guide for Health Promotion Practice*; Lulu. com, 2018; ISBN 0359244343.
53. Wayne W. LaMorte The Health Belief Model Available online: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/behavioralchangetheories2.html (accessed on 11 August 2022).
54. Rosenstock, I.M. The Health Belief Model and Preventive Health Behavior. *Health Education & Behavior* **1974**, *2*, 354–386, doi:10.1177/109019817400200405.
55. Limbu, Y.B.; Gautam, R.K.; Pham, L. The Health Belief Model Applied to COVID-19 Vaccine Hesitancy: A Systematic Review. *Vaccines (Basel)* **2022**, *10*, doi:10.3390/vaccines10060973.
56. Smith, P.J.; Humiston, S.G.; Marcuse, E.K.; Zhao, Z.; Dorell, C.G.; Howes, C.; Hibbs, B. Parental Delay or Refusal of Vaccine Doses, Childhood Vaccination Coverage at 24 Months of Age, and the Health Belief Model. *Public Health Rep* **2011**, *126 Suppl 2*, 135–146, doi:10.1177/00333549111260S215.
57. Grinberg, K.; Sela, Y. What Affects Maternal Response to Measles Vaccinations? Examining the Health Beliefs Model (HBM). *Sci* **2021**, *3*, 20, doi:10.3390/SCI3020020.
58. Donadiki, E.M.; Jiménez-García, R.; Hernández-Barrera, V.; Sourtzi, P.; Carrasco-Garrido, P.; López de Andrés, A.; Jimenez-Trujillo, I.; Velonakis, E.G. Health Belief Model Applied to Non-Compliance with HPV Vaccine among Female University Students. *Public Health* **2014**, *128*, 268–273, doi:10.1016/J.PUHE.2013.12.004.
59. Mehta, P.; Sharma, M.; Lee, R.C. Designing and Evaluating a Health Belief Model-Based Intervention to Increase Intent of HPV Vaccination among College Males. *Community Health Equity Research & Policy* **2013**, *34*, 101–117, doi:10.2190/IQ.34.1.H.
60. Chen, M.F.; Wang, R.H.; Schneider, J.K.; Tsai, C.T.; Dah-Shyong Jiang, D.; Hung, M.N.; Lin, L.J. Using the Health Belief Model to Understand Caregiver Factors Influencing Childhood Influenza Vaccinations. *J Community Health Nurs* **2011**, *28*, 29–40, doi:10.1080/07370016.2011.539087.
61. Coe, A.B.; Gatewood, S.B.S.; Moczygemba, L.R.; Goode, J.-V. "Kelly" R.; Beckner, J.O. The Use of the Health Belief Model to Assess Predictors of Intent to Receive the Novel (2009) H1N1 Influenza Vaccine. *Innov Pharm* **2012**, *3*, 1, doi:10.24926/IIP.V3I2.257.
62. Riad, A.; Drobov, A.; Rozmarinová, J.; Drapáčová, P.; Klugarová, J.; Dušek, L.; Pokorná, A.; Klugar, M. Monkeypox Knowledge and Vaccine Hesitancy of Czech Healthcare Workers: A Health Belief Model (HBM)-Based Study. *Vaccines (Basel)* **2022**, *10*, 2022, doi:10.3390/vaccines10122022.

63. Ajzen, I. From Intentions to Actions: A Theory of Planned Behavior. In *Action Control: From Cognition to Behavior*; Kuhl, J., Beckmann, J., Eds.; Springer Berlin Heidelberg: Berlin, Heidelberg, 1985; pp. 11–39 ISBN 978-3-642-69746-3.
64. Wayne W. LaMorte The Theory of Planned Behavior Available online: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/BehavioralChangeTheories3.html (accessed on 29 June 2023).
65. Ajzen, I. The Theory of Planned Behavior. *Organ Behav Hum Decis Process* **1991**, *50*, 179–211, doi:10.1016/0749-5978(91)90020-T.
66. Hossain, M.B.; Alam, M.Z.; Islam, M.S.; Sultan, S.; Faysal, M.M.; Rima, S.; Hossain, M.A.; Mamun, A. Al Health Belief Model, Theory of Planned Behavior, or Psychological Antecedents: What Predicts COVID-19 Vaccine Hesitancy Better Among the Bangladeshi Adults? *Front Public Health* **2021**, *9*, 711066, doi:10.3389/FPUBH.2021.711066/BIBTEX.
67. Yahaghi, R.; Ahmadizade, S.; Fotuhi, R.; Taherkhani, E.; Ranjbaran, M.; Buchali, Z.; Jafari, R.; Zamani, N.; Shahbazkhania, A.; Simiari, H.; et al. Fear of COVID-19 and Perceived COVID-19 Infectability Supplement Theory of Planned Behavior to Explain Iranians' Intention to Get COVID-19 Vaccinated. *Vaccines (Basel)* **2021**, *9*, 684, doi:10.3390/VACCINES9070684.
68. Dou, K.; Yang, J.; Wang, L.X.; Li, J. Bin Theory of Planned Behavior Explains Males' and Females' Intention to Receive COVID-19 Vaccines Differently. *Hum Vaccin Immunother* **2022**, *18*, doi:10.1080/21645515.2022.2086393.
69. Fan, C.-W.; Chen, I.-H.; Ko, N.-Y.; Yen, C.-F.; Lin, C.-Y.; Griffiths, M.D.; Pakpour, A.H. Extended Theory of Planned Behavior in Explaining the Intention to COVID-19 Vaccination Uptake among Mainland Chinese University Students: An Online Survey Study. *Hum Vaccin Immunother* **2021**, *17*, 3413–3420, doi:10.1080/21645515.2021.1933687.
70. Fisher, W.A.; Kohut, T.; Salisbury, C.M.A.; Salvadori, M.I. Understanding Human Papillomavirus Vaccination Intentions: Comparative Utility of the Theory of Reasoned Action and the Theory of Planned Behavior in Vaccine Target Age Women and Men. *J Sex Med* **2013**, *10*, 2455–2464, doi:10.1111/JSM.12211.
71. Askelson, N.M.; Campo, S.; Lowe, J.B.; Smith, S.; Dennis, L.K.; Andsager, J. Using the Theory of Planned Behavior to Predict Mothers' Intentions to Vaccinate Their Daughters Against HPV. *The Journal of School Nursing* **2010**, *26*, 194–202, doi:10.1177/1059840510366022.
72. Catalano, H.P.; Knowlden, A.P.; Birch, D.A.; Leeper, J.D.; Paschal, A.M.; Usdan, S.L. Using the Theory of Planned Behavior to Predict HPV Vaccination Intentions of College Men. *Journal of American College Health* **2017**, *65*, 197–207.
73. Chu, A.; Gupta, V.; Unni, E.J. Utilizing the Theory of Planned Behavior to Determine the Intentions to Receive the Influenza Vaccine during COVID-19: A Cross-Sectional Survey of US Adults. *Prev Med Rep* **2021**, *23*, 101417, doi:https://doi.org/10.1016/j.pmedr.2021.101417.
74. Agarwal, V. A/H1N1 Vaccine Intentions in College Students: An Application of the Theory of Planned Behavior. *Journal of American College Health* **2014**, *62*, 416–424.
75. Wayne W. LaMorte The Transtheoretical Model (Stages of Change) Available online: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/BehavioralChangeTheories6.html (accessed on 30 June 2023).
76. Sutton, S. Transtheoretical Model of Behaviour Change. In *Cambridge Handbook of Psychology, Health and Medicine*; Baum, A., McManus, C., Weinman, J., Wallston,

K., West, R., Newman, S., Ayers, S., Eds.; Cambridge University Press: Cambridge, 2007; pp. 228–232 ISBN 9780511543579.

77. DiClemente, C.C.; Prochaska, J.O. Self-Change and Therapy Change of Smoking Behavior: A Comparison of Processes of Change in Cessation and Maintenance. *Addictive behaviors* **1982**, *7*, 133–142, doi:10.1016/0306-4603(82)90038-7.
78. Prochaska, J.O.; DiClemente, C.C. Stages and Processes of Self-Change of Smoking: Toward an Integrative Model of Change. *J Consult Clin Psychol* **1983**, *51*, 390–395, doi:10.1037//0022-006X.51.3.390.
79. Prochaska, J.O.; Velicer, W.F. The Transtheoretical Model of Health Behavior Change. *Am J Health Promot* **1997**, *12*, 38–48, doi:10.4278/0890-1171-12.1.38.
80. Lipschitz, J.M.; Fernandez, A.C.; Elsa Larson, H.; Blaney, C.L.; Meier, K.S.; Redding, C.A.; Prochaska, J.O.; Paiva, A.L. Validation of Decisional Balance and Self-Efficacy Measures for HPV Vaccination in College Women. *Am J Health Promot* **2013**, *27*, 299–307, doi:10.4278/ajhp.110606-quan-240.
81. Fernandez, A.C.; Amoyal, N.R.; Paiva, A.L.; Prochaska, J.O. Motivation for HPV Vaccination Among Young Adult Men: Validation of TTM Decisional Balance and Self-Efficacy Constructs. *Am J Health Promot* **2016**, *30*, 163–171, doi:10.4278/AJHP.131108-QUAN-570.
82. Stein, M.; Sabo, M.; Caverly, J. Relationship Between Stages of Change and HPV Vaccine Attitudes and Beliefs in Baccalaureate Nursing Students. *Williams Honors College, Honors Research Projects* **2015**.
83. Lachance-Grzela, M.; Charbonneau, A.; Jbilou, J.; Dubé, A.; Richard, J. Factors Related to the Intention to Get Vaccinated Against COVID-19 in the Province of New Brunswick, Canada. *J Community Health* **2022**, *47*, 674–679, doi:10.1007/S10900-022-01093-5/TABLES/2.
84. Weinstein, N.D. The Precaution Adoption Process. *Health Psychol* **1988**, *7*, 355–386, doi:10.1037/0278-6133.7.4.355.
85. Brewer, N.T.; Chapman, G.B.; Gibbons, F.X.; Gerrard, M.; McCaul, K.D.; Weinstein, N.D. Meta-Analysis of the Relationship between Risk Perception and Health Behavior: The Example of Vaccination. *Health Psychology* **2007**, *26*, 136–145, doi:10.1037/0278-6133.26.2.136.
86. Karen Glanz; Barbara K. Rimer; K. Viswanath The Precaution Adoption Process Model. In *Health Behavior and Health Education*; Jossey-Bass: Hoboken, NJ, 2008 ISBN 978-0787996147.
87. Weinstein, N.D.; Sandman, P.M. A Model of the Precaution Adoption Process: Evidence from Home Radon Testing. *Health Psychol* **1992**, *11*, 170–180, doi:10.1037/0278-6133.11.3.170.
88. Meyer, C.; Goffe, L.; Antonopoulou, V.; Graham, F.; Tang, M.Y.; Lecouturier, J.; Grimani, A.; Chadwick, P.; Sniehotta, F.F. Using the Precaution Adoption Process Model to Understand Decision-Making about the COVID-19 Booster Vaccine in England. *Vaccine* **2023**, *41*, 2466, doi:10.1016/j.vaccine.2023.02.047.
89. Lee, E.N.; Bae, S.H.; Choi, E.H.; Hwang, H.J.; Lee, Y.O.; Cho, J.L. Factors Influencing Human Papillomavirus Vaccination Adoption Stages Based on the Precaution Adoption Process Model. *aon* **2015**, *15*, 89–96, doi:10.5388/aon.2015.15.2.89.
90. Barnard, M.; George, P.; Perryman, M.L.; Wolff, L.A. Human Papillomavirus (HPV) Vaccine Knowledge, Attitudes, and Uptake in College Students: Implications from the Precaution Adoption Process Model. *PLoS One* **2017**, *12*, e0182266-.
91. Tatar, O.; Shapiro, G.K.; Perez, S.; Wade, K.; Rosberger, Z. Using the Precaution Adoption Process Model to Clarify Human Papillomavirus Vaccine Hesitancy in

Canadian Parents of Girls and Parents of Boys. *Human Vaccines & Immunotherapeutics* **2019**, *15*, 1803–1814, doi:10.1080/21645515.2019.1575711.
92. Bandura, A. Social Foundations of Thought and Action. *Englewood Cliffs, NJ* **1986**, *1986*.
93. Wayne W. LaMorte The Social Cognitive Theory Available online: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/behavioralchangetheories5.html (accessed on 30 June 2023).
94. Catalano, H.P.; Knowlden, A.P.; Sharma, M.; Franzidis, A. A Pilot Study Applying Social Cognitive Theory to Predict HPV Vaccination Intentions of Unvaccinated College Women. *Am J Sex Educ* **2016**, *11*, 287–305, doi:10.1080/15546128.2016.1231648.
95. Priest, H.M.; Knowlden, A.P.; Sharma, M. Social Cognitive Theory Predictors of Human Papillomavirus Vaccination Intentions of College Men at a Southeastern University. *Community Health Equity Research & Policy* **2015**, *35*, 371–385, doi:10.1177/0272684X15583289.
96. Alsaeed, A.A.; Rabbani, U. Explaining COVID-19 Vaccine Rejection Using Social Cognitive Theory in Qassim, Saudi Arabia. *Vaccines (Basel)* **2021**, *9*, 1304, doi:10.3390/VACCINES9111304.
97. She, R.; Chen, X.; Li, L.; Li, L.; Huang, Z.; Lau, J.T.F. Factors Associated with Behavioral Intention of Free and Self-Paid Severe Acute Respiratory Coronavirus Virus 2 (SARS-CoV-2) Vaccination Based on the Social Cognitive Theory among Nurses and Doctors in China. *Infect Control Hosp Epidemiol* **2022**, *43*, 609–615, doi:10.1017/ICE.2021.201.
98. Zhu, Y.; Beam, M.; Ming, Y.; Egbert, N.; Smith, T.C. A Social Cognitive Theory Approach to Understanding Parental Attitudes and Intentions to Vaccinate Children during the COVID-19 Pandemic. *Vaccines (Basel)* **2022**, *10*, 1876, doi:10.3390/VACCINES10111876.
99. Wayne W. LaMorte Diffusion of Innovation Theory Available online: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/behavioralchangetheories4.html (accessed on 1 July 2023).
100. Rogers, E.M. *Diffusion of Innovations*; 5th ed.; Free Press: New York, 2003; ISBN 0743222091; 9780743222099.
101. Dearing, J.W.; Cox, J.G. Diffusion Of Innovations Theory, Principles, And Practice. *Health Aff* **2018**, *37*, 183–190, doi:10.1377/hlthaff.2017.1104.
102. Rosen, B.; Goodson, P. A Recommendation to Use the Diffusion of Innovations Theory to Understand School Nurses' Role in HPV Vaccine Uptake. *Community Health Equity Research & Policy* **2013**, *34*, 37–49, doi:10.2190/IQ.34.1.D.
103. Cohen, E.L.; Head, K.J. Identifying Knowledge-Attitude-Practice Gaps to Enhance HPV Vaccine Diffusion. *J Health Commun* **2013**, *18*, 1221–1234, doi:10.1080/10810730.2013.778357.
104. Pinariya, J.M.; Ikhsano, A.; Sutjipto, A.M. Accelerating Diffusion Innovation Using Celebritites as Opinion Leader Millenials: HPV Vaccines in Indonesia. *Malaysian Journal of Communication* **2020**, *36*, 32–48.
105. Still, J.E. Explaining HPV Vaccine Uptake among African American Adolescent Females Using The Diffusion of Innovations Theory, Emory University, 2014.
106. Mo, P.K.H.; Luo, S.; Wang, S.; Zhao, J.; Zhang, G.; Li, L.; Li, L.; Xie, L.; Lau, J.T.F. Intention to Receive the COVID-19 Vaccination in China: Application of the Diffusion of Innovations Theory and the Moderating Role of Openness to Experience. *Vaccines (Basel)* **2021**, *9*, 129, doi:10.3390/VACCINES9020129.

107. Hunter-Mullis, K.; Macy, J.T.; Greene, A.; Simon, K. Perceived COVID-19 Vaccine Attributes Associated with Early Adoption among Adults in Rural Indiana. *Health Educ Res* **2022**, *37*, 466–475, doi:10.1093/HER/CYAC029.
108. Hensel, D.; Springmyer, J. Do Perinatal Nurses Still Check for Blood Return When Administering the Hepatitis B Vaccine? *Journal of Obstetric, Gynecologic & Neonatal Nursing* **2011**, *40*, 589–594, doi:10.1111/J.1552-6909.2011.01277.X.
109. US Health Resources and Services Administration (HRSA) Community Organization Model Available online: https://www.ruralhealthinfo.org/toolkits/health-promotion/2/program-models/community-organization (accessed on 1 July 2023).
110. Bracht, N.F.; Kingsbury, L.; Rissel, C. A Five-Stage Community Organization Model for Health Promotion: Empowerment and Partnership Strategies.; 1999.
111. Minkler, M.; Wallerstein, N.; Wilson, N. Improving Health Through Community Organization and Community Building. In *Health Behavior and Health Education*.
112. Rothman, J.; Erlich, J.; Tropman, J.E. *Strategies of Community Intervention*; F.E. Peacock Publishers, 2001; ISBN 9780875814360.
113. Kadariya, S.; Ball, L.; Chua, D.; Ryding, H.; Hobby, J.; Marsh, J.; Bartrim, K.; Mitchell, L.; Parkinson, J. Community Organising Frameworks, Models, and Processes to Improve Health: A Systematic Scoping Review. *Int J Environ Res Public Health* **2023**, *20*, 5341, doi:10.3390/IJERPH20075341.
114. Santilli, A.; Carroll-Scott, A.; Ickovics, J.R. Applying Community Organizing Principles to Assess Health Needs in New Haven, Connecticut. *Am J Public Health* **2016**, *106*, 841, doi:10.2105/AJPH.2016.303050.
115. Bronfenbrenner, U. Toward an Experimental Ecology of Human Development. *American Psychologist* **1977**, *32*, 513–531, doi:10.1037/0003-066X.32.7.513.
116. McLeroy, K.R.; Bibeau, D.; Steckler, A.; Glanz, K. An Ecological Perspective on Health Promotion Programs. *Health Educ Q* **1988**, *15*, 351–377.
117. Golden, S.D.; Earp, J.A.L. Social Ecological Approaches to Individuals and Their Contexts: Twenty Years of Health Education & Behavior Health Promotion Interventions. *Health education & behavior* **2012**, *39*, 364–372.
118. Al-Jayyousi, G.F.; Sherbash, M.A.M.; Ali, L.A.M.; El-Heneidy, A.; Alhussaini, N.W.Z.; Elhassan, M.E.A.; Nazzal, M.A. Factors Influencing Public Attitudes towards COVID-19 Vaccination: A Scoping Review Informed by the Socio-Ecological Model. *Vaccines (Basel)* **2021**, *9*, 548, doi:10.3390/VACCINES9060548/S1.
119. Dayton, L.; Miller, J.; Strickland, J.; Davey-Rothwell, M.; Latkin, C. A Socio-Ecological Perspective on Parents' Intentions to Vaccinate Their Children against COVID-19. *Vaccine* **2022**, *40*, 4432–4439, doi:10.1016/j.vaccine.2022.05.089.
120. Limaye, R.J.; Paul, A.; Gur-Arie, R.; Zavala, E.; Lee, C.; Fesshaye, B.; Singh, P.; Njagi, W.; Odila, P.; Munyao, P.; et al. A Socio-Ecological Exploration to Identify Factors Influencing the COVID-19 Vaccine Decision-Making Process among Pregnant and Lactating Women: Findings from Kenya. *Vaccine* **2022**, *40*, 7305–7311, doi:10.1016/j.vaccine.2022.10.068.
121. Riad, A.; Huang, Y.; Abdulqader, H.; Morgado, M.; Domnori, S.; Koščík, M.; Mendes, J.J.; Klugar, M.; Kateeb, E.; IADS-SCORE Universal Predictors of Dental Students' Attitudes towards COVID-19 Vaccination: Machine Learning-Based Approach. *Vaccines (Basel)* **2021**, *9*, 1158, doi:10.3390/VACCINES9101158.
122. Tostrud, L.; Thelen, J.; Palatnik, A. Models of Determinants of COVID-19 Vaccine Hesitancy in Non-Pregnant and Pregnant Population: Review of Current Literature". *Hum Vaccin Immunother* **2022**, *18*, doi:10.1080/21645515.2022.2138047.

123. Geiger, M.; Rees, F.; Lilleholt, L.; Santana, A.P.; Zettler, I.; Wilhelm, O.; Betsch, C.; Böhm, R. Measuring the 7Cs of Vaccination Readiness. *European Journal of Psychological Assessment* **2022**, *38*, 261–269, doi:10.1027/1015-5759/a000663.
124. Shapiro, G.K.; Kaufman, J.; Brewer, N.T.; Wiley, K.; Menning, L.; Leask, J.; Abad, N.; Betsch, C.; Bura, V.; Correa, G.; et al. A Critical Review of Measures of Childhood Vaccine Confidence. *Curr Opin Immunol* **2021**, *71*, 34–45, doi:10.1016/J.COI.2021.04.002.
125. Strategic Advisory Group of Experts on Immunization (SAGE) *Report of the Sage Working Group on Vaccine Hesitancy*; 2014;
126. Strategic Advisory Group of Experts on Immunization (SAGE) *Vaccine Hesitancy Survey Questions Related to SAGE Vaccine Hesitancy Matrix*;
127. Larson, H.J.; Jarrett, C.; Eckersberger, E.; Smith, D.M.D.; Paterson, P. Understanding Vaccine Hesitancy around Vaccines and Vaccination from a Global Perspective: A Systematic Review of Published Literature, 2007-2012. *Vaccine* **2014**, *32*, 2150–2159, doi:10.1016/j.vaccine.2014.01.081.
128. Quinn, S.C.; Jamison, A.M.; An, J.; Hancock, G.R.; Freimuth, V.S. Measuring Vaccine Hesitancy, Confidence, Trust and Flu Vaccine Uptake: Results of a National Survey of White and African American Adults. *Vaccine* **2019**, *37*, 1168–1173, doi:10.1016/j.vaccine.2019.01.033.
129. Betsch, C.; Schmid, P.; Heinemeier, D.; Korn, L.; Holtmann, C.; Böhm, R. Beyond Confidence: Development of a Measure Assessing the 5C Psychological Antecedents of Vaccination. *PLoS One* **2018**, *13*, doi:10.1371/journal.pone.0208601.
130. Turner, P.J.; Larson, H.; Dubé, È.; Fisher, A. Vaccine Hesitancy: Drivers and How the Allergy Community Can Help. *J Allergy Clin Immunol Pract* **2021**, *9*, 3568–3574, doi:10.1016/j.jaip.2021.06.035.
131. Nicholls, L.A.B.; Gallant, A.J.; Cogan, N.; Rasmussen, S.; Young, D.; Williams, L. Older Adults' Vaccine Hesitancy: Psychosocial Factors Associated with Influenza, Pneumococcal, and Shingles Vaccine Uptake. *Vaccine* **2021**, *39*, 3520–3527, doi:10.1016/j.vaccine.2021.04.062.
132. COSMO Authors Available online: https://vaccination-readiness.com/authors/ (accessed on 2 July 2023).
133. COSMO Development of the 7C Scale Available online: https://vaccination-readiness.com/development/ (accessed on 2 July 2023).
134. Thomson, A.; Robinson, K.; Vallée-Tourangeau, G. The 5As: A Practical Taxonomy for the Determinants of Vaccine Uptake. *Vaccine* **2016**, *34*, 1018–1024, doi:10.1016/j.vaccine.2015.11.065.
135. Butler, R.; MacDonald, N.E.; Eskola, J.; Liang, X.; Chaudhuri, M.; Dube, E.; Gellin, B.; Goldstein, S.; Larson, H.; Manzo, M.L.; et al. Diagnosing the Determinants of Vaccine Hesitancy in Specific Subgroups: The Guide to Tailoring Immunization Programmes (TIP). *Vaccine* **2015**, *33*, 4176–4179, doi:10.1016/j.vaccine.2015.04.038.
136. WHO Strategic Advisory Group of Experts on Immunization (SAGE) Understanding the Behavioural and Social Drivers of Vaccine Uptake WHO Position Paper – May 2022 Available online: https://www.who.int/publications/i/item/who-wer9720-209-224 (accessed on 3 July 2023).
137. Brewer, N.T.; Chapman, G.B.; Rothman, A.J.; Leask, J.; Kempe, A. Increasing Vaccination: Putting Psychological Science Into Action. *Psychological Science in the Public Interest* **2017**, *18*, 149–207, doi:10.1177/1529100618760521.
138. World Health Organisation (WHO) *Behavioural and Social Drivers of Vaccination: Tools and Practical Guidance for Achieving High Uptake*; World Health Organization: Geneva, 2022; ISBN 9789240049680 (electronic version).

139. Jarrett, C.; Wilson, R.; O'Leary, M.; Eckersberger, E.; Larson, H.J.; Eskola, J.; Liang, X.; Chaudhuri, M.; Dube, E.; Gellin, B.; et al. Strategies for Addressing Vaccine Hesitancy - A Systematic Review. *Vaccine* 2015, *33*, 4180–4190.
140. Sekera, J.C.; Preis, J.; Pazdiora, P. Health Literacy on Hiv Infection among Adolescents in the Czech Republic: A Case Study of Two Czech Cities Plzen and Ceské Budejovice | Zdravotní Gramotnost Týkající Se Infekce Hiv Mezi Adolescenty v České Republice: Případová Studie Ze Dvou Českých Měst . *Epidemiologie, Mikrobiologie, Imunologie* **2020**, *69*, 182–188.
141. Agrinier, N.; Le Maréchal, M.; Fressard, L.; Verger, P.; Pulcini, C. Discrepancies between General Practitioners' Vaccination Recommendations for Their Patients and Practices for Their Children. *Clinical Microbiology and Infection* **2017**, *23*, 311–317, doi:10.1016/J.CMI.2016.08.019.
142. Dubé, E. Addressing Vaccine Hesitancy: The Crucial Role of Healthcare Providers. *Clinical Microbiology and Infection* **2017**, *23*, 279–280, doi:10.1016/J.CMI.2016.11.007.
143. Finney Rutten, L.J.; Zhu, X.; Leppin, A.L.; Ridgeway, J.L.; Swift, M.D.; Griffin, J.M.; St Sauver, J.L.; Virk, A.; Jacobson, R.M. Evidence-Based Strategies for Clinical Organizations to Address COVID-19 Vaccine Hesitancy. *Mayo Clin Proc* **2021**, *96*, 699–707, doi:10.1016/J.MAYOCP.2020.12.024.
144. Vocelka, K.; Heller, L. *Die Private Welt Der Habsburger. Leben Und Alltag Einer Familie*; Graz/Wien, 1998;
145. Wimmer, J. *Gesundheit, Krankheit Und Tod Im Zeitalter Der Aufklärung. Fallstudien Aus Den Habsburgischen Erbländern*; Wien/Köln, 1991;
146. Moser, M.W.; Patzak, B. Variola: Zur Geschichte Einer Museal Präsenten Seuche. *Zeitschrift Wiener Klinische Wochenschrift* **2008**, *120*, 3–10.
147. Beran, J.; Havlík, J.; Vonka, V. *Očkování: Minulost, Přítomnost, Budoucnost*; Galén: Praha, 2005; ISBN 8072623613.
148. Beran, J. *Očkování v Otázkách a Odpovědích*; Albatros Media a.s., 2023; ISBN 9788020461179.
149. Petráš, M.; Domorázková, E.; Hobstová, J. *Co by Rodiče Měli Vědět o Očkování*; TANGO: Praha, 1999; ISBN 8023845330.
150. Dáňová, J.; Částková, J. *Očkování v České Republice*; Částková, J., Ed.; 1st ed.; Triton: Praha, 2008; ISBN 9788073871222.
151. Tomaskova, H.; Ovesna, V.; Kloudova, A.; Hozak, A.; Janout, V. The History of Serological Surveys in the Czech Republic. *Hygiena* **2016**, *61*, 161–166.
152. Marešová, V. A Short History of Infectious Diseases since the Fifties of the Last Century and the Importance of Vaccination. *Cas Lek Cesk* **2015**, *154*, 156–160.
153. Trebichavský, I. Lži a Mýty Proti Očkování. *Živa* **2016**, *Not availa*, 53–55.
154. Janda, J. Očkování Dětí a Dorostu–Alternativní Rodiče, Odpůrci Očkování. *Tempus Medicorum* **2015**, *24*, 16–17.
155. Suchánková, M.; Sláčalová, D. Rozalio.Cz 2023.
156. Paracelsus - Detail Firmy 2023.
157. O Povinném Očkování Dětí Se Rozhořel Prudký Spor 2023.
158. Suchánková, M.; Sláčalová, D. Návrhy Změn Systému Očkování 2023.
159. European Centre for Disease Prevention and Control (ECDC) Czech Republic: Recommended Vaccinations Available online: https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByCountry?SelectedCountryId=201&IncludeChildAgeGroup=true&IncludeChildAgeGroup=false&IncludeAdultAgeGroup=true&IncludeAdultAgeGroup=false (accessed on 7 July 2023).
160. *Health at a Glance 2021*; Health at a Glance; OECD, 2021; ISBN 9789264961012.

161. Chlíbek, R.; Cabrnochová, H.; Dušek, L. Results of Vaccination Coverage in the Czech Republic. *Vakcinologie* **2021**, 82–90.
162. Vaz, O.M.; Ellingson, M.K.; Weiss, P.; Jenness, S.M.; Bardají, A.; Bednarczyk, R.A.; Omer, S.B. Mandatory Vaccination in Europe. *Pediatrics* **2020**, *145*, e20190620, doi:10.1542/peds.2019-0620.
163. Smetana, J.; Chlibek, R.; Hanovcova, I.; Sosovickova, R.; Smetanova, L.; Gal, P.; Dite, P. Decreasing Seroprevalence of Measles Antibodies after Vaccination – Possible Gap in Measles Protection in Adults in the Czech Republic. *PLoS One* **2017**, *12*, e0170257.
164. Duval, L.; Wolff, F.-C.; McKee, M.; Roberts, B. The Roma Vaccination Gap: Evidence from Twelve Countries in Central and South-East Europe. *Vaccine* **2016**, *34*, 5524–5530, doi:https://doi.org/10.1016/j.vaccine.2016.10.003.
165. Nguyen-Huu, N.-H.; Thilly, N.; Derrough, T.; Sdona, E.; Claudot, F.; Pulcini, C.; Agrinier, N. Human Papillomavirus Vaccination Coverage, Policies, and Practical Implementation across Europe. *Vaccine* **2020**, *38*, 1315–1331, doi:https://doi.org/10.1016/j.vaccine.2019.11.081.
166. Ústav zdravotnických informací a statistiky České republiky (ÚZIS) Příloha 2. Nově Dostupná Data: Proočkovanost České Populace Proti HPV. **2018**.
167. Blank, P.R.; van Essen, G.A.; Ortiz de Lejarazu, R.; Kyncl, J.; Nitsch-Osuch, A.; Kuchar, E.P.; Falup-Pecurariu, O.; Maltezou, H.C.; Zavadska, D.; Kristufkova, Z.; et al. Impact of European Vaccination Policies on Seasonal Influenza Vaccination Coverage Rates: An Update Seven Years Later. *Hum Vaccin Immunother* **2018**, *14*, 2706–2714, doi:10.1080/21645515.2018.1489948.
168. Blank, P.R.; Schwenkglenks, M.; Szucs, T.D. Vaccination Coverage Rates in Eleven European Countries during Two Consecutive Influenza Seasons. *Journal of Infection* **2009**, *58*, 446–458, doi:https://doi.org/10.1016/j.jinf.2009.04.001.
169. Kynčl, J.; Liptáková, M.; Košťálová, J.; Malý, M.; Křížová, M.; Heřman, H.; Fabiánová, K. Vaccination against Influenza in Pregnant Women in a Maternity Hospital in the Czech Republic in the Season 2020–2021. *BMC Public Health* **2023**, *23*, 1029, doi:10.1186/s12889-023-15911-5.
170. (VCP), T.V.C.P. State of Vaccine Confidence in the EU Available online: https://www.vaccineconfidence.org/our-work/projects/state-of-vaccine-confidence-in-the-eu/.
171. (EC), E.C. State of Vaccine Confidence in the EU 2022 Available online: https://health.ec.europa.eu/publications/state-vaccine-confidence-eu-2022_en.
172. (EC), E.C. State of Vaccine Confidence in the EU and the UK (2020) Available online: https://health.ec.europa.eu/vaccination/state-vaccine-confidence_en.
173. (VCP), T.V.C.P. The State of Vaccine Confidence in the EU 2020 2020.
174. Larson, H.; de Figueiredo, A.; Xiahong, Z.; Schulz, W.S.; Verger, P.; Johnston, I.G.; Cook, A.R.; Jones, N.S. *The State of Vaccine Confidence in the EU 2018*; European Commission: Brussels, 2018;
175. Mascherini, M.; Nivakoski, S. Social Media Use and Vaccine Hesitancy in the European Union. *Vaccine* **2022**, *40*, 2215–2225, doi:https://doi.org/10.1016/j.vaccine.2022.02.059.
176. Tolstrup Wester, C.; Lybecker Scheel-Hincke, L.; Bovil, T.; Andersen-Ranberg, K.; Juel Ahrenfeldt, L.; Christian Hvidt, N. Prayer Frequency and COVID-19 Vaccine Hesitancy among Older Adults in Europe. *Vaccine* **2022**, *40*, 6383–6390, doi:https://doi.org/10.1016/j.vaccine.2022.09.044.
177. Recio-Román, A.; Recio-Menéndez, M.; Román-González, M. V Vaccine Hesitancy and Political Populism. An Invariant Cross-European Perspective. *Int J Environ Res Public Health* 2021, *18*.

178. Agosti, F.; Toffolutti, V.; Cavalli, N.; Nivakoski, S.; Mascherini, M.; Aassve, A. Information and Vaccine Hesitancy: Evidence from the Early Stage of the Vaccine Roll-out in 28 European Countries. *PLoS One* **2022**, *17*, e0273555.
179. Toshkov, D. What Accounts for the Variation in COVID-19 Vaccine Hesitancy in Eastern, Southern and Western Europe? *Vaccine* **2023**, *41*, 3178–3188, doi:https://doi.org/10.1016/j.vaccine.2023.03.030.
180. Tomaskova, H.; Bohacova, S.; Slachtova, H. Attitudes of the Medical Students from Two Czech Universities to Pandemic Flu A (H1N1) 2009 and to Influenza Vaccination. *Cent Eur J Public Health* **2012**, *20*, 215–218.
181. Prymula, R.; Usluer, G.; Altinel, S.; Sichova, R.; Weber, F. Acceptance and Opinions of Intanza/IDflu Intradermal Influenza Vaccine in the Czech Republic and Turkey. *Adv Ther* **2012**, *29*, 41–52, doi:10.1007/s12325-011-0090-5.
182. Pazdiora, P.; Skalova, J.; Kubatova, A.; Ježová, I.; Moravkova, I.; Podlesna, I.; Průchová, J.; Spáčilová, M.; Švecová, M. Mumps Outbreak in the Plzeň Region in 2011. *Epidemiol Mikrobiol Imunol* **2015**, *64*, 242–249.
183. Šálek, J.; Čelko, A.M.; Dáňová, J. Vaccination Perception and Attitude among Undergraduate Medical and Teacher Education Students at Charles University, Prague, Czech Republic. *Vaccines (Basel)* 2020, *8*.
184. Vochocová, L.; Numerato, D.; Sedláčková, T. Opting for Polarizing Emotions: Strategies of Czech pro-Vaccination Discussants in the Emotionalized Public Sphere and Debate on a Measles Epidemic. *Int J Commun* **2022**, *16*, 21.
185. Liptakova, M.; Kostalova, J.; Kyncl, J.; Maly, M.; Krizova, M.; Herman, H.; Fabianova, K. Monitoring the Vaccination of Pregnant Women against Pertussis-Single-Centre One-Year Study in the Czech Republic. *Bratislava Medical Journal/Bratislavske Lekarske Listy* **2023**, *124*.
186. Strachoňová, J. Současná Právní Úprava Povinného Očkování v České Republice a Důsledky Vedoucí z Jeho Odmítnutí Available online: https://dspace.jcu.cz/handle/123456789/17774.
187. Vokrouhlíková, M. Informovanost Veřejnosti o Onemocnění Klíšťovou Encefalitidou Available online: https://dspace.jcu.cz/handle/123456789/17781.
188. Sýkorová, M. Hodnocení Prevence u Cestovatelů Do Zahraničí Available online: https://dspace.jcu.cz/handle/123456789/17775.
189. Zemanová, I. Analýza Zájmu Zdravotnických Pracovníků o Očkován Proti Chřipce v Nemocnici Rudolfa a Stefanie Benešov. Available online: https://dspace.jcu.cz/handle/123456789/20087.
190. Maxová, M. Studie Proočkovanosti a Vakcinační Disciplíny u Povinného Očkování, 2013.
191. Palátová, I. Odmítání Očkování v Kraji Vysočina v Období Let 2010 - 2013 Available online: https://dspace.jcu.cz/handle/123456789/21939.
192. Chocholová, B. Význam Kontroly Proočkovanosti u Dětí Available online: https://dspace.jcu.cz/handle/123456789/34457.
193. Mejtská, P. Role Otců Při Váhání o Očkování Available online: https://dspace.cuni.cz/handle/20.500.11956/122126.
194. Martinková, M. Postoje Rodičů k Očkování Dětí Available online: https://dspace.cuni.cz/handle/20.500.11956/173401.
195. Dziadková, K. Postoje Rodičů k Povinnénu Očkování Dětí Available online: https://dspace.cuni.cz/handle/20.500.11956/180209.
196. Štěpánek, L.; Janošíková, M.; Nakládalová, M.; Štěpánek, L.; Boriková, A.; Vildová, H. Motivation to COVID-19 Vaccination and Reasons for Hesitancy in Employees of a Czech Tertiary Care Hospital: A Cross-Sectional Survey. *Vaccines (Basel)* 2021, *9*.

197. Kupsova, B.; Pavlik, V.; Horacek, J.M.; Stepanek, L. Vaccination against COVID-19 as Prevention of Occupational Disease in University of Defence Members in the Czech Republic-Motivation for Vaccination and Reasons for Hesitancy. *Bratislava Medical Journal/Bratislavske Lekarske Listy* **2022**, *123*.
198. Kosarkova, A.; Malinakova, K.; van Dijk, J.P.; Tavel, P. Vaccine Refusal in the Czech Republic Is Associated with Being Spiritual but Not Religiously Affiliated. *Vaccines 2021* **2021**, *9*, 1157, doi:10.3390/VACCINES9101157.
199. Zidkova, R.; Malinakova, K.; van Dijk, J.P.; Tavel, P. COVID-19 Vaccination Refusal—Which Factors Are Related in the Czech Republic, One of the Most Affected Countries in the World? . *International Journal of Public Health* 2023, *68*.
200. Šerek, J.; Klicperová-Baker, M. Health Worries, Sociopolitical Attitudes, or Both? Prospective Predictors of COVID-19 Vaccine Uptake in the Czech Republic. *Soc Personal Psychol Compass* **2023**, *n/a*, e12803, doi:https://doi.org/10.1111/spc3.12803.
201. Zapletal, J.; Drochýtek, V.; Vařbuchtová, A.; Rob, L. Analysis of Awareness and Acceptance of SARS-CoV-2 Vaccination among Pregnant Women. *Ceska Gynekol* **2022**, *87*, 100–103.
202. Spiteri, G.; Fielding, J.; Diercke, M.; Campese, C.; Enouf, V.; Gaymard, A.; Bella, A.; Sognamiglio, P.; Moros, M.J.S.; Riutort, A.N. First Cases of Coronavirus Disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. *Eurosurveillance* **2020**, *25*, 2000178.
203. Nadeau, S.A.; Vaughan, T.G.; Scire, J.; Huisman, J.S.; Stadler, T. The Origin and Early Spread of SARS-CoV-2 in Europe. *Proc Natl Acad Sci U S A* **2021**, *118*, e2012008118, doi:10.1073/PNAS.2012008118/SUPPL_FILE/PNAS.2012008118.SAPP.PDF.
204. World Health Organization (WHO); World Health Organization; WHO; World Health Organization (WHO); World Health Organization WHO Director-General's Opening Remarks at the Media Briefing on COVID-19 - 13 March 2020 Available online: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-mission-briefing-on-covid-19---13-march-2020 (accessed on 1 May 2020).
205. Philip Schellekens COVID Waves: Europe and US Compared Available online: https://pandem-ic.com/covid-waves-europe-and-us-compared/ (accessed on 12 July 2023).
206. World Health Organisation (WHO) WHO Coronavirus (COVID-19) Dashboard Available online: https://covid19.who.int/ (accessed on 12 July 2023).
207. European Centre for Disease Prevention and Control (ECDC) Weekly COVID-19 Country Overview Available online: https://www.ecdc.europa.eu/en/covid-19/country-overviews (accessed on 12 July 2023).
208. Global Change Data Lab (GCDL) Coronavirus (COVID-19) Cases Available online: https://ourworldindata.org/covid-cases (accessed on 12 July 2023).
209. Česká televize V Česku Jsou Tři Lidé Nakažení Koronavirem. Předtím Byli v Itálii Available online: https://ct24.ceskatelevize.cz/domaci/3056228-v-cesku-jsou-tri-lide-nakazeni-koronavirem (accessed on 12 July 2023).
210. Vláda ČR Vládní Usnesení Související s Bojem Proti Epidemii - Rok 2020 Available online: https://www.vlada.cz/cz/epidemie-koronaviru/dulezite-informace/vladni-usneseni-souvisejici-s-bojem-proti-epidemii-koronaviru-rok-2020-186999/ (accessed on 12 July 2023).
211. Komenda, M.; Jarkovský, J.; Klimeš, D.; Panoška, P.; Šanca, O.; Gregor, J.; Mužík, J.; Karolyi, M.; Májek, O.; Blaha, M.; et al. Sharing Datasets of the COVID-19 Epidemic in the Czech Republic. *PLoS One* **2022**, *17*, e0267397-.

212. COVID-19: Přehled Očkování | Onemocnění Aktuálně Od MZČR Available online: https://onemocneni-aktualne.mzcr.cz/vakcinace-cr (accessed on 22 July 2021).
213. Tuček, M.; Vaněček, V. COVID-19 in the Czech Republic 2020 and 2021: Comparative Analysis of Probable Work-Related Transmission of the Coronavirus SARS-CoV-2. *Cent Eur J Public Health* **2022**, *30*, 201–204.
214. European Commission (EC) Timeline of EU Action Available online: https://commission.europa.eu/strategy-and-policy/coronavirus-response/timeline-eu-action_en (accessed on 13 July 2023).
215. European Centre for Disease Prevention and Control (ECDC) Timeline of ECDC's Response to COVID-19 Available online: https://www.ecdc.europa.eu/en/covid-19/timeline-ecdc-response (accessed on 13 July 2023).
216. Government of the Czech Republic Measures Adopted by the Czech Government against the Coronavirus Available online: https://www.vlada.cz/en/media-centrum/aktualne/measures-adopted-by-the-czech-government-against-coronavirus-180545/ (accessed on 13 July 2023).
217. Europen Council COVID-19: The EU's Response to the Economic Fallout Available online: https://www.consilium.europa.eu/en/policies/coronavirus/covid-19-economy/ (accessed on 13 July 2023).
218. Santomauro, D.F.; Mantilla Herrera, A.M.; Shadid, J.; Zheng, P.; Ashbaugh, C.; Pigott, D.M.; Abbafati, C.; Adolph, C.; Amlag, J.O.; Aravkin, A.Y.; et al. Global Prevalence and Burden of Depressive and Anxiety Disorders in 204 Countries and Territories in 2020 Due to the COVID-19 Pandemic. *The Lancet* **2021**, *398*, 1700–1712, doi:10.1016/S0140-6736(21)02143-7.
219. Meinck, S.Ed.; Fraillon, J.Ed.; Strietholt, R.Ed. The Impact of the COVID-19 Pandemic on Education: International Evidence from the Responses to Educational Disruption Survey (REDS). *International Association for the Evaluation of Educational Achievement* **2022**, 126–150.
220. Alfred Kammer Europe's Post-Pandemic Economic Challenges Available online: https://www.imf.org/en/Blogs/Articles/2021/10/20/europes-post-pandemic-economic-challenges (accessed on 13 July 2023).
221. Maarten Verwey; Allen Monks The EU Economy after COVID-19: Implications for Economic Governance Available online: https://cepr.org/voxeu/columns/eu-economy-after-covid-19-implications-economic-governance (accessed on 13 July 2023).
222. Kneip, T.; Börsch-Supan, A.; Andersen-Ranberg, K. Social, Health and Economic Impact of the COVID-19 Pandemic from a European Perspective. *Eur J Ageing* **2022**, *19*, 789–792, doi:10.1007/s10433-022-00744-9.
223. Cook, R.; Grimshaw, D. A Gendered Lens on COVID-19 Employment and Social Policies in Europe. *European Societies* **2020**, *23*, S215–S227, doi:10.1080/14616696.2020.1822538.
224. Kovacs, V.A.; Starc, G.; Brandes, M.; Kaj, M.; Blagus, R.; Leskošek, B.; Suesse, T.; Dinya, E.; Guinhouya, B.C.; Zito, V.; et al. Physical Activity, Screen Time and the COVID-19 School Closures in Europe – An Observational Study in 10 Countries. *European Journal of Sport Science* **2021**, *22*, 1094–1103, doi:10.1080/17461391.2021.1897166.
225. Blaskó, Z.; Costa, P. da; Schnepf, S. V. Learning Losses and Educational Inequalities in Europe: Mapping the Potential Consequences of the COVID-19 Crisis. *J Eur Soc Policy* **2022**, *32*, 361–375, doi:10.1177/09589287221091687.
226. World Health Organisation (WHO) Coronavirus Disease (COVID-19): Vaccines and Vaccine Safety Available online: https://www.who.int/emergencies/diseases/novel-

coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-(covid-19)-vaccines (accessed on 14 July 2023).
227. World Health Organisation (WHO) COVID-19 Vaccine Tracker and Landscape Available online: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines (accessed on 14 July 2023).
228. Gavi the Vaccine Alliance There Are Four Types of COVID-19 Vaccines: Here's How They Work Available online: https://www.gavi.org/vaccineswork/there-are-four-types-covid-19-vaccines-heres-how-they-work (accessed on 29 July 2021).
229. European Medicines Agency (EMA) EMA Recommends First COVID-19 Vaccine for Authorisation in the EU Available online: https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu (accessed on 1 August 2021).
230. European Medicines Agency (EMA) Spikevax (Previously COVID-19 Vaccine Moderna) Available online: https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax-previously-covid-19-vaccine-moderna (accessed on 1 August 2021).
231. European Medicines Agency (EMA) Authorised COVID-19 Vaccines Available online: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#authorised-covid-19-vaccines-section (accessed on 29 July 2021).
232. Burckhardt, R.M.; Dennehy, J.J.; Poon, L.L.M.; Saif, L.J.; Enquist, L.W. Are COVID-19 Vaccine Boosters Needed? The Science behind Boosters. *J Virol* **2021**, doi:10.1128/JVI.01973-21.
233. Rzymski, P.; Camargo, C.A.; Fal, A.; Flisiak, R.; Gwenzi, W.; Kelishadi, R.; Leemans, A.; Nieto, J.J.; Ozen, A.; Perc, M.; et al. COVID-19 Vaccine Boosters: The Good, the Bad, and the Ugly. *Vaccines (Basel)* **2021**, *9*, 1299, doi:10.3390/VACCINES9111299.
234. European Medicines Agency (EMA) Comirnaty Available online: https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty (accessed on 1 August 2021).
235. World Health Organisation (WHO) Vaccine Efficacy, Effectiveness and Protection Available online: https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection (accessed on 14 July 2023).
236. Polack, F.P.; Thomas, S.J.; Kitchin, N.; Absalon, J.; Gurtman, A.; Lockhart, S.; Perez, J.L.; Pérez Marc, G.; Moreira, E.D.; Zerbini, C.; et al. Safety and Efficacy of the BNT162b2 MRNA Covid-19 Vaccine. *New England Journal of Medicine* **2020**, *383*, 2603–2615, doi:10.1056/NEJMOA2034577.
237. Baden, L.R.; El Sahly, H.M.; Essink, B.; Kotloff, K.; Frey, S.; Novak, R.; Diemert, D.; Spector, S.A.; Rouphael, N.; Creech, C.B.; et al. Efficacy and Safety of the MRNA-1273 SARS-CoV-2 Vaccine. *New England Journal of Medicine* **2021**, *384*, 403–416, doi:10.1056/NEJMOA2035389.
238. Voysey, M.; Clemens, S.A.C.; Madhi, S.A.; Weckx, L.Y.; Folegatti, P.M.; Aley, P.K.; Angus, B.; Baillie, V.L.; Barnabas, S.L.; Bhorat, Q.E.; et al. Safety and Efficacy of the ChAdOx1 NCoV-19 Vaccine (AZD1222) against SARS-CoV-2: An Interim Analysis of Four Randomised Controlled Trials in Brazil, South Africa, and the UK. *The Lancet* **2021**, *397*, 99–111, doi:10.1016/S0140-6736(20)32661-1.
239. Oliver, S.E.; Gargano, J.W.; Scobie, H.; Wallace, M.; Hadler, S.C.; Leung, J.; Blain, A.E.; McClung, N.; Campos-Outcalt, D.; Morgan, R.L.; et al. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Janssen

COVID-19 Vaccine — United States, February 2021. *MMWR Morb Mortal Wkly Rep* **2021**, *70*, 329–332, doi:10.15585/MMWR.MM7009E4.

240. Teerawattananon, Y.; Anothaisintawee, T.; Pheerapanyawaranun, C.; Botwright, S.; Akksilp, K.; Sirichumroonwit, N.; Budtarad, N.; Isaranuwatchai, W. A Systematic Review of Methodological Approaches for Evaluating Real-World Effectiveness of COVID-19 Vaccines: Advising Resource-Constrained Settings. *PLoS One* **2022**, *17*, e0261930, doi:10.1371/JOURNAL.PONE.0261930.
241. Self, W.H.; Tenforde, M.W.; Rhoads, J.P.; Gaglani, M.; Ginde, A.A.; Douin, D.J.; Olson, S.M.; Talbot, H.K.; Casey, J.D.; Mohr, N.M.; et al. Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March–August 2021. *Morbidity and Mortality Weekly Report* **2021**, *70*, 1337, doi:10.15585/MMWR.MM7038E1.
242. Wallace, M.; Collins, J.P.; Moline, H.; Plumb, I.D.; Godfrey, M.; Morgan, R.L.; Campos-Outcalt, D.; Oliver, S.E.; Dooling, K.; Gargano, J.W. Effectiveness of Pfizer-BioNTech COVID-19 Vaccine as Evidence for Policy Action: A Rapid Systematic Review and Meta-Analysis of Non-Randomized Studies. *PLoS One* **2022**, *17*, e0278624, doi:10.1371/JOURNAL.PONE.0278624.
243. Andrews, N.; Stowe, J.; Kirsebom, F.; Toffa, S.; Rickeard, T.; Gallagher, E.; Gower, C.; Kall, M.; Groves, N.; O'Connell, A.-M.; et al. Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. *New England Journal of Medicine* **2022**, *386*, 1532–1546, doi:10.1056/nejmoa2119451.
244. Link-Gelles, R.; Levy, M.E.; Natarajan, K.; Reese, S.E.; Naleway, A.L.; Grannis, S.J.; Klein, N.P.; Desilva, M.B.; Ong, T.C.; Gaglani, M.; et al. Estimation of COVID-19 MRNA Vaccine Effectiveness and COVID-19 Illness and Severity by Vaccination Status During Omicron BA.4 and BA.5 Sublineage Periods. *JAMA Netw Open* **2023**, *6*, e232598–e232598, doi:10.1001/JAMANETWORKOPEN.2023.2598.
245. European Medicines Agency (EMA) Pharmacovigilance: Overview Available online: https://www.ema.europa.eu/en/human-regulatory/overview/pharmacovigilance-overview (accessed on 14 July 2023).
246. US Food & Drug Administration (FDA) COVID-19 Vaccine Safety Surveillance Available online: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance (accessed on 14 July 2023).
247. Riad, A.; Hocková, B.; Kantorová, L.; Slávik, R.; Spurná, L.; Stebel, A.; Havriľak, M.; Klugar, M. Side Effects of MRNA-Based COVID-19 Vaccine: Nationwide Phase IV Study among Healthcare Workers in Slovakia. *Pharmaceuticals 2021, Vol. 14, Page 873* **2021**, *14*, 873, doi:10.3390/PH14090873.
248. Riad, A.; Schulz-Weidner, N.; Dziedzic, A.; Howaldt, H.-P.; Attia, S.; Školství, M.; Telovýchovy, M. Oral Side Effects of COVID-19 Vaccines in 32 European Countries: Analysis of EudraVigilance Reports. *J Med Virol* **2023**, *95*, e28771, doi:10.1002/JMV.28771.
249. Riad, A.; Põld, A.; Kateeb, E.; Attia, S. Oral Adverse Events Following COVID-19 Vaccination: Analysis of VAERS Reports. *Front Public Health* **2022**, *10*, 2230, doi:10.3389/FPUBH.2022.952781/BIBTEX.
250. Gee, J.; Marquez, P.; Su, J.; Calvert, G.M.; Liu, R.; Myers, T.; Nair, N.; Martin, S.; Clark, T.; Markowitz, L.; et al. First Month of COVID-19 Vaccine Safety Monitoring — United States, December 14, 2020–January 13, 2021. *MMWR Morb Mortal Wkly Rep* **2021**, *70*, 283–288, doi:10.15585/MMWR.MM7008E3.
251. Shimabukuro, T.T.; Cole, M.; Su, J.R. Reports of Anaphylaxis After Receipt of MRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021. *JAMA* **2021**, *325*, 1101–1102, doi:10.1001/JAMA.2021.1967.

252. Boufidou, F.; Hatziantoniou, S.; Theodoridou, K.; Maltezou, H.C.; Vasileiou, K.; Anastassopoulou, C.; Medić, S.; Tsakris, A. Anaphylactic Reactions to COVID-19 Vaccines: An Updated Assessment Based on Pharmacovigilance Data. *Vaccines (Basel)* **2023**, *11*, 613, doi:10.3390/VACCINES11030613.
253. Riad, A.; Schünemann, H.; Attia, S.; Peričić, T.P.; Žuljević, M.F.; Jürisson, M.; Kalda, R.; Lang, K.; Morankar, S.; Yesuf, E.A.; et al. COVID-19 Vaccines Safety Tracking (CoVaST): Protocol of a Multi-Center Prospective Cohort Study for Active Surveillance of COVID-19 Vaccines' Side Effects. *International Journal of Environmental Research and Public Health 2021, Vol. 18, Page 7859* **2021**, *18*, 7859, doi:10.3390/ijerph18157859.
254. Riad, A.; Pokorná, A.; Attia, S.; Klugarová, J.; Koščík, M.; Klugar, M. Prevalence of COVID-19 Vaccine Side Effects among Healthcare Workers in the Czech Republic. *J. Clin. Med* **2021**, *10*, 1428, doi:10.3390/jcm10071428.
255. Riad, A.; Pokorná, A.; Klugarová, J.; Antalová, N.; Kantorová, L.; Koščík, M.; Klugar, M. Side Effects of MRNA-Based COVID-19 Vaccines among Young Adults (18–30 Years Old): An Independent Post-Marketing Study. *Pharmaceuticals* **2021**, *14*, 1049, doi:10.3390/PH14101049.
256. Dziedzic, A.; Riad, A.; Attia, S.; Klugar, M.; Tanasiewicz, M. Self-Reported Adverse Events of COVID-19 Vaccines in Polish Healthcare Workers and Medical Students. Cross-Sectional Study and Pooled Analysis of CoVaST Project Results in Central Europe. *J Clin Med* **2021**, *10*, 5338, doi:10.3390/JCM10225338.
257. Riad, A.; Pokorná, A.; Antalová, N.; Krobot, M.; Zviadadze, N.; Serdiuk, I.; Koščík, M.; Klugar, M. Prevalence and Drivers of COVID-19 Vaccine Hesitancy among Czech University Students: National Cross-Sectional Study. *Vaccines (Basel)* **2021**, *9*, 948, doi:10.3390/VACCINES9090948.
258. Riad, A.; Jouzová, A.; Üstün, B.; Lagová, E.; Hruban, L.; Janků, P.; Pokorná, A.; Klugarová, J.; Koščík, M.; Klugar, M. COVID-19 Vaccine Acceptance of Pregnant and Lactating Women (PLW) in Czechia: An Analytical Cross-Sectional Study. *International Journal of Environmental Research and Public Health 2021, Vol. 18, Page 13373* **2021**, *18*, 13373, doi:10.3390/IJERPH182413373.
259. Klugar, M.; Riad, A.; Mohanan, L.; Pokorná, A. COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Workers in Czechia: National Cross-Sectional Study. *Vaccines (Basel)* **2021**, *9*, 1437, doi:10.3390/VACCINES9121437.
260. Riad, A.; Abdulqader, H.; Morgado, M.; Domnori, S.; Koščík, M.; Mendes, J.J.; Klugar, M.; Kateeb, E. Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy. *Vaccines (Basel)* **2021**, *9*, 566, doi:10.3390/vaccines9060566.
261. Kateeb, E.; Danadneh, M.; Pokorná, A.; Klugarová, J.; Abdulqader, H.; Klugar, M.; Riad, A. Predictors of Willingness to Receive COVID-19 Vaccine: Cross-Sectional Study of Palestinian Dental Students. *Vaccines (Basel)* **2021**, *9*, 954, doi:10.3390/VACCINES9090954.
262. Attia, S.; Mausbach, K.; Klugar, M.; Howaldt, H.-P.; Riad, A. Prevalence and Drivers of COVID-19 Vaccine Booster Hesitancy (VBH) among German University Students and Employees. *Front Public Health 0*, 706, doi:10.3389/FPUBH.2022.846861.
263. Dziedzic, A.; Issa, J.; Hussain, S.; Tanasiewicz, M.; Wojtyczka, R.; Kubina, R.; Konwinska, M.D.; Riad, A. COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Professionals and Students in Poland: Cross-Sectional Survey-Based Study. *Front Public Health* **2022**, *10*, 2391, doi:10.3389/FPUBH.2022.938067/BIBTEX.
264. Lounis, M.; Bencherit, D.; Rais, M.A.; Riad, A. COVID-19 Vaccine Booster Hesitancy (VBH) and Its Drivers in Algeria: National Cross-Sectional Survey-Based Study. *Vaccines (Basel)* **2022**, *10*, 621, doi:10.3390/VACCINES10040621.

265. Harvard Humanitarian Initiative Welcome to KoBoToolbox Available online: https://support.kobotoolbox.org/welcome.html (accessed on 4 January 2022).
266. Von Elm, E.; Altman, D.G.; Egger, M.; Pocock, S.J.; Gøtzsche, P.C.; Vandenbroucke, J.P. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. *UroToday International Journal* **2007**, *335*, 806–808, doi:10.1136/bmj.39335.541782.ad.
267. (WMA), W.M.A. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA - Journal of the American Medical Association* **2013**, *310*, 2191–2194, doi:10.1001/jama.2013.281053.
268. SPSS Inc. IBM SPSS Statistics 28 Available online: https://www.ibm.com/support/pages/ibm-spss-statistics-28-documentation (accessed on 7 January 2023).
269. The jamovi project. Jamovi (Version 2.3) [Computer Software] Available online: https://www.jamovi.org (accessed on 7 January 2023).
270. Organisation for Economic Cooperation and Development (OECD) Advancing Patient Safety Governance in the COVID-19 Response Available online: https://www.oecd-ilibrary.org/social-issues-migration-health/advancing-patient-safety-governance-in-the-covid-19-response_9b4a9484-en (accessed on 16 July 2023).
271. Chlíbek, R.; Stříž, I.; Dlouhý, P.; Pazdiora, P. Doporučení k Přeočkování a Aplikaci Dodatečných (Třetích) Dávek Vakcíny Proti Onemocnění Covid-19. *Vakcinologie* **2021**, *15*, 73–75.
272. Starke, K.R.; Reissig, D.; Petereit-Haack, G.; Schmauder, S.; Nienhaus, A.; Seidler, A. The Isolated Effect of Age on the Risk of COVID-19 Severe Outcomes: A Systematic Review with Meta-Analysis. *BMJ Glob Health* **2021**, *6*, e006434, doi:10.1136/BMJGH-2021-006434.
273. Organization, P.A.H. Introducing COVID-19 Vaccination: Guidance for Determining Priority Groups and Microplanning. Version 1, 18 January 2021. **2021**.
274. De Bruin, W.B. Age Differences in COVID-19 Risk Perceptions and Mental Health: Evidence From a National U.S. Survey Conducted in March 2020. *The Journals of Gerontology: Series B* **2021**, *76*, e24–e29, doi:10.1093/GERONB/GBAA074.
275. Lu, P.; Kong, D.; Shelley, M. Risk Perception, Preventive Behavior, and Medical Care Avoidance among American Older Adults During the COVID-19 Pandemic. *J Aging Health* **2021**, *33*, 577–584, doi:10.1177/08982643211002084.
276. Rosi, A.; van Vugt, F.T.; Lecce, S.; Ceccato, I.; Vallarino, M.; Rapisarda, F.; Vecchi, T.; Cavallini, E. Risk Perception in a Real-World Situation (COVID-19): How It Changes From 18 to 87 Years Old. *Front Psychol* **2021**, *12*, 646558, doi:10.3389/fpsyg.2021.646558.
277. European Centre for Disease Prevention and Control (ECDC) COVID-19 Vaccine Tracker Available online: https://vaccinetracker.ecdc.europa.eu/public/extensions/COVID-19/vaccine-tracker.html#uptake-tab (accessed on 23 October 2022).
278. Erega, B.B.; Ferede, W.Y.; Sisay, F.A.; Tiruneh, G.A.; Ayalew, A.B.; Malka, E. shigign; Tassew, H.A.; Alemu, A. COVID-19 Vaccine Hesitancy in Ethiopia in 2021: A Multicenter Cross-Sectional Study. *IJID Regions* **2023**, *6*, 120, doi:10.1016/J.IJREGI.2022.11.006.
279. Al-Ghabeesh, S.H.; Al-Awayssa, R.M.; Rayan, A.H.; Assaf, E.A. Perceived Occupational Stressors and the General Health of Critical Care Nurses During COVID-19 Pandemic. *SAGE Open Nurs* **2022**, *8*, doi:10.1177/23779608221134770.

280. Abu-Snieneh, H.M. Psychological Factors Associated with the Spread of Coronavirus Disease 2019 (COVID-19) among Nurses Working in Health Sectors in Saudi Arabia. *Perspect Psychiatr Care* **2021**, *57*, 1399–1408, doi:10.1111/PPC.12705.
281. Kwok, K.O.; Li, K.K.; WEI, W.I.; Tang, A.; Wong, S.Y.S.; Lee, S.S. Influenza Vaccine Uptake, COVID-19 Vaccination Intention and Vaccine Hesitancy among Nurses: A Survey. *Int J Nurs Stud* **2021**, *114*, 103854, doi:10.1016/J.IJNURSTU.2020.103854.
282. Barello, S.; Palamenghi, L.; Graffigna, G. Looking inside the 'Black Box' of Vaccine Hesitancy: Unlocking the Effect of Psychological Attitudes and Beliefs on COVID-19 Vaccine Acceptance and Implications for Public Health Communication. *Psychol Med* **2023**, *53*, 1120–1121, doi:10.1017/S003329172100101X.
283. Rancher, C.; Moreland, A.D.; Smith, D.W.; Cornelison, V.; Schmidt, M.G.; Boyle, J.; Dayton, J.; Kilpatrick, D.G. Using the 5C Model to Understand COVID-19 Vaccine Hesitancy across a National and South Carolina Sample. *J Psychiatr Res* **2023**, *160*, 180–186, doi:10.1016/j.jpsychires.2023.02.018.
284. Fleming, P.J.; Agnew-Brune, C. Current Trends in the Study of Gender Norms and Health Behaviors. *Curr Opin Psychol* **2015**, *5*, 72–77, doi:10.1016/J.COPSYC.2015.05.001.
285. Green, M.S.; Abdullah, R.; Vered, S.; Nitzan, D. A Study of Ethnic, Gender and Educational Differences in Attitudes toward COVID-19 Vaccines in Israel – Implications for Vaccination Implementation Policies. *Isr J Health Policy Res* **2021**, *10*, 1–12, doi:10.1186/s13584-021-00458-w.
286. Horiuchi, S.; Sakamoto, H.; Abe, S.K.; Shinohara, R.; Kushima, M.; Otawa, S.; Yui, H.; Akiyama, Y.; Ooka, T.; Kojima, R.; et al. Factors of Parental COVID-19 Vaccine Hesitancy: A Cross Sectional Study in Japan. *PLoS One* **2021**, *16*, e0261121, doi:10.1371/JOURNAL.PONE.0261121.
287. Wang, Q.; Hu, S.; Du, F.; Zang, S.; Xing, Y.; Qu, Z.; Zhang, X.; Lin, L.; Hou, Z. Mapping Global Acceptance and Uptake of COVID-19 Vaccination: A Systematic Review and Meta-Analysis. *Communications Medicine 2022 2:1* **2022**, *2*, 1–10, doi:10.1038/s43856-022-00177-6.
288. Yasmin, F.; Najeeb, H.; Moeed, A.; Naeem, U.; Asghar, M.S.; Chughtai, N.U.; Yousaf, Z.; Seboka, B.T.; Ullah, I.; Lin, C.Y.; et al. COVID-19 Vaccine Hesitancy in the United States: A Systematic Review. *Front Public Health* **2021**, *9*, 770985, doi:10.3389/FPUBH.2021.770985/BIBTEX.
289. Noushad, M.; Rastam, S.; Nassani, M.Z.; Al-Saqqaf, I.S.; Hussain, M.; Yaroko, A.A.; Arshad, M.; Kirfi, A.M.; Koppolu, P.; Niazi, F.H.; et al. A Global Survey of COVID-19 Vaccine Acceptance Among Healthcare Workers. *Front Public Health* **2022**, *9*, 794673, doi:10.3389/fpubh.2021.794673.
290. Bono, S.A.; Villela, E.F. de M.; Siau, C.S.; Chen, W.S.; Pengpid, S.; Hasan, M.T.; Sessou, P.; Ditekemena, J.D.; Amodan, B.O.; Hosseinipour, M.C.; et al. Factors Affecting COVID-19 Vaccine Acceptance: An International Survey among Low- and Middle-Income Countries. *Vaccines (Basel)* **2021**, *9*, 515, doi:10.3390/VACCINES9050515.
291. Toshkov, D. Explaining the Gender Gap in COVID-19 Vaccination Attitudes. *Eur J Public Health* **2023**, *33*, 490–495, doi:10.1093/EURPUB/CKAD052.
292. Morales, D.X.; Beltran, T.F.; Morales, S.A. Gender, Socioeconomic Status, and COVID-19 Vaccine Hesitancy in the US: An Intersectionality Approach. *Sociol Health Illn* **2022**, *44*, 953–971, doi:10.1111/1467-9566.13474.
293. Centers for Disease Control and Prevention (CDC) COVID-19 Vaccination Age and Sex Trends in the United States, National and Jurisdictional Available online:

https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-Age-and-Sex-Trends-in-the-Uni/5i5k-6cmh/data (accessed on 20 July 2023).
294. Garg, I.; Hanif, H.; Javed, N.; Abbas, R.; Mirza, S.; Javaid, M.A.; Pal, S.; Shekhar, R.; Sheikh, A.B. COVID-19 Vaccine Hesitancy in the LGBTQ+ Population: A Systematic Review. *Infect Dis Rep* **2021**, *13*, 872–887, doi:10.3390/IDR13040079.
295. Balaji, J.N.; Prakash, S.; Joshi, A.; Surapaneni, K.M. A Scoping Review on COVID-19 Vaccine Hesitancy among the Lesbian, Gay, Bisexual, Transgender, Queer, Intersex and Asexual (LGBTQIA+) Community and Factors Fostering Its Refusal. *Healthcare* **2023**, *11*, 245, doi:10.3390/healthcare11020245.
296. Low, A.; Wright, C.; Platt, J.; Chang, C.; Mantell, J.E.; Romero, E.; Hoos, D.; Mannheimer, S.; Greenleaf, A.; Castor, D.; et al. COVID-19 Vaccine Uptake and Factors Associated With Being Unvaccinated Among Lesbian, Gay, Bisexual, Transgender, Queer, and Other Sexual Identities (LGBTQ+) New Yorkers. *Open Forum Infect Dis* **2022**, *9*, doi:10.1093/OFID/OFAC260.
297. Holt, M.; MacGibbon, J.; Bavinton, B.; Broady, T.; Clackett, S.; Ellard, J.; Kolstee, J.; Molyneux, A.; Murphy, D.; Power, C.; et al. COVID-19 Vaccination Uptake and Hesitancy in a National Sample of Australian Gay and Bisexual Men. *AIDS Behav* **2022**, *26*, 2531–2538, doi:10.1007/S10461-022-03603-X.
298. Azarpanah, H.; Farhadloo, M.; Vahidov, R.; Pilote, L. Vaccine Hesitancy: Evidence from an Adverse Events Following Immunization Database, and the Role of Cognitive Biases. *BMC Public Health* **2021**, *21*, 1–13, doi:10.1186/S12889-021-11745-1/FIGURES/2.
299. Soares, P.; Rocha, J.V.; Moniz, M.; Gama, A.; Laires, P.A.; Pedro, A.R.; Dias, S.; Leite, A.; Nunes, C. Factors Associated with COVID-19 Vaccine Hesitancy. *Vaccines (Basel)* **2021**, *9*, 300, doi:10.3390/vaccines9030300.
300. Reno, C.; Maietti, E.; Fantini, M.P.; Savoia, E.; Manzoli, L.; Montalti, M.; Gori, D. Enhancing COVID-19 Vaccines Acceptance: Results from a Survey on Vaccine Hesitancy in Northern Italy. *Vaccines (Basel)* **2021**, *9*, 378, doi:10.3390/vaccines9040378.
301. Leigh, J.P.; Moss, S.J.; White, T.M.; Picchio, C.A.; Rabin, K.H.; Ratzan, S.C.; Wyka, K.; El-Mohandes, A.; Lazarus, J. V. Factors Affecting COVID-19 Vaccine Hesitancy among Healthcare Providers in 23 Countries. *Vaccine* **2022**, *40*, 4081–4089, doi:10.1016/j.vaccine.2022.04.097.
302. Solís Arce, J.S.; Warren, S.S.; Meriggi, N.F.; Scacco, A.; McMurry, N.; Voors, M.; Syunyaev, G.; Malik, A.A.; Aboutajdine, S.; Adeojo, O.; et al. COVID-19 Vaccine Acceptance and Hesitancy in Low- and Middle-Income Countries. **2021**, *27*, 1385–1394, doi:10.1038/s41591-021-01454-y.
303. Zhao, S.; Hu, S.; Zhou, X.; Song, S.; Wang, Q.; Zheng, H.; Zhang, Y.; Hou, Z. The Prevalence, Features, Influencing Factors, and Solutions for COVID-19 Vaccine Misinformation: Systematic Review. *JMIR Public Health Surveill* **2023**, *9*, e40201, doi:10.2196/40201.
304. Schwarzinger, M.; Watson, V.; Arwidson, P.; Alla, F.; Luchini, S. COVID-19 Vaccine Hesitancy in a Representative Working-Age Population in France: A Survey Experiment Based on Vaccine Characteristics. *Lancet Public Health* **2021**, *6*, e210–e221, doi:https://doi.org/10.1016/S2468-2667(21)00012-8.
305. Shih, S.F.; Wagner, A.L.; Masters, N.B.; Prosser, L.A.; Lu, Y.; Zikmund-Fisher, B.J. Vaccine Hesitancy and Rejection of a Vaccine for the Novel Coronavirus in the United States. *Front Immunol* **2021**, *12*, 558270, doi:10.3389/fimmu.2021.558270.
306. Rosiello, D.F.; Anwar, S.; Yufika, A.; Adam, R.Y.; Ismaeil, M.IH.; Ismail, A.Y.; Dahman, N.BH.; Hafsi, M.; Ferjani, M.; Sami, F.S.; et al. Acceptance of COVID-19

Vaccination at Different Hypothetical Efficacy and Safety Levels in Ten Countries in Asia, Africa, and South America. *Narra J* **2021**, *1*, doi:10.52225/narra.v1I3.55.

307. Lazarus, J. V.; Wyka, K.; White, T.M.; Picchio, C.A.; Rabin, K.; Ratzan, S.C.; Parsons Leigh, J.; Hu, J.; El-Mohandes, A. Revisiting COVID-19 Vaccine Hesitancy around the World Using Data from 23 Countries in 2021. *Nat Commun* **2022**, *13*, 1–14, doi:10.1038/s41467-022-31441-x.
308. Khatatbeh, M.; Albalas, S.; Khatatbeh, H.; Momani, W.; Melhem, O.; Al Omari, O.; Tarhini, Z.; A'aqoulah, A.; Al-Jubouri, M.; Nashwan, A.J.; et al. Children's Rates of COVID-19 Vaccination as Reported by Parents, Vaccine Hesitancy, and Determinants of COVID-19 Vaccine Uptake among Children: A Multi-Country Study from the Eastern Mediterranean Region. *BMC Public Health* **2022**, *22*, 1–11, doi:10.1186/s12889-022-13798-2.
309. Marzo, R.R.; Sami, W.; Alam, M.Z.; Acharya, S.; Jermsittiparsert, K.; Songwathana, K.; Pham, N.T.; Respati, T.; Faller, E.M.; Baldonado, A.M.; et al. Hesitancy in COVID-19 Vaccine Uptake and Its Associated Factors among the General Adult Population: A Cross-Sectional Study in Six Southeast Asian Countries. *Trop Med Health* **2022**, *50*, 1–10, doi:10.1186/s41182-021-00393-1.
310. Gostin, L.O.; Salmon, D.A.; Larson, H.J. Mandating COVID-19 Vaccines. *JAMA* **2021**, *325*, 532–533, doi:10.1001/jama.2020.26553.
311. Klompas, M.; Pearson, M.; Morris, C. The Case for Mandating COVID-19 Vaccines for Health Care Workers. *Ann Intern Med* **2021**, *174*, 1305–1307, doi:10.7326/M21-2366.
312. Mayan, D.; Nguyen, K.; Keisler, B. National Attitudes of Medical Students towards Mandating the COVID-19 Vaccine and Its Association with Knowledge of the Vaccine. *PLoS One* **2021**, *16*, e0260898, doi:10.1371/journal.pone.0260898.
313. Smith, D.T.; Attwell, K.; Evers, U. Support for a COVID-19 Vaccine Mandate in the Face of Safety Concerns and Political Affiliations: An Australian Study. *Politics* **2021**, *42*, 480–491, doi:10.1177/02633957211009066.
314. Lazarus, J. V.; Wyka, K.; White, T.M.; Picchio, C.A.; Gostin, L.O.; Larson, H.J.; Rabin, K.; Ratzan, S.C.; Kamarulzaman, A.; El-Mohandes, A. A Survey of COVID-19 Vaccine Acceptance across 23 Countries in 2022. *Nat Med* **2023**, *29*, 366–375, doi:10.1038/s41591-022-02185-4.
315. Shah, A.; Coiado, O.C. COVID-19 Vaccine and Booster Hesitation around the World: A Literature Review. *Front Med (Lausanne)* **2023**, *9*, 1054557, doi:10.3389/fmed.2022.1054557.
316. Peterson, C.J.; Lee, B.; Nugent, K. COVID-19 Vaccination Hesitancy among Healthcare Workers—A Review. *Vaccines (Basel)* **2022**, *10*, 948, doi:10.3390/VACCINES10060948.
317. Šimánek, V.; Pecen, L.; Řezáčková, H.; Topolčan, O.; Fajfrlík, K.; Sedláček, D.; Šín, R.; Bludovská, M.; Pazdiora, P.; Slouka, D.; et al. Long-Term Monitoring of the Antibody Response to a Sars-Cov-2 Infection. *Diagnostics* **2021**, *11*, 1915, doi:10.3390/DIAGNOSTICS11101915/S1.