Efficacy of the second COVID-19 vaccine booster dose in older persons

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Short Report

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Efficacy of the second COVID-19 vaccine booster dose in older persons

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Key summary points

- The second COVID-19 vaccine booster maintains high effectiveness against adverse COVID-19 outcomes
- Protection of second COVID-19 vaccine booster seems higher than that of the first booster
- Regular boosting with COVID-19 vaccines is advisable in older persons
Abstract

**Purpose:** We analyzed coronavirus disease 2019 (COVID-19) vaccine efficacy in older persons who received the second booster compared to unvaccinated people and those receiving only a single COVID-19 vaccine booster.

**Methods:** We collected information on vaccine efficacy from the ongoing Italian nationwide COVID-19 vaccination campaign in subjects aged 80 years or older from official data published by the Italian National Institute of Health.

**Results:** The second vaccine booster maintained high effectiveness against adverse COVID-19 outcomes such as hospitalization, intensive care unit admission and death (i.e., between 77-86%), showing also around 10% higher efficacy than the single booster. Nonetheless, the efficacy of the second vaccine booster declined over time, decreasing by 33-46% when assessed at >120 days from administration.

**Conclusions:** The results of our ad interim analysis of the ongoing Italian nationwide COVID-19 vaccination campaign suggest that regular boosting with COVID-19 vaccines may be advisable in older persons.

**Key words:** COVID-19; SARS-COV-2; Vaccination; Booster; Older people
Introduction

Coronavirus disease 2019 (COVID-19), a life-threatening infectious pathology first identified in the Chinese town of Wuhan in 2019, has since spread all over the world, becoming the seventh more lethal pandemics throughout the known human history [1]. Although widespread COVID-19 vaccination combined with gradual mitigation of virus aggressiveness over time have indeed contributed to reduce the clinical and social impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection over time, reliable evidence suggests that older and especially frail individuals remain at an exceptionally enhanced risk of developing unfavourable COVID-19 progression, as recently highlighted by Maynou et al. [2].

We have previously emphasized that the risk of COVID-19 related hospitalization, intensive care unit (ICU) admission and death was 80% lower in older Italian persons who received the first COVID-19 vaccine booster compared to those who earlier completed the primary vaccination [3]. Since the administration of a second COVID-19 booster dose of mRNA-based vaccines (i.e., Pfizer/BioNTech Comirnaty and Moderna Spikevax) has been initiated in Italy from April 2022 in persons aged 80 years or older, we provide here an update statistics of vaccine efficacy in this high-risk category.

Materials and Methods

Our analysis is based on official data of the COVID-19 national integrated surveillance program, regularly updated by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS; Last available update, November 18, 2022) [4]. The official ISS bulletin contains updated nationwide information on the cumulative burden of COVID-19 related hospitalizations, intensive care unit (ICU) admissions and deaths. The official data of the ISS bulletin were retrieved and transcribed into an Excel
Worksheet (Microsoft Excel; Microsoft, Redmond, WA, US), whilst vaccine efficacy over time was estimated by calculating the odds ratio (OR) and 95% confidence interval (95%CI) for each of the three major endpoints (COVID-19 related hospitalizations, ICU admissions and deaths) with MedCalc (Version 20.015; MedCalc Software Ltd., Ostend, Belgium).

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 [4], so that Ethical Committee approval and informed consent were both unnecessary.

**Results**

According to the official statistics of the Italian National Institute of Health, the number of older persons (i.e., aged ≥80 years) who were still unvaccinated, who received the first and the second COVID-19 vaccine boosters at November 18, 2022 were 140,164, 2,542,606 and 1,536,464, respectively. The results of our analysis are summarized in table 1 and figure 1.

As specifically shown in figure 1, the rate of COVID-19 related hospitalizations, ICU admissions and deaths progressively declined from people who did not underwent COVID-19 vaccination, to those who received a single COVID-19 vaccine booster, and finally to those who received the second vaccine booster. The risk of COVID-19 related hospitalization, ICU admission and death was also nearly 10% lower in those who received the second COVID-19 vaccine booster dose compared to those who only received the first booster, with such difference achieving statistical significance for COVID-19 related hospitalizations. A sub-analysis of older people who received the second COVID-19 vaccine booster also showed that vaccine efficacy declined over time, in that the risk of COVID-19 related hospitalizations, ICU admissions and deaths increased by 33%, 47% and 44% in older subjects who had received the second
COVID-19 vaccine booster after 120 days compared to those who instead received the second vaccine booster within 120 days, respectively (Table 2).

**Discussion**

The results of our ad interim analysis of the ongoing Italian nationwide COVID-19 vaccination campaign [5] provide clear evidence that the administration of a second COVID-19 vaccine booster dose may be substantially advantageous in older persons. In particular, we showed that vaccine efficacy against all the most important endpoints (i.e., COVID-19 related hospitalizations, ICU admissions and deaths) not only could be restored at exceptionally high levels (i.e., between 77-86%) in those who received the second COVID-19 vaccine booster, but was also constantly higher (by around 11-13%, in absolute terms) compared to that only conferred by the first single booster. These results are well aligned to those very recently published by Kislaya et al, who also showed that the second COVID-19 vaccine booster in older Portuguese individuals (i.e., aged ≥80 years) conferred 81-82% protection against the risk of hospitalization or death compared to a vaccine efficacy of around 63-64% in those who only received the first COVID-19 vaccine booster [6]. Unlike this report, however, we also found that the efficacy of the second COVID-19 vaccine booster gradually declined over time, with a trend mirroring that seen already for primary vaccination and for the first vaccine booster [7]. This is quite understandable, considering that both humoral and cellular immunity against SARS-CoV-2 tend to decline over time, even after vaccine boosters, as clearly demonstrated by many recent studies [8-10]. Importantly, cellular immunity and immunological memory seem to wane slower and/or at lower extent compared to humoral immunity, and this evidence provides a reasonable explanation to the fact that vaccine efficacy after the second COVID-19 vaccine booster is not exceptionally superior to that conferred by the single booster [10].
Thus, the results of our ad interim analysis of the ongoing Italian nationwide COVID-19 vaccination campaign suggest that regular boosting with COVID-19 vaccines may be advisable in older individuals, for clinical, social and even economic motivations. To this end, the cost-effectiveness of administering a second COVID-19 vaccine booster dose has been recently highlighted by Mungmunpuntipantip and Wiwanitkit [11], who concluded that the cost per effectiveness of this practice is 66% higher than limiting vaccine coverage to administration of the first vaccine booster (i.e., 28.68 vs. 47.56 US$). We also emphasize that further and future boosters should be preferably administered using COVID-19 bivalent vaccines, since their efficacy in neutralizing emerging and highly mutated SARS-CoV-2 sublineages seems considerably higher than that of the previous monovalent formulations [12].

Acknowledgements None

Declarations

Conflicts of interest Authors have no conflicts of interests.

References


immune responses measured using the QuantiFERON SARS-CoV-2 assay.


Figure 1. Cases per 100,000 of coronavirus disease 2019 (COVID-19) related hospitalizations, intensive care unit (ICU) admissions and deaths within the nationwide COVID-19 vaccination campaign in older Italian persons (i.e., aged >80 years).

COVID-19, coronavirus disease 2019; ICU, intensive care unit
Table 1. Efficacy of the first and second coronavirus disease 2019 (COVID-19) vaccine booster doses in older Italian persons (i.e., aged ≥80 years).

<table>
<thead>
<tr>
<th>OR (95% CI) COVID-19 related hospitalizations</th>
<th>Unvaccinated</th>
<th>2nd vaccine booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st vaccine booster</td>
<td>0.26 (95% CI, 0.24-0.28; p&lt;0.001)</td>
<td>0.89 (95% CI, 0.84-0.94; p&lt;0.001)</td>
</tr>
<tr>
<td>2nd vaccine booster</td>
<td>0.23 (95% CI, 0.21-0.25; p&lt;0.001)</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OR (95% CI) COVID-19 related ICU admissions</th>
<th>Unvaccinated</th>
<th>2nd vaccine booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st vaccine booster</td>
<td>0.17 (95% CI, 0.11-0.26; p&lt;0.001)</td>
<td>0.87 (95% CI, 0.61-1.24; p=0.443)</td>
</tr>
<tr>
<td>2nd vaccine booster</td>
<td>0.15 (95% CI, 0.09-0.24; p&lt;0.001)</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OR (95% CI) COVID-19 related deaths</th>
<th>Unvaccinated</th>
<th>2nd vaccine booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st vaccine booster</td>
<td>0.16 (95% CI, 0.14-0.19; p&lt;0.001)</td>
<td>0.89 (95% CI, 0.78-1.01; p=0.074)</td>
</tr>
<tr>
<td>2nd vaccine booster</td>
<td>0.14 (95% CI, 0.12-0.17; p&lt;0.001)</td>
<td>-</td>
</tr>
</tbody>
</table>

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.
Table 2. Efficacy the second coronavirus disease 2019 (COVID-19) vaccine booster within or after 120 days in older Italian persons (i.e., aged ≥80 years).

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Rate (×100,000)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI) COVID-19 related hospitalizations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤120 days</td>
<td>1.14</td>
<td>0.67 (95% CI, 0.61-0.73; p&lt;0.001)</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>1.71</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) COVID-19 related ICU admissions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤120 days</td>
<td>0.02</td>
<td>0.53 (95% CI, 0.29-0.99; p=0.045)</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) COVID-19 related deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤120 days</td>
<td>0.17</td>
<td>0.56 (95% CI, 0.45-0.69; p&lt;0.001)</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>0.30</td>
<td></td>
</tr>
</tbody>
</table>

OR, odds ratio; 95% CI, 95% confidence interval; COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-CoV-2.