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Editorial: First Full Regulatory Approval of a COVID-19 Vaccine, the BNT162b2 Pfizer-BioNTech Vaccine, and the Real-World Implications for Public Health Policy

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Abstract

In the past 18 months, accelerated vaccine development to prevent or reduce the severity of coronavirus disease 2019 (COVID-19) has resulted in rapid global emergency regulatory approvals, including the US Food and Drug Administration (FDA) emergency use authorization (EUA) approvals. On August 23, 2021, the US FDA gave the first full regulatory approval for a COVID-19 vaccine and approved the Pfizer-BioNTech COVID-19 vaccine (Comirnaty) for individuals 16 years and older. In the US, there is a continued EUA for individuals aged 12-15 years of age. Also, the EUA includes the administration of a third or booster dose in immunocompromised individuals at increased risk for severe COVID-19. This Editorial aims to present an update on the first COVID-19 vaccine to receive full regulatory approval, the Pfizer-BioNTech vaccine, and the implications for real-world public health during the global COVID-19 pandemic and increasing concerns for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern.

Keywords:

Editorial • COVID-19 • Severe Acute Respiratory Syndrome Coronavirus 2 • COVID-19 Vaccine

In the past 18 months, accelerated vaccine development to prevent or reduce the severity of coronavirus disease 2019 (COVID-19) has resulted in rapid global emergency regulatory approvals, including the US Food and Drug Administration (FDA) emergency use authorization (EUA) approvals [1]. There are now several mRNA vaccines to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which were the first to undergo FDA EUA [1]. Now, ahead of the field is the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, which contains single-stranded mRNA produced by in vitro transcription from a DNA template encodes the viral spike protein (S protein) [2]. The Pfizer-BioNTech COVID-19 vaccine, BNT162b2, is marketed under the brand name Comirnaty, which is derived from the words COVID, immunity, mRNA, and community [3].

Since December 11, 2020, the Pfizer-BioNTech COVID-19 vaccine has been administered to individuals 16 years of age and older under an FDA EUA [4]. On May 10, 2021, an expanded authorization included children aged 12-15 years of age [5]. In Europe, the vaccine received conditional marketing authorization from the European Medicines Agency (EMA) and is currently also under additional monitoring by the EMA [6]. In the UK, the Medicines and Healthcare Products Regulatory Agency (MHRA) emergency use approval of Pfizer and BioNTech's Covid-19 vaccine, Comirnaty, has recently been expanded to include children between 12-15 years of age [7].

On August 23, 2021, the US FDA gave the first full regulatory approval for a COVID-19 vaccine and approved the Pfizer-BioNTech COVID-19 vaccine (Comirnaty) for individuals 16 years and older [8]. In the US, there is a continued EUA for individuals aged 12-15 years of age [8]. Also, the EUA includes the administration of a third or booster dose in immunocompromised individuals at increased risk for severe COVID-19 [8]. This full authorization was approved following the submission of a comprehensive data package from Pfizer and BioNTech that included additional long-term follow-up data on the safety and efficacy of the vaccine from a key phase 3 trial [2,9]. Full regulatory approval for a vaccine to SARS-CoV-2 may have implications for public health and vaccine uptake at a time of uncertainty regarding the safety and efficacy of new vaccines that have undergone rapid development and clinical evaluation [8,10].

Vaccine hesitancy, or the reluctance to attend COVID-19 vaccination programs, when available, is a public health concern at this time [10]. Studies on vaccine hesitancy in healthcare professionals and support staff have identified a lack of knowledge about the benefits of the vaccines in reducing hospitalization and mortality from SARS-CoV-2 infection [10]. The accelerated development of COVID-19 vaccines has resulted in vaccine safety concerns, particularly when these vaccines await full authorization [10,11]. As shown by full regulatory approvals,

public health education and information to provide reassurance on vaccine safety may reduce vaccine hesitancy [11].

In advance of the recent full regulatory approval of the Pfizer-BioNTech COVID-19 vaccine, some real-world studies have shown the efficacy of this vaccine in populations where vaccine compliance has been high [12-14]. In April 2021, Fabiani and colleagues published real-world data on the effectiveness of the Pfizer-BioNTech COVID-19 vaccine in a study of 6,423 healthcare workers in the Treviso Province, Italy [12]. This study showed that at between 14-21 days from the first vaccine dose and at least seven days from the second vaccine dose, the effectiveness in preventing SARS-CoV-2 infection was 84% and 95%, respectively [12].

In May 2021, Lopez-Bernal et al. reported the findings from a real-world study on the effectiveness of the Pfizer-BioNTech BNT162b2 vaccine and Oxford-AstraZeneca ChAdOx1-S vaccine in confirmed cases of SARS-CoV-2 infection, including the B.1.1.7 (alpha or UK) variant of concern, on hospital admissions and patient mortality [13]. This UK community-based study included 156,930 adults 70 years and older with symptoms of COVID-19 between December 2020 and February 2021 [13]. The effects of vaccination occurred between 10-13 days after vaccination, with an effectiveness of 70% [13]. At 14 days after the second dose, the Pfizer-BioNTech BNT162b2 vaccine effectiveness of the second dose of the BNT162b2 vaccine was 51-69% from 28-34 days after vaccination, which then plateaued [13]. In addition to the protection from symptomatic disease, a further 33-52% had a reduced risk of emergency hospital admission, and 37-62% had a reduced risk of death following the Pfizer-BioNTech BNT162b2 vaccine [13]. Combined with the effect against symptomatic COVID-19, a single dose of either vaccine was 80% effective at preventing admission to hospital, and a single dose of the Pfizer-BioNTech BNT162b2 vaccine was 85% effective at preventing death from COVID-19 [13]. The authors from this real-world study concluded that vaccination with either one dose of the Pfizer-BioNTech BNT162b2 vaccine or ChAdOx1-S was associated with a reduction in symptomatic COVID-19 in older adult individuals [13]. Also, a second dose of the Pfizer-BioNTech BNT162b2 vaccine was associated with further protection against symptomatic disease, including the B.1.1.7 (alpha, or UK Kent) variant of SARS-CoV-2 [13].

Angel et al. published the findings from a real-world retrospective cohort study on the effectiveness of the Pfizer-BioNTech COVID-19 vaccine in healthcare workers based in Tel Aviv, Israel [14]. Symptomatic and asymptomatic SARS-CoV-2 infections were identified by regular screening between December 2020 and February 2021 [14]. From a total of 6,710 healthcare workers who were followed up for a median period of 63 days, 5,953 received at least one dose of the Pfizer-BioNTech COVID-19 vaccine, 5,517 (82.2%) received two doses, and

757 (11.3%) had not been vaccinated [14]. Vaccination compliance was associated with older age and male gender [14]. Symptomatic SARS-CoV-2 infection occurred in 8 fully vaccinated healthcare workers and 38 unvaccinated health care workers, with an incidence rate of 4.7 per 100,000 person-days compared with 149.8 per 100,000 person-days, respectively [14]. Symptomatic SARS-CoV-2 infection occurred in 19 fully vaccinated healthcare workers and 17 unvaccinated healthcare workers [14]. These findings supported that vaccination significantly reduced the incidence of symptomatic and asymptomatic SARS-CoV-2 infection more than seven days after the second dose of the Pfizer-BioNTech COVID-19 vaccine [14].

Population studies in epidemiology and public health in all areas of human disease, including infectious disease, have an important role in developing public health policy and identifying therapeutic and vaccine safety concerns [15]. Goldshtein and colleagues retrospectively evaluated the safety and efficacy of the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, in a cohort of women in an extensive pregnancy registry in Israel [16]. The study included 7,530 vaccinated women and 7,530 matched unvaccinated women, with a mean age of 31.1 years (± 4.9 years), who were vaccinated with the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, between December 2020 and February 2021 and were followed up to April 2021 [16]. Pregnant women were 1:1 matched to unvaccinated pregnant women by age, gestational age, parity, primary demographics, and influenza vaccination status, 46% were in the second trimester, and 33% were in the third trimester of pregnancy [16]. Vaccination with the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, compared with no vaccination, was associated with a significantly reduced risk of SARS-CoV-2 infection, with minor adverse events that included headache (0.1%), and abdominal discomfort ($<0.1\%$), with no reported serious adverse events [16].

However, due to the rapidity of vaccine development during the COVID-19 pandemic, preapproval clinical trials that show good safety profiles may be limited by study size and lack clinical and sociodemographic variables that exist within a population [17]. At the same time as the announcement of full FDA approval for the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, data from the largest health care organization in Israel have been published from a real-world evaluation of the safety of this mRNA-based vaccine [17]. Barda and colleagues recently reported the findings from 884,828 vaccinated individuals to unvaccinated individuals matched according to clinical and sociodemographic variables [17]. Risk ratios and differences were evaluated at 42 days following vaccination [17]. A similar analysis was performed that included individuals infected with SARS-CoV-2 who were matched to uninfected individuals [17]. Vaccination with the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, was associated with an increased risk of myocarditis with 1-5 events per 100,000 population [17]. Other adverse

events included pericarditis, arrhythmia, deep vein thrombosis, pulmonary embolism, and myocardial infarction [17]. The risk of post-vaccine myocarditis and other adverse events was significantly increased following SARS-CoV-2 infection [17]. Population studies will be of increasing importance in monitoring the effectiveness of SARS-CoV-2 vaccines in response to the challenges of increasing SARS-CoV-2 variants [18].

The American Society of Health-System Pharmacists (ASHP) has recently produced guidelines to optimize mass COVID-19 vaccination rates [19]. Best practice requires that lessons are continually learned in preparedness for pandemics, management of vaccine supply chains, vaccine distribution, and clinical guidelines for population vaccination [19]. The ASHP has emphasized that the US and international collaboration is important to coordinate vaccine distribution to hundreds of millions of people as efficiently and safely as possible [19]. Of the ten principles that ASHP has developed for safe and effective

mass COVID-19 vaccination, the importance of a transparent and rigorous process for the development, approval, post-marketing surveillance, and ensuring public trust have been highlighted by the ASHP [19].

Conclusions

The first COVID-19 vaccine to receive full regulatory approval, the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, has implications for real-world public health during the global COVID-19 pandemic and increasing SARS-CoV-2 variants. As further full regulatory approvals for COVID-19 vaccines are anticipated, population studies may identify which populations benefit the most from different vaccines and may identify risk factors for adverse events. Surveillance of vaccine efficacy against emerging variants of SARS-CoV-2 will require viral genotyping to be incorporated into global post-marketing vaccine guidelines.

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