



# Efficacy of COVID-19 vaccine booster doses in older people

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## Key summary points

**Aim** COVID-19 vaccine efficacy is high in older people, but declines after 4–6 months.

**Findings** Booster doses are effective for restoring COVID-19 vaccine efficacy in older people.

**Message** COVID-19 vaccine boosters generate higher protection than primary vaccination.

## Abstract

**Purpose** We provide here an updated analysis on efficacy of COVID-19 vaccine booster doses in older people (i.e., aged  $\geq 80$  years) based on ongoing Italian nationwide COVID-19 vaccination campaign.

**Methods** Data were obtained from the COVID-19 national integrated surveillance program, made available and regularly updated by the Italian National Institute of Health.

**Results** Compared to those who completed the COVID-19 vaccination cycle for  $\geq 5$  months ( $n = 2,385,897$ ), those receiving booster doses ( $n = 1,549,747$ ) had 75% lower risk of SARS-CoV-2 infection, 82–83% lower risk of COVID-19 hospitalization and ICU admission, and 81% lower risk of death. Administration of COVID-19 vaccine boosters generated also greater protection (between 63 and 87% higher) against all these same endpoints compared to early completing (i.e.,  $< 5$  months;  $n = 335,458$ ) a primary COVID-19 vaccination cycle.

**Conclusions** The administration of COVID-19 vaccine booster doses is advisable for reducing the risk of morbidity and mortality in older people.

**Keywords** COVID-19 · SARS-COV-2 · Vaccination · Booster · Older people

## Introduction

It is now virtually undeniable that the ongoing coronavirus disease 2019 (COVID-19) pandemic is one of the most dramatic events that has challenged humanity since the former Spanish flu pandemic outbreak, in 1918–1919 [1]. One of the most important aspects of this infectious respiratory disease, sustained by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is that older, fragile and comorbid people represent the most vulnerable part of the

population, whereby the vast majority of COVID-19-related hospitalizations, intensive care unit (ICU) admissions and even deaths involve people aged 65 years or older [2, 3]. Several lines of evidence now attest that SARS-CoV-2 has a devastating impact on older adults, by increasing several folds their risk of unfavourable outcomes such as the need of hospitalization, respiratory support, intensive care, and ultimately magnifying their risk of death [4]. Last but not least, increased frailty and loss of function are commonplace in older people after recovering from COVID-19, thus generating dramatic consequences on healthcare, society and economy, since these older patients may need closer follow-up, as well as reinforced functional and psychologic support [5, 6].

The clinical evidence accumulated so far would hence suggest that older people should be especially protected from SARS-CoV-2 infection. Nonetheless, physical measures such as wearing face mask, social distancing, hand hygiene and so forth are only partially effective for preventing viral

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infection and COVID-19-related complications [7], so that widespread administration of COVID-19 vaccines is now regarded as the most effective preventive strategy in older persons [8], as already proven for other infectious diseases such as influenza, meningococcal and pneumococcal diseases, hepatitis, herpes zoster, diphtheria and tetanus [9].

Although the efficacy of COVID-19 vaccines against the risk of developing symptomatic disease is noteworthy, even higher than that of other vaccines such as those against Influenza (i.e., 80–90% vs. 50–60% efficacy) [10], waned post-vaccination immunity has been widely reported between 4 and 6 months after completing a primary COVID-19 vaccination cycle, with the risk of developing severe COVID-19 illness becoming nearly twofold higher after such period in people aged 60 years or older [11]. One of the potential solutions to contrast such decline of post-vaccine immunity encompasses the administration of additional vaccine doses (i.e., the so-called “boosters”), with the aim of restoring immunity to levels similar to, or even greater than, those achieved immediately after completing a primary COVID-19 vaccination. This article is hence aimed at providing an analysis on efficacy of COVID-19 vaccine booster doses in older people based on data retrieved from the ongoing nationwide Italian COVID-19 vaccination campaign.

## Methods

This analysis was based on the official statistics of the COVID-19 national integrated surveillance program, which is made available and regularly updated by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS; Last available update, December 17, 2021) [12]. This official bulletin includes complete nationwide epidemiologic information concerning the cumulative burden of COVID-19 cases, hospitalizations, ICU admissions and deaths, together with data on advancement of the nationwide COVID-19 vaccination campaign, which started on December 27, 2020. Vaccine administration in Italy was essentially based on two mRNA-based formulations (Pfizer/BioNTech Comirnaty and Moderna Spikevax) and two adenovirus-based vaccines (AstraZeneca Vaxzevria and Janssen Ad26.COV2-S). Starting from October 2021, an additional vaccination campaign has begun, with administration of vaccine booster doses (i.e., Pfizer/BioNTech Comirnaty or Moderna Spikevax) to older (i.e., > 60 years) and fragile individuals.

The official information available in the ISS bulletin was downloaded within an Excel Worksheet (Microsoft Excel; Microsoft, Redmond, WA, US) and statistical analysis (calculation of the odds ratio [OR] and 95% confidence interval [95%CI]) was carried out using MedCalc (Version 20.015; MedCalc Software Ltd., Ostend, Belgium). Statistical significance was set at  $p < 0.05$ . The study was performed in

accordance with the Declaration of Helsinki, under all relevant terms of the local legislation. The research was based on public ISS data [12], so that Ethical Committee approval was unnecessary.

## Results

The total number of people aged 80 years or older who were unvaccinated, who completed the primary COVID-19 vaccination cycle < 5 or  $\geq 5$  months and those who received a COVID-19 vaccine booster dose were 216,424, 335,458, 2,385,897 and 1,549,747, respectively. Vaccine coverage was as follows: Pfizer/BioNTech Comirnaty 70.1%, Moderna Spikevax 16.9%, AstraZeneca Vaxzevria 11.6% and Janssen Ad26.COV2-S 1.4%, respectively. As shown in Table 1 and Fig. 1, the overall COVID-19 vaccine efficacy within 5 months from completing a primary vaccination cycle was considerably high in this older population, associated with 80% lower risk of SARS-CoV-2 infection, 86% lower risk of COVID-19 hospitalization and ICU admission and 88% lower risk of death compared to unvaccinated people. Nonetheless, this protection tended to slightly wane after 5 months since the efficacy against the risk of SARS-CoV-2 infection, COVID-19 hospitalization, ICU admission and death was 70%, 83%, 86% and 88%, respectively. Compared to those who had completed the COVID-19 vaccination cycle for more than 5 months those who received vaccine booster doses had 75% lower risk of SARS-CoV-2 infections, and between 81 and 83% lower risk of COVID-19 hospitalization, ICU admission and death, respectively. The administration of COVID-19 vaccine boosters generated also greater protection (i.e., between 63 and 87% higher) against all these same endpoints compared to people who early completed (i.e., < 5 months) a primary COVID-19 vaccination cycle.

## Discussion

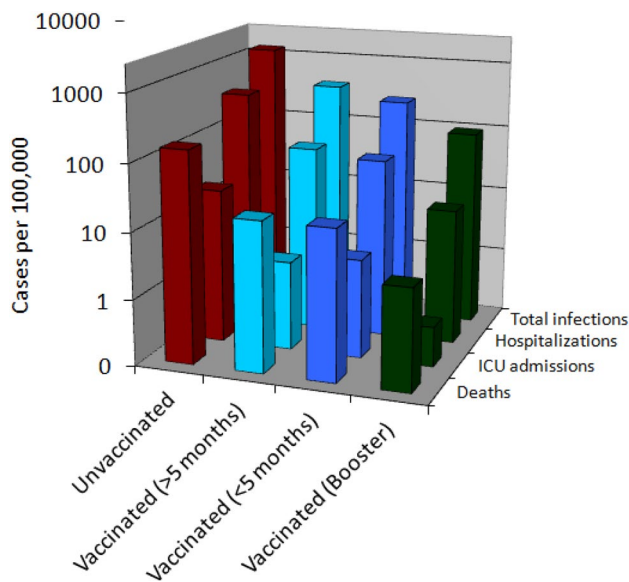
The results of our investigation based on data garnered from the ongoing nationwide COVID-19 vaccination campaign in Italy are in keeping with those reported in Israel [13, 14], and confirm that the efficacy of COVID-19 vaccines tends to decrease over time, especially against the risk of developing SARS-CoV-2 infection and COVID-19-related hospitalization. However, the administration of vaccine booster doses not only was found effective for restoring high protection against all unfavourable COVID-19 outcomes in older people (i.e.,  $\geq 97\%$  efficacy compared to unvaccinated people), but was also associated with a considerably decreased vulnerability to SARS-CoV-2 infections and complications (i.e., between 63 and

**Table 1** Efficacy of primary COVID-19 vaccine cycle and vaccine boosters from the ongoing Italian nationwide COVID-19 vaccination campaign

	Unvaccinated	Vaccinated ( $\geq 5$ months)	Vaccinated ( $< 5$ months)
OR (95%CI) total SARS-CoV-2 infections			
Vaccinated ( $\geq 5$ months)	<b>0.30 (0.2900–0.31; <math>p &lt; 0.001</math>)</b>	–	–
Vaccinated ( $< 5$ months)	<b>0.20 (0.19–0.21; <math>p &lt; 0.001</math>)</b>	<b>0.66 (0.63–0.69; <math>p &lt; 0.001</math>)</b>	–
Vaccinated (Booster)	<b>0.07 (0.06–0.08; <math>p &lt; 0.001</math>)</b>	<b>0.25 (0.23–0.27; <math>p &lt; 0.001</math>)</b>	<b>0.37 (0.35–0.40; <math>p &lt; 0.001</math>)</b>
OR (95%CI) COVID-19-related hospitalizations			
Vaccinated ( $\geq 5$ months)	<b>0.17 (0.16–0.19; <math>p &lt; 0.0019</math>)</b>	–	–
Vaccinated ( $< 5$ months)	<b>0.14 (0.13–0.15; <math>p &lt; 0.001</math>)</b>	<b>0.80 (0.71–0.90; <math>p &lt; 0.001</math>)</b>	–
Vaccinated (Booster)	<b>0.03 (0.02–0.04; <math>p &lt; 0.001</math>)</b>	<b>0.17 (0.14–0.21; <math>p &lt; 0.001</math>)</b>	<b>0.21 (0.17–0.26; <math>p &lt; 0.001</math>)</b>
OR (95%CI) COVID-19 related ICU admissions			
Vaccinated ( $\geq 5$ months)	<b>0.10 (0.07–0.16; <math>p &lt; 0.001</math>)</b>	–	–
Vaccinated ( $< 5$ months)	<b>0.14 (0.10–0.21; <math>p &lt; 0.001</math>)</b>	1.41 (0.82–2.43; $p = 0.210$ )	–
Vaccinated (Booster)	<b>0.02 (0.01–0.04; <math>p &lt; 0.001</math>)</b>	<b>0.18 (0.06–0.53; <math>p &lt; 0.001</math>)</b>	<b>0.13 (0.04–0.37; <math>p &lt; 0.001</math>)</b>
OR (95%CI) COVID-19 related deaths			
Vaccinated ( $\geq 5$ months)	<b>0.12 (0.10–0.14; <math>p &lt; 0.001</math>)</b>	–	–
Vaccinated ( $< 5$ months)	<b>0.12 (0.10–0.14; <math>p &lt; 0.001</math>)</b>	0.99 (0.81–1.22; $p = 0.958$ )	–
Vaccinated (Booster)	<b>0.02 (0.01–0.03; <math>p &lt; 0.001</math>)</b>	<b>0.19 (0.13–0.27; <math>p &lt; 0.001</math>)</b>	<b>0.19 (0.13–0.27; <math>p &lt; 0.001</math>)</b>

Statistically significant values ( $p < 0.05$ ) are reported in bold

OR odds ratio, 95%CI 95% confidence interval, COVID-19 coronavirus disease 2019, ICU intensive care unit, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2



**Fig. 1** Cases per 100,000 of SARS-CoV-2 infection, COVID-19-related hospitalizations, intensive care unit admissions and deaths reported from the ongoing nationwide COVID-19 vaccination campaign in older Italian people (i.e., aged  $> 80$  years). SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, COVID-19 coronavirus disease 2019; ICU, intensive care unit

87% lower) compared to what is commonly observed shortly after (i.e., within 5 months) completing a primary COVID-19 vaccination cycle. Unfortunately, no specific

information could be garnered from the official ISS bulletin on the outcome of different vaccines as well as on the frail status of the population, two pivotal aspects in influencing vaccination efficacy, as shown in a recent study in residents of long-term care facilities in Israel [15].

A plausible biological explanation supports these findings, wherein the serum levels of anti-SARS-CoV-2 neutralizing antibodies tends to gradually decline over time, and such reduction seems even amplified in older people, as we have recently demonstrated [16]. The efficacy of COVID-19 vaccines largely depends on anti-SARS-CoV-2 neutralizing antibodies titer, irrespective of the type of vaccine [17], and COVID-19 vaccine boosters are especially effective to increase the serum levels of these antibodies by over two-fold in older people (i.e., aged 65–85 years) compared to younger subjects [18]. It is hence advisable that COVID-19 vaccine booster doses shall be urgently made available to older people, who seem to display a more rapid decline of post-vaccine immunity and protection, and are also much more vulnerable to SARS-CoV-2 complications.

## Declarations

**Conflict of interest** The authors have no conflicts of interests.

**Ethical approval** Not applicable.

**Informed consent** Not applicable.

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