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Primary COVID-19 vaccine cycle and booster doses efficacy: analysis of Italian nationwide vaccination campaign

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Abstract

We provide here an updated analysis of primary COVID-19 vaccination and vaccine booster doses efficacy, emerging from the ongoing Italian nationwide COVID-19 vaccination campaign. Primary COVID-19 vaccination efficacy was 76-92% within 6 months, decreasing to 34-80% after 6 months. Administration of vaccine booster doses decreased SARS-CoV-2 infections by 65%, COVID-19 related hospitalizations and deaths by 69% and 97% compared to vaccine efficacy after 6 months, but also decreased SARS-CoV-2 infections by 39% compared to vaccine efficacy within 6 months. These results suggest that COVID-19 vaccine booster doses are important for restoring vaccine efficacy and further limiting virus circulation.

Key words: COVID-19; SARS-COV-2; Vaccination; Booster

Introduction

As brilliantly highlighted in many articles, such as that published by Zeegers Paget et al.,¹ many important things have been learned nearly 2 years after the emergence of the coronavirus disease (COVID-19) pandemic outbreak, though several aspects remained unrevealed. Several lines of evidence now attest that physical measures (e.g., social distancing, face masking, and so forth) are only partially effective for preventing SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection and complications,² so that widespread COVID-19 vaccination shall be considered the most effective strategy for decreasing virus circulation and preventing or limiting the risk of developing severe COVID-19 illness.³ Despite the efficacy of COVID-19 vaccines is now straightforward and unquestionable, even higher than that of vaccines used for preventing other respiratory infectious diseases such as Influenza,⁴ waning immunity against SARS-CoV-2 has been widely reported, especially 4 to 6 months after completing the primary COVID-19 vaccination cycle,⁵ so that there is ongoing debate as to whether additional vaccine booster doses may be necessary to restore the immune response to levels similar to or even greater than those achievable immediately after completing a primary COVID-19 vaccination.⁵ This article is hence aimed at providing an updated analysis of primary COVID-19 vaccination and vaccine booster doses efficacy by analyzing data emerging from the ongoing Italian nationwide COVID-19 vaccination campaign.

Methods

We downloaded and analytically reviewed the official statistics of the COVID-19 national integrated surveillance program, published and regularly updated by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS; Last available update, November 19, 2021).⁶ This bulletin contains comprehensive nationwide

epidemiological data related to overall number of SARS-CoV-2 infections, COVID-19 related hospitalizations, intensive care unit (ICU) admissions and deaths, along with information on progression of the COVID-19 vaccination campaign, which started on December 27, 2020, and was originally based on administration of the two mRNA-based COVID-19 vaccines manufactured by Pfizer/BioNTech and Moderna, and the two adenovirus-based COVID-19 vaccines manufactured by AstraZeneca and Johnson & Johnson. From October 2021, a national campaign of booster vaccine doses administration has been also initiated in older (i.e., >60 years old) and fragile people (i.e., immunocompromised, with cancer and/or multiple co-morbidities), extended to the entire national population from December 2021. At the time of this analysis, 45.6 million people have completed the primary COVID-19 vaccination cycle (84.4% of the national population in which COVID-19 vaccination is made available; 71.9% with Pfizer/BioNTech, 13.4% with AstraZeneca, 13.0% with Moderna and 1.7% with Johnson & Johnson, respectively), while 5.2 million people have already received a COVID-19 vaccine booster dose.

The official ISS data were imported into an Excel Worksheet (Microsoft Excel; Microsoft, Redmond, WA, US) and analyzed with MedCalc (Version 20.015; MedCalc Software Ltd., Ostend, Belgium). Statistical significance was set at $p < 0.05$. The study was carried out in accordance with Helsinki Declaration, under terms of relevant local legislation. The research was based on public ISS data,⁶ so that Ethical Committee approval was unnecessary.

Results

As shown in table 1 (and Supplementary Figure 1), the cumulative primary COVID-19 vaccine cycle efficacy within 6 months from administration was effective to reduce all SARS-CoV-2 infections by 76%, COVID-19 related hospitalizations by 87%,

ICU admissions by 92% and deaths by 84%, respectively. After 6 months from completing the primary COVID-19 vaccine cycle the protection declined to 59% against the risk of developing SARS-CoV-2 infections, 52% against COVID-19 related hospitalizations and 34% against deaths, but remained considerably high, up to 80%, for preventing COVID-19 related ICU admissions.

The cumulative efficacy of COVID-19 vaccine booster dose is summarized in Table 1 (and Supplementary Figure 1). Compared to COVID-19 vaccine efficacy recorded 6 months after completing the primary vaccination cycle, the administration of COVID-19 vaccine booster doses was effective to reduce SARS-CoV-2 infections by 65%, COVID-19 related hospitalizations by 69% and deaths by 97%. A trend towards reduction of COVID-19 related ICU admissions could also be observed (i.e., -67%), though failing to reach statistical significance. Notably, the efficacy of COVID-19 vaccine booster doses did not significantly differ from that recorded within 6 months after completing the primary COVID-19 vaccination (Table 1), though it was further effective for significantly reducing (by 39%) the risk of developing SARS-CoV-2 infection.

Discussion

The results of this updated analysis of the ongoing Italian nationwide COVID-19 vaccination campaign are in keeping with those recently emerged from the analogous nationwide vaccination campaign carried out in Israel,^{7,8} and underlie some essential aspects. After 2 years from initiation of nationwide vaccination, with over 45 million COVID-19 vaccine recipients at present out of a national population of nearly 59.2 inhabitants, the primary vaccine efficacy against the risk of developing severe COVID-19 illness (i.e., COVID-19 related hospitalization, ICU admission or death) in Italy is confirmed to be over 84%, and is also associated with a remarkable 76% reduced risk of

developing SARS-CoV-2 infection. Despite primary vaccine efficacy at 6 months after completing the primary vaccination cycle remains sizeable, a substantial decline could be observed when all endpoints were compared to those observed within 6 months after primary vaccination (Table 1). Such reduction seems however completely reversible by administering COVID-19 vaccine booster doses, which are seemingly effective to generate a cumulative protection very similar (or even better) than that achievable immediately after completing primary COVID-19 vaccination.

Notably, the administration of additional COVID-19 vaccine booster doses seems also effective to substantially diminish the risk of developing SARS-CoV-2 infection compared to immediate (i.e., within 6 months) primary vaccination efficacy, with such efficacy further increasing to 65% in people who had received a primary COVID-19 vaccination over 6 months before. This aspect is of paramount importance, since reducing the circulation of the virus in the community not only remains a primary target of SARS-CoV-2 eradication campaigns, but may also generate additional advantages such as reducing the likelihood of emergence of new variants and the risk of mandating social limitations such as lockdowns or partial closures.⁹

Conflicts of interest: None declared

Key points

- Primary COVID-19 vaccine efficacy is high but declines over time
- COVID-19 vaccine boosters restore or even enhance efficacy
- COVID-19 vaccine booster may further reduce SARS-CoV-2 circulation

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

OR (and 95% CI) - Total SARS-CoV-2 infections

	Unvaccinated	Vaccinated (>6 months)	Vaccinated (<6 months)
Vaccinated (>6 months)	0.41 (0.41-0.42)	-	-
Vaccinated (<6 months)	0.24 (0.24-0.24)	0.58 (0.57-0.59)	-
Vaccinated (Booster)	0.15 (0.13-0.16)	0.35 (0.32-0.38)	0.61 (0.56-0.66)

OR (and 95% CI) COVID-19 related hospitalizations

	Unvaccinated	Vaccinated (>6 months)	Vaccinated (<6 months)
Vaccinated (>6 months)	0.48 (0.45-0.52)	-	-
Vaccinated (<6 months)	0.13 (0.12-0.14)	0.27 (0.25-0.29)	-
Vaccinated (Booster)	0.15 (0.11-0.20)	0.31 (0.22-0.44)	1.15 (0.83-1.61)

OR (and 95% CI) – COVID-19 related ICU admissions

	Unvaccinated	Vaccinated (>6 months)	Vaccinated (<6 months)
Vaccinated (>6 months)	0.20 (0.15-0.27)	-	-
Vaccinated (<6 months)	0.08 (0.07-0.10)	0.42 (0.30-0.59)	-
Vaccinated (Booster)	0.07 (0.02-0.26)	0.33 (0.08-1.35)	0.77 (0.19-3.11)

OR (and 95% CI) – COVID-19 related deaths

	Unvaccinated	Vaccinated (>6 months)	Vaccinated (<6 months)
Vaccinated (>6 months)	0.66 (0.54-0.80)	-	-
Vaccinated (<6 months)	0.16 (0.14-0.19)	0.25 (0.20-0.30)	-
Vaccinated (Booster)	0.02 (0.00-0.29)	0.03 (0.00-0.44)	0.11 (0.01-1.77)

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.

Supplementary Figure 1. Cases per 100,000 of SARS-CoV-2 infection, COVID-19 related hospitalizations, intensive care unit (ICU) admissions and deaths reported from the ongoing Italian nationwide COVID-19 vaccination campaign.

