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Review Article

The Significance of COVID-19 Vaccine Booster Dose. A Comparative Review

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Abstract

Background: The COVID-19 epidemic affects practically every aspect of human activity**.** The pandemic effect will continue until development of proper vaccine that neutralize different emerging viral variants.

Discussion: Different studies showed an advantage for COVID-19 vaccine third "booster" dose regarding decreased infection rates, hospitalization rates, and morality rates. Furthermore, booster doses showed an enhanced neutralizing antibodies against new emerging Omicron variant. Absolute vaccine effectiveness for BioNTech/Pfizer (BNT162b2) or Moderna (mRNA-1273) booster ranged from 94 to 97 percent. Besides, the 10-fold decrease in infection rate for the boosted with BNT162b2.

Conclusion: It can be concluded that booster doses of COVID-19 vaccine showed beneficial and significant positive effects that we are in need nowadays to overcome the spread of new emerging variants, reducing infection rates, and the burden on health care facilities.

Keywords: COVID-19; Omicron; BioNTech/Pfizer Vaccine; AstraZeneca ChAdOx1

Abbreviations

COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; ACE2: Angiotensin-converting Enzyme-2; BNT162b2: BioNTech/Pfizer COVID-19 Vaccine; mRNA-1273: Moderna COVID-19 Vaccine; ChAdOx1 nCoV-19: AstraZeneca COVID-19 Vaccine; mRNA: Messenger RNA; Ad26: Johnson and Johnson COVID-19 Vaccine; NVX: NVX-CoV2373 Novavax Vaccine; VLA: VLA2001 Valneva Vaccine; CVn: CVnCoV Curevac Vaccine; ELU: ELISA laboratory Units

Introduction

The COVID-19 pandemic has an impact on nearly every component of human activity and will continue to do so until suitable vaccinations or therapies are produced. The trimeric "spike" glycoprotein on the virion surface contacts angiotensin-converting enzyme-2 (ACE2), facilitating viral entrance and commencing viral replication [1].

Following an uneventful incubation phase, the infection can result in a wide range of clinical outcomes, ranging from insignificant or moderate symptoms to severe illness that results in mortality [2].

One concern that may have an impact on vaccination effectiveness is the possibility that induced immunity will deteriorate over time and become less effective against increasingly aggressive strains. As a result, sub-strains can form as a result of genetic changes that impart functional variations in infectivity and transmissibility [3]. Furthermore, Genetic polymorphisms showed to contribute in wide variation in anesthetic responses in ICUs ventilation of severe COVID-19 cases [4].

Despite the fact that most studies results revealed that utilized immunizations offer the proper protection against severe COVID-19 illness and fatality, even when the delta (B.1.617.2) strain is widespread, observational data indicated that a continuous decrease in vaccination protection occurs after a period of time [5].

Real-world trials reveal that, despite the fact that BioNTech/Pfizer vaccine (BNT162b2) generates many times more neutralizing antibodies than AstraZeneca's ChAdOx1 nCoV-19 vaccine (ChAd), there is no difference in early protection against infection, severe illness, or mortality following vaccination with either two ChAd or BNT162b2 doses [6-8].

Boosting may be appropriate for certain people whose primary immunization did not provide adequate protection for example, individuals of low-efficacy vaccines or immune-compromised individuals. The primary immunization in this context is defined as a single-dose or a two-dose vaccination regimen [9].

Boosting vaccine dose may be necessary for community in the future. The reason for that may be attributed to the primary vaccination diminished immunity or because evolution of new variants expressing different antigens where immune responses to the original vaccine antigens no longer provide adequately protection against currently new muted circulating virus [10].

Recent surveillance has shown the appearance of the Omicron variant, which has different spike protein mutations that reaches up to 36 mutations, which is the target of neutralizing antibodies. This will give the new Omicron variant the probability to escape vaccine-induced immunity [11].

Although the advantages of initial COVID-19 immunization obviously outweigh the risks, there may be potential dangers if booster doses are widely used too quickly or too frequently, especially with vaccinations that might produce immune mediated adverse effects (such as myocarditis, which is more common after the second dose of some mRNA vaccines) [12].

Discussion

A clinical study investigated the immunogenic and reactogenic effect of seven brands of COVID-19 vaccines administered as a third dose following two vaccination doses of AstraZeneca ChAdOx1 nCov-19 (ChAd) or Pfizer/BioNtech (BNT162b2). Participants age were above 30 years, and at least 70 days' post two doses of ChAd or 84 days following two doses of BNT162B2 main vaccination course. There is no proven infection history of SARS-CoV-2 among the participating individuals. The findings revealed that three vaccinations had an overall higher reactogenicity. These three vaccines are Moderna vaccine (mRNA1273) boost following two ChAd doses or two BNT162B2 doses, ChAd and Johnson and Johnson vaccine (Ad26) boost following two doses of BNT162B2. The most prevalent local and systemic adverse effects were fatigue and pain, which were more common in persons aged 30-69 years than in those aged 70 years or more. All vaccinations in the trial increased antibody and neutralizing responses following two doses of ChAd and all but one following two BNT162B2 doses, with no safety issues [13].

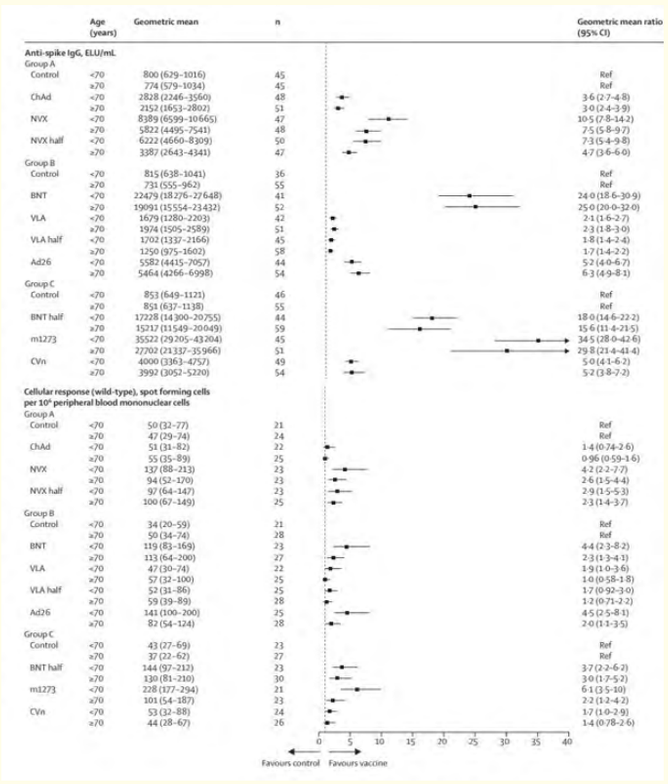
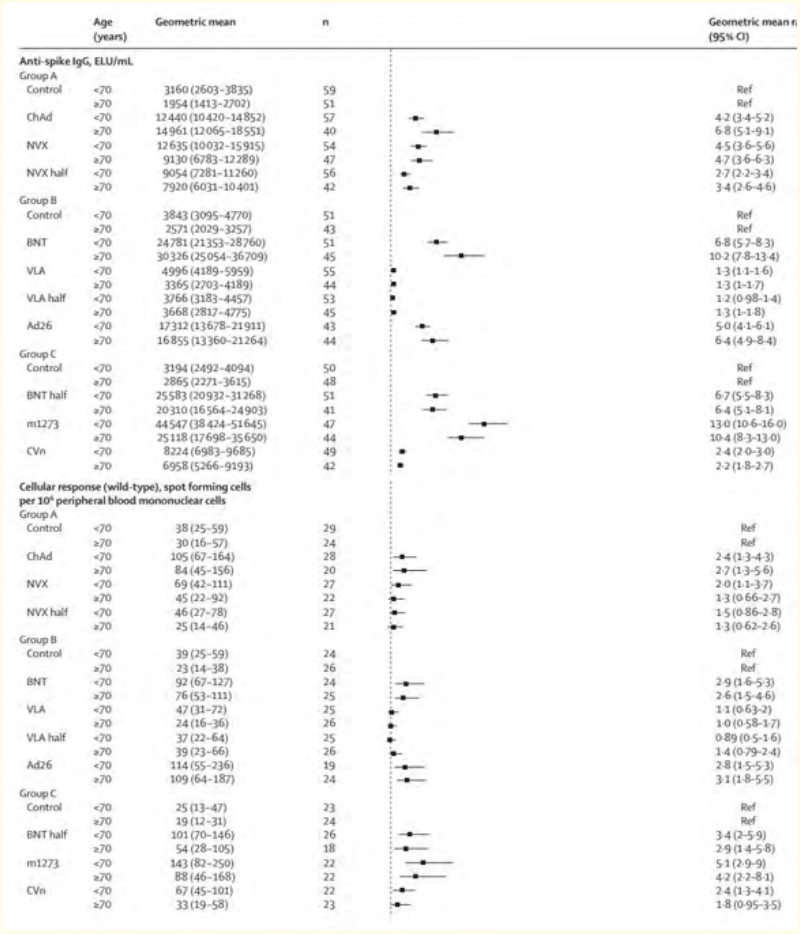


Figure 1: Subgroup immunogenicity analyses by age for anti-spike IgG and cellular response at 28 days post third dose between study vaccines and controls for the ChAd/ChAd-primed population (A) [13].



	Age (years)	Geometric mean	n	Geometric mean r (95% CI)
Anti-spike IgG, ELU/mL				
Group A				
Control	<70	3160 (2603–3835)	59	Ref
	≥70	1954 (1413–2702)	51	Ref
ChAd	<70	12440 (10420–14852)	57	4·2 (3·4–5·2)
	≥70	14961 (12065–18551)	40	6·8 (5·1–9·1)
NVX	<70	12635 (10032–15915)	54	4·5 (3·6–5·6)
	≥70	9130 (6783–12289)	47	4·7 (3·6–6·3)
NVX half	<70	9054 (7281–11260)	56	2·7 (2·2–3·4)
	≥70	7920 (6031–10401)	42	3·4 (2·6–4·6)
Group B				
Control	<70	3843 (3095–4770)	51	Ref
	≥70	2571 (2029–3257)	43	Ref
BNT	<70	24781 (21353–28760)	51	6·8 (5·7–8·3)
	≥70	30326 (25054–36709)	45	10·2 (7·8–13·4)
VLA	<70	4996 (4189–5959)	55	1·3 (1·1–1·6)
	≥70	3365 (2703–4189)	44	1·3 (1–1·7)
VLA half	<70	3766 (3183–4457)	53	1·2 (0·98–1·4)
	≥70	3668 (2817–4775)	45	1·3 (1–1·8)
Ad26	<70	17312 (13678–21911)	43	5·0 (4·1–6·1)
	≥70	16855 (13360–21264)	44	6·4 (4·9–8·4)
Group C				
Control	<70	3194 (2492–4094)	50	Ref
	≥70	2865 (2271–3615)	48	Ref
BNT half	<70	25583 (20932–31268)	51	6·7 (5·5–8·3)
	≥70	20310 (16564–24903)	41	6·4 (5·1–8·1)
m1273	<70	44547 (38424–51645)	47	13·0 (10·6–16·0)
	≥70	25118 (17698–35650)	44	10·4 (8·3–13·0)
CVn	<70	8224 (6983–9685)	49	2·4 (2·0–3·0)
	≥70	6958 (5266–9193)	42	2·2 (1·8–2·7)
Cellular response (wild-type), spot forming cells per 10^6 peripheral blood mononuclear cells				
Group A				
Control	<70	38 (25–59)	29	Ref
	≥70	30 (16–57)	24	Ref
ChAd	<70	105 (67–164)	28	2·4 (1·3–4·3)
	≥70	84 (45–156)	20	2·7 (1·3–5·6)
NVX	<70	69 (42–111)	27	2·0 (1·1–3·7)
	≥70	45 (22–92)	22	1·3 (0·66–2·7)
NVX half	<70	46 (27–78)	27	1·5 (0·86–2·8)
	≥70	25 (14–46)	21	1·3 (0·62–2·6)
Group B				
Control	<70	39 (25–59)	24	Ref
	≥70	23 (14–38)	26	Ref
BNT	<70	92 (67–127)	24	2·9 (1·6–5·3)
	≥70	76 (53–111)	25	2·6 (1·5–4·6)
VLA	<70	47 (31–72)	25	1·1 (0·63–2)
	≥70	24 (16–36)	26	1·0 (0·58–1·7)
VLA half	<70	37 (22–64)	25	0·89 (0·5–1·6)
	≥70	39 (23–66)	26	1·4 (0·79–2·4)
Ad26	<70	114 (55–236)	19	2·8 (1·5–5·3)
	≥70	109 (64–187)	24	3·1 (1·8–5·5)
Group C				
Control	<70	25 (13–47)	23	Ref
	≥70	19 (12–31)	24	Ref
BNT half	<70	101 (70–146)	26	3·4 (2·5·9)
	≥70	54 (28–105)	18	2·9 (1·4–5·8)
m1273	<70	143 (82–250)	22	5·1 (2·9–9)
	≥70	88 (46–168)	22	4·2 (2·2–8·1)
CVn	<70	67 (45–101)	22	2·4 (1·3–4·1)
	≥70	33 (19–58)	23	1·8 (0·95–3·5)

Figure 2: Subgroup immunogenicity analyses by age for anti-spike IgG and cellular response at 28 days post third dose between study vaccines and controls for the BNT/BNT-primed population (B) [13].

Another clinical trial in England used a test-negative case-control design to evaluate the relative efficacy of Pfizer/BioNTech (BNT162B2) booster dose against merely primary vaccination course (2-doses) at a 175 days' minimum period after the second dose. The relative effectiveness of BNT162B2 or mRNA-1273 booster against symptomatic disease 14 to 34 days after ChAd and BNT162B2 primary vaccination course varied from 85 to 95 percent. Absolute vaccine effectiveness ranged from 94 to 97 percent and was consistent across all age groups. There was a very little decline in antibodies after 10 weeks of the booster dose. Regarding hospitalization and mortality, the absolute effectiveness of BNT162B2 booster varied from roughly 97 to 99 percent in all age categories regardless of the primary vaccination course with no signs of decreasing antibodies up to 10 weeks [14].

A clinical trial was conducted to highlight the importance of boosting vaccination against emerging new viral variants. Serum neutralization potency against wild-type, Delta, and Omicron SARS-CoV-2 pseudo viruses was assessed in 88 mRNA-1273 vaccinated, 111 BNT162B2 vaccinated, and 40 Ad26 vaccinated people. The trial included individuals that received their primary vaccination series (less than 3 months), (6 to 12 months), or an additional "booster" dose. The results showed that Omicron variant neutralization was significantly undetectable in most primary vaccination series. Individuals boosted with mRNA vaccinations, displayed considerable Omicron neutralization that was lower than the wild type by only 4 to 6 fold. Furthermore, the results indicated that the Omicron pseudo-virus is more infective than the other variants types studied [11].

An investigation was conducted to determine the efficacy of the third dose of BNT162B2 vaccination in avoiding severe COVID-19 results. The evaluation included 1,158,269 individuals that were eligible for the third boosting dose. The median participants age was 52 years and 51 percent of them were females. The median follow-up time was 13 days in both boosted and control groups. Effectiveness of the vaccine was evaluated at a minimum 7 days after the third booster vaccine dose compared with those individuals with the (two vaccine doses regimen) received at a minimum 5 months ago. The booster effectiveness was estimated to be 93 percent for hospital admission (231 events for the two doses regimen against 29 events for the three doses), 92 percent for severe disease (157 versus 17 events), and 81 percent for disease related death (44 versus 7 events) [15].

In a primary analysis, the rates of COVID-19 infection, severe illness, and death among individuals received BNT162b2 vaccine booster dose of 12 days earlier at minimum were compared against the rates in individuals that had not received a booster vaccine dose. The analysis results showed that the rate of infection was approximately 10 fold lower in the boosted individuals than in the non-boosted ones. Furthermore, the infection rate was ranged from 4.9 to 10.8 fold lower in the boosted individuals than in the early post boosted ones [16].

The clinical trial comprised 1928 health workers, with 1650 (85.6 percent) receiving a booster dosage throughout the course of the study. The overall follow-up time (median data) was 39 days, while for boosted individuals, commencing seven days or more after receiving the booster immunization, was 26 days. The results revealed that 44 people tested positive for SARS-CoV-2, including 31 people who exhibited COVID-19 symptoms during the follow-up period. SARS-CoV-2 incidence was 116 per 100000 person-days before to booster immunization and 12.8 per 100000 following booster vaccination, representing a 93 percent relative decrease. The booster vaccination doses lowered the risk of both symptomatic and asymptomatic illness equally [17].

Generally speaking, vulnerable persons should be mass vaccinated first to acquire immunity as fast as we can. By this way we can bring COVID-19 spreading under control and reduce the load on health-care sites [18]. Besides, this will reduce the development of new viral variants.

Conclusion

It may be concluded that booster doses of COVID-19 vaccine demonstrated favourable and considerable positive benefits that are required today to combat the spread of new developing viral variants like Omicron, reduce infection rates, disease severity, mortality rates, and reduce the burden on health care facilities.

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