Use of COVID-19 Boosters among Health Care Providers

Subjects: Infectious Diseases

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While the World Health Organization (WHO) has de-escalated coronavirus disease 2019 (COVID-19) from a global health emergency, ongoing discussions persist as new viral variants.

health care provider COVID-19 vaccine booster

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has posed challenges to healthcare systems globally, significantly impacting public health, economies, and daily life. Although public health measures such as maskwearing, social distancing, and lockdowns have been extensively implemented to control the virus' spread, vaccination remains the primary prevention method. Vaccination campaigns have been used to achieve widespread immunity and mitigate the burden of COVID-19. The development of the initial vaccines brought hope for controlling the pandemic [1][2].

2. Current German Recommendations

On 11 January 2024, the Robert Koch Institute (RKI), responsible for managing infectious diseases in Germany, released its latest recommendations [2]. These recommendations can be summarised as follows:

- Despite Despite the transition from a pandemic level (defined as "the infection characterised by widespread international impact causing social disruption, economic loss, and general hardship") to the endemic level (defined as "the outbreak with the consistent presence of the disease limited to a specific region, and predictable spread and rates"), the epidemiological situation of COVID-19 remains strongly distributed around the population.

The objectives of the recommendations made by the RKI's Standing Committee on Vaccination (STIKO) for COVID-19 are threefold: (1) to reduce the severity of symptoms, specifically targeting reductions in hospitalisation and mortality, (2) to minimise the potential long-term complications of COVID-19, and (3) to protect healthcare providers at all levels from COVID-19.

According to the STIKO, the immunity against COVID-19 is divided into the basic and hybrid immunity (**Table 1**). Achieving "basic immunity" in all adults aged ≥18 years, including women of childbearing age and pregnant women without underlying diseases, requires two initial doses of vaccine and at least one booster dose. In this context, one infection is considered equivalent to one dose of vaccine. Therefore, the STIKO recommends that all adults with "basic immunity" should either receive the vaccine or be infected "at least three times" (i.e., three antigen [Ag] contacts); one of these three times should be vaccine immunity, e.g., two vaccinations plus one infection, or one vaccination plus two infections. The interval between a vaccination and an infection must be at least 3 months; otherwise the vaccination and the infection are counted as a single immunisation.

Table 1. The immunity types according to the German Standing Committee on Vaccination (STIKO) [2].

Basic Immunity	Hybrid Immunity
- 2 initial doses + 1 booster dose	- 2 initial doses + 1 infection - 1 initial dose + 1 infection + 1 booster dose - 1 initial dose + 2 infections - 1 infection + 1 initial dose + 1 booster dose - 1 infection + 1 initial dose + 1 infection - 2 or 3 infections + 1 booster dose

Basic Immunity	Hybrid Immunity

enhanced protection against severe symptoms. This phenomenon is attributed to a broader recognition of different Ags not included in the vaccine design by the subsequent boosting of mucosal immunity [2][3][4][5]. The (2) emergence of the Omicron variant (B.1.1.529) suggests that the spike protein of the viral entry mediated SARS-CoV-2 protection (1) individuals who have had COVID-19 [4] previously have hybrid immunity can last for at least 12 months [3]. Therefore, it is recommended that the next booster should not be administered before 12 months have passed since the last vaccination or infection.

2. The updated recommendations include the introduction of a new booster for specific population groups who received their last vaccination booster or had an infection 12 months ago or longer. The targeted groups are as follows:

   (1) Individuals aged ≥60 years;

   (2) Residents in nursing homes;

   (3) HCPs who have direct contact with patients and/or nursing home residents;

   (4) All individuals aged ≥6 months with underlying diseases, encompassing bedridden conditions, chronic obstructive lung disease (COPD), chronic cardiovascular, hepatic and renal diseases, diabetes mellitus and other metabolic diseases, obesity, chronic neurological diseases (e.g., dementia, stroke, mental retardation, psychological diseases), immunodeficiency (e.g., human immunodeficiency virus [HIV] infection, chronic inflammatory diseases under immunosuppressive therapy including post-organ transplantation), and active cancer;

   (5) Family members and individuals with direct contact with immunocompromised persons (e.g., after organ or stem cell transplantation, haemodialysis) aged ≥6 months.

These specific groups are identified based on increased vulnerability to severe outcomes from COVID-19 and the potential complications associated with their health conditions. The targeted approach aims to provide enhanced protection to those most at risk within the population.

3. The administration timing of the “yearly” booster is recommended during the autumn, aligning with statistical evidence indicating that disease waves tend to peak during the winter months. This strategic timing aims to maximise the effectiveness of the booster in preparation for the seasonal increase in COVID-19 cases. Additionally, it is suggested that, when indicated, the COVID-19 booster may be administered concurrently with the influenza or pneumococcal vaccine. This co-administration approach aims to optimise protection aims to optimise protection against both COVID-19 and influenza or pneumonia, particularly during periods of heightened respiratory pathogen activity, i.e., in the winter.

4. The choice of vaccine for the booster is recommended to be adapted to the prevalent viral variants in the region. The current variant in Germany is XBB.1.5 (as of 11.01.2024). In European Union (EU) countries, including Germany, the approved booster vaccines encompass various categories:

   - (monovalent) mRNA vaccines: Comirnaty Original and Comirnaty XBB.1.5 (BioNTech/Pfizer), Spikevax (Moderna; cautioned against use as a booster for individuals aged between 6 months and 5 years), and Spikevax XBB.1.5 (Moderna).

The use of monovalent vaccines during the Omicron wave has faced some hesitation. However, a randomised controlled trial conducted in the UK demonstrated that both Comirnaty Original and Spikevax were well tolerated. The fold change in anti-spike protein immunoglobulin (Ig) G titres from before (day 0: 1.59, 1.41–1.78; 2.19, 95% confidence interval [CI], 1.90–2.52) to after (day 14: 12.19, 95% CI, 10.37–14.32; 15.90, 12.92–19.58) the fourth dose was significantly greater than that 28 days after the third dose. Additionally, both mRNA vaccine groups showed significant increases in neutralising antibodies (nAb) and T-cell responses after the fourth dose (7.32, 95% CI, 3.24–16.54; 6.22, 95% CI, 3.90–9.92). The research also reported that Spikevax induced higher antibody (Ab) titres than Comirnaty Original after the fourth dose [6][7].

   - bivalent mRNA vaccines: Comirnaty Original/Omicron BA.4/5 and Comirnaty Original/Omicron BA.1 (BioNTech/Pfizer), Spikevax bivalent Original/Omicron BA.4/5 and Spikevax bivalent Original/Omicron BA.1 (Moderna). Notably, Moderna vaccines should be administered carefully to individuals aged < 30 years due to the risk of peri- and myocarditis.

When comparing the monovalent Moderna with the bivalent Moderna after 28 days of the fourth dose of the bivalent vaccine as a second booster, this exhibited significantly greater nAb titres against Omicron BA.1 and other variants (BA.4/5, alpha, beta, gamma, and delta), maintaining a safety and reactogenicity profile akin to that of the monovalent vaccine [7][8].

- viral vector vaccines: Vaxzevria (AstraZeneca) and JCOVDEN (Janssen Cilag International), recommended only for individuals aged ≥60 years due to the risk of thromboembolic events in younger individuals. Moreover, JCOVDEN must not be used as a booster in individuals who previously received mRNA or viral vector vaccines.

- protein-based vaccines: Nuvaxovid (only for individuals aged ≥18 years) and Novaxovid XBB 1.5 (Novavax), seemingly suitable for young individuals due to the very low risk of peri- and myocarditis. However, there are limited scientific data on the use of these vaccines in pregnant and breastfeeding women.

- inactivated whole-virus vaccine: COVID-19 vaccine Valneva (Valneva) is recommended only for individuals with contraindications to other vaccines and unsuitable for those who have already received Valneva or viral vector vaccines as part of their basic immunisation. Limited scientific data are available regarding the use of this vaccine in pregnant and breastfeeding women.

5. Pre-exposure prophylaxis (PEP) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is designed to complement vaccination and hygiene practices, not replace them. In specific cases, such as after stem cell transplantation (prior to immunological reconstitution), B-cell depletion therapies (when B-cell reconstitution is absent), CAR-T-cell therapies, severe immunosuppression (e.g., after solid organ transplantation or ongoing chemotherapy), and those with genetically-related immune defects leading to poor antiviral immunity, the use of Evusheld (AstraZeneca) may be considered. This agent comprises two monoclonal Ab, namely, tixagevimab and cilgavimab. However, it is crucial to note that the efficacy of this drug preparation is significantly reduced or non-existent against the currently circulating Omicron sublineages.

6. According to Section 22a of the German Infection Protection Law, foreign nationals residing in EU countries who have been vaccinated with vaccines not approved by the EU, such as Sinovac (Sinovac Biotech Ltd. SVA:NASDAQ GS, Beijing, China), Sinopharm (China National Pharmaceutical Group Co., Beijing, China), COVAXIN, (Bharat Biotech International Ltd., Turkapally, India), and Sputnik V (Russian Gamaleya Research Institute of Epidemiology and Microbiology), are required to repeat the EU-approved vaccination [2], even though some investigators found that the Sinopharm booster is safe and capable of rescuing immune signals and further strengthening the protective immune response by increasing nAb levels against some Omicron sublineages [7][9].

Individuals who have only received one non-EU-approved vaccine dose, including those who have received intranasal vaccines like BBV154-adenovirus-vectored vaccine (Bharat Biotech International Ltd.), are considered unimmunised and must complete the full course of EU-approved triple vaccines. For those who have received two or more non-EU-approved vaccine doses, a booster with at least one EU-approved vaccine dose is recommended. This approach aims to enhance their immunity to a level similar to individuals who have received three mRNA vaccine doses (termed as “3-dose” vaccinees). It is noteworthy that pure mRNA vaccines provide comparable protection to partial mRNA vaccines, but both offer higher protection than non-mRNA vaccines [10].

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