Estimating averted COVID-19 cases, hospitalisations, intensive care unit admissions and deaths by COVID-19 vaccination, Italy, January–September 2021

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We assessed the impact of COVID-19 vaccination in Italy, by estimating numbers of averted COVID-19 cases, hospitalisations, ICU admissions and deaths between January and September 2021, by age group and geographical macro areas. Timing and speed of vaccination programme implementation varied slightly between geographical areas, particularly for older adults. We estimated that 445,193 (17% of expected; range: 331,059−616,054) cases, 79,152 (32%; range: 53,209−148,756) hospitalisations, 9,839 ICU admissions (29%; range: 6,434−16,276) and 22,067 (38%; range: 13,571−48,026) deaths were prevented by vaccination.

We evaluated the direct impact of the Italian vaccination programme on the number of cases, on hospitalisations, on admissions to intensive care units (ICU) and on deaths, by estimating the numbers of these outcomes prevented (averted events) by COVID-19 vaccination between January (week 2/2021) and the end of September 2021 (week 38/2021) by age groups and geographical macro area.

Vaccine deployment and uptake

The target groups for COVID-19 vaccination followed the recommendations of the Ministry of Health [5], with healthcare workers, residents in long-term care facilities and persons aged over 80 years being the first to receive the vaccines. Successively, the vaccine roll-out was extended to clinically extremely vulnerable groups and younger age groups in descending order, prioritising those with multiple comorbidities. The present vaccination programme in Italy targets the whole population aged 12 years and older with access to the national healthcare. About 80% of the vaccinated population has received the mRNA vaccines Comirnaty (BNT162b2 mRNA, BioNTech-Pfizer, Mainz, Germany/New York, United States (US)) or Spikevax (mRNA-1273, Moderna, Cambridge, US), whereas the rest of the population has received Vaxzevria (ChAdOx1 nCoV-19, Oxford-AstraZeneca, Cambridge, United Kingdom (UK) or COVID-19 Vaccine Janssen (Ad26.COV2-S, Janssen-Cilag International NV, Beerse, Belgium).

There was notable heterogeneity in the pace of vaccine uptake both across Italian regions and across Italian macro areas (North-West, North-East, Centre, and South-Islands, based on nomenclature for territories for statistics (NUTS)3 areas for Italy [6]). While vaccine uptake was faster in the Centre of Italy, particularly in those aged 60–79 years, the South-Islands area has consistently reached lower levels of vaccine uptake in those aged 80 years and older compared to the other macro areas (Figure 1). By the end of September (week 38), 65% (ranging from 63% in the North-East to 66% in the North-West and in the Centre) of those aged under 60 years, 84% (ranging from 82% in the South-Islands to 87% in the Centre) of those aged between 60 and 69 years, 89% (ranging from 87% in...
**Figure 1**
Cumulative monthly full vaccination coverage by age group and geographical macro area, Italy, week 2/2021–week 38/2021

NUTS: nomenclature of territorial units for statistics.

* Based on NUTS1 areas for Italy [6].
To account for the time-lag between vaccination and the development of immunity, we assumed a delay of 2 weeks for each of the vaccine doses \([7,8]\). Thus, we defined as partially vaccinated those in the period between 14 days post-first dose and 13 days post-second dose; and as fully vaccinated those who had received the second dose or a single dose least 14 days earlier.

**Estimation of events averted by the vaccination programme**

To measure the events averted, we obtained data on all notified COVID-19 cases exploiting the case-based national COVID-19 integrated surveillance system \([9]\), and data from vaccine coverage through the national vaccination portal of the Ministry of Health \([10]\), both updated on 11 November 2021. We focused on data covering the population aged 12 years and older, for the period between 11 January (week 2) and 30 September (week 38) 2021. The weekly number of COVID-19 cases, hospitalisations, ICU admissions and deaths averted by the vaccination campaign was estimated using a method widely used in the study of the impact of the vaccination during the influenza season \([11,12]\) and recently applied to calculate vaccine-prevented COVID-19 deaths \([13]\). Details can be found in the Supplementary Material 2.

The weekly number of observed COVID-19 cases, hospitalisations, ICU admissions and deaths were summarised by date of diagnosis or sampling since we were interested in measuring the number of cases hospitalised, admitted to ICU and died and not when these events took place. We included in our analysis only hospitalisations, ICU admissions and deaths that occurred within 30 days of the COVID-19 diagnosis, which account for ca 96%, 97%, and 88% of the total numbers reported in the study period, respectively (Supplementary Figure S1). All analyses were stratified by age group (<60 years, 60–69 years, 70–79 years, and 80 years and older), and geographical macro area. The results were further analysed by splitting the study period into three phases (January–March, April–June, July–September) characterised by different epidemiological situations and different levels of vaccination coverage (Table S1).

Details about VE estimation, methods and results used in this study can be found in the Supplementary Material 3. We also performed a sensitivity analysis varying the VE in an interval of \(+/-10\) percentage points, considering as max upper limit 100%. The results of the sensitivity analyses are presented as ranges of the estimated averted events to indicate uncertainties.

All the analysis were performed using R (version 4.1.1) \([14]\). The list of the R packages used is available in the Supplementary Material.

**COVID-19 cases, hospitalisations, ICU admissions and deaths observed and averted**

A total of 445,193 (range: 331,059–616,054) cases, 79,152 (range: 53,209–148,756) hospitalisations, 9,839 (range: 6,434–16,276) ICU admissions and 22,067 (range: 13,571–48,026) deaths were estimated to have been averted by the vaccination campaign (Table), which account for 17% (range: 14%–23%), 32% (range: 24%–47%), 29% (range: 21%–41%) and 38% (range: 28%–57%) of the expected events (observed plus averted), respectively.

**Age-stratified hospitalisations, ICU admissions and deaths**

Without vaccination, the expected hospitalisation rate would have been 214, 595, 871, 1,592 per 100,000 respectively for those aged under 60, 60–69, 70–79 and 80 years and older the observed rate of 163, 421, 618, 886 per 100,000 (ranges see Table). In terms of admissions to ICU, we observed a differences of 5 (range: 4–6), 37 (range: 24–48), 50 (range: 31–80) and 50 (range: 30–128) events per 100,000 between the expected and the observed cumulative rate among those under 60, 60–69, 70–79 years old and those aged 80 years and older, respectively. We estimated that 71% (range: 69–79) of the overall deaths were averted for those aged 80 years and older, and that 18% (range: 14–19), 8% (range: 5–9) and 2% (range: 1–3) were averted for those aged 70–79, 60–69 and under 60 years, respectively.

**COVID-19 cases, hospitalisations, ICU admissions and deaths by geographical macro area**

We observed large differences between observed and expected cumulative rates for the four studied outcomes by geographical macro area according to their vaccination coverage (Figures 2 and 3). Areas that achieved high vaccination coverage (around 90%) by the end of June in those aged 80 years and older (North-East, North-West and Centre) already had an estimated percentage of averted events for all outcomes together of over 50% in the period between April and June.

Without vaccination, between July and September, the overall expected mortality rate for those aged 80 years and older would have been 224 (range: 128–669) per 100,000 vs the observed rate of 32 per 100,000 during the same months (Figure 3). In the South and Islands we observed the lowest difference between the expected, 157 (range: 117–233) and the observed mortality rate, 52; whereas in the Centre we observed the largest difference, 332 (range: 170–1,170) vs 27. In the same period, for people aged 60–69 and 70–79 years in all the geographical areas, we estimated a percentage of averted hospitalisations and ICU admissions...
### Table

Cumulative number of COVID-19 cases, hospitalisations, ICU admissions and deaths observed and averted by vaccination and observed and expected incidence rates, by geographical macro area and age group, Italy, week 2/2021–week 38/2021

| Geographical macro area | Age group (years) | COVID-19 cases | Hospitalisations | ICU admissions | Draths |
|-------------------------|------------------|----------------|-----------------|---------------|--------|
|                         | Observed         | Averted        | Expected incidence rate | Observed        | Averted        | Expected incidence rate | Observed         | Averted        | Expected incidence rate |
|                         | n                | n              | Range (95% VEB) | n                | n              | Range (95% VEB) | n                | n              | Range (95% VEB) |
|                         | Per 100,000      | Per 100,000    | Per 100,000      | Per 100,000      | Per 100,000      | Per 100,000      | Per 100,000      | Per 100,000      | Per 100,000      |
| South and Islands       | < 60             | 516,578        | 62,460          | 35,888–89,093    | 4,187.2          | 4,744.2         | 4,679–4,807.7    | 4,178.7          | 4,744.2         | 4,679–4,807.7    | 13,986          | 4,571          | 3,599–5,648    | 121.3            | 152.2          | 115.0–162.6   | 1,437            | 476.2          | 395–525.7   | 11.6            | 14.7          | 14.0–15.9   | 1.792            | 3.13          | 2.93–3.28   | 0.88            | 1.27          | 1.18–1.35   |
|                         | 60–69            | 79,060         | 8,283           | 34,854–19,924    | 2,915.3          | 3,697.2         | 2,949–3,853      | 3,951.3          | 5,913          | 2,749–3,326      | 35.32           | 48.6           | 44.6–52.1    | 1,554            | 65.8           | 44.9–83.1   | 56.4            | 91.0          | 72.9–74.1   | 1,985            | 5.19          | 3.89–7.2    | 8.54            | 10.5         | 9.5–10.0   |
|                         | 70–79            | 51,034         | 5,261           | 3,153,6–16,361   | 29,83           | 3,609.9         | 2,760–3,325      | 50,66           | 4,982          | 3,372–5,726      | 9.85            | 18.9           | 15.5–22.1    | 18.35           | 71.1           | 94.3–108.3   | 95.1            | 131.8         | 115.5–178.2 | 1,947            | 3.16          | 2.86–3.48   | 118.8           | 244.1         | 239.3–251.1 |
|                         | Total (< 60)     | 393,453        | 25,424          | 3,436,9–12,122   | 8,382.5          | 9,596.8         | 8,957–10,347     | 23,793          | 2,949          | 2,589–3,326      | 11.5            | 14.7           | 11.7–16.5    | 1,274           | 10.4          | 8.9–13.6    | 17.8            | 23.7          | 21.5–26.2   | 9.34             | 13.0          | 11.5–14.1   | 13,524           | 314.7         | 272.5–341.1 |
|                         | Total (60–69)    | 53,010         | 5,392           | 3,156,1–5,398    | 5,851.2          | 6,542           | 5,407–7,617      | 8,983           | 6,699          | 6,260–8,617      | 36.5            | 49.7           | 44.9–54.5    | 20.10           | 4,468          | 3,698–5,241   | 21.8            | 30.7          | 26.7–34.5   | 3.12             | 3.92          | 3.72–4.12   | 26,46           | 513.2         | 458.1–540.6 |
|                         | Total (70–79)    | 27,555         | 2,816           | 2,473,5–4,257    | 8,983           | 9,596.8         | 8,957–10,347     | 23,793          | 2,949          | 2,589–3,326      | 11.5            | 14.7           | 11.7–16.5    | 1,274           | 10.4          | 8.9–13.6    | 17.8            | 23.7          | 21.5–26.2   | 9.34             | 13.0          | 11.5–14.1   | 13,524           | 314.7         | 272.5–341.1 |
|                         | Total (Total)    | 3,081,352      | 152,120         | 3,860,9–5,669,7   | 12,362.7         | 13,460         | 11,819–15,101    | 82,949          | 12,492         | 10,057–14,927    | 121.3           | 152.2          | 115.0–162.6  | 1,437            | 476.2          | 395–525.7   | 11.6            | 14.7          | 14.0–15.9   | 1.792            | 3.13          | 2.93–3.28   | 0.88            | 1.27          | 1.18–1.35   | 1.040            | 1.17          | 0.99–1.34   | 0.33             | 0.43          | 0.36–0.51   |

COVID-19: coronavirus disease; ICU: intensive care unit; NUTS: nomenclature of territorial units for statistics; VE: vaccine effectiveness.
higher than 60%. Furthermore, for those aged under 60 years, the observed mortality rate and the observed hospital rate was less than half of the expected one by week 38 at the end of September, in all the geographical areas.

Overall, we estimated that 74% (range: 72–77), 70% (range: 66–80), 75% (range: 71–82) and 62% (range: 55–78) of cases, hospitalisations, ICU admissions and deaths were, respectively, averted between July and September, given that the average full vaccination coverage at the end of September was higher than 60% in all age groups. Indeed in this period 48% (range: 40–57), 73% (range: 63–85), 78% (range: 68–86) and 83% (range: 73–93) of the expected cases, hospitalisations, ICU admissions and deaths were averted, respectively.

Ethical statement
The dissemination of COVID-19 surveillance data was authorised by the Italian Presidency of the Council of Ministers on 27 February 2020 (Ordinance number 640).

Discussion
The pace of the roll-out of COVID-19 mass vaccination varied by age group and across geographical macro areas in Italy, particularly in people aged 80 years and older, and influenced the magnitude of prevented infections, hospitalisations, ICU admissions and deaths. The South-Islands experienced less averted events than other macro areas mainly because of a slower vaccination uptake in those at higher risk and the high incidence of COVID-19 cases observed during the tourist season (July–August). Rates of expected and observed events for all four outcomes started to diverge in the
period between January and March in those aged 80 years older; and between April and June in the other age groups. Our model estimations show that without vaccination, peaks in hospitalisations, ICU admissions and deaths higher than those observed would have been detected for people aged 80 years and older starting from April and for other age groups from July to September. Overall, the largest proportions of hospitalisations and deaths prevented by the vaccination was observed in the oldest age group (41%; range 38−53 and 71%; range 69−79, respectively), whereas the largest number of averted ICU admissions has been observed in those aged between 60 and 79 years (59%; range: 52−57).

Our results are consistent with the current literature that demonstrates a positive impact of COVID-19 vaccination in preventing infections [4] and severe disease [13,15], with a larger reduction in the COVID-19 burden in older adults [16,17]. Furthermore, previous studies have estimated the number of deaths averted as a result of the vaccination roll-out [13,15,17,18]. However, to the best of our knowledge, this is the first study that, exploiting a standard approach, estimates the impact of the COVID-19 vaccinations in terms of prevented events in Italy for all the age groups eligible for vaccination and which analyses geographical differences.

The analysis has several limitations. The method used assumes that vaccination impact is only driven by its direct effects and does not take into account its potential indirect effects such as impact on the overall transmissibility and/or relaxation of restriction measures.
The proposed calculation may therefore have underestimated the number of avoided events. Moreover, since our approach is not based on a dynamic-transmission model, it is not able to predict future behavioural changes of the population in the counterfactual situation of no-vaccination having been available in 2021, as Italy may have implemented multiple restriction measures over 2021 had the vaccines not been available. Although we performed a sensitivity analysis to determine how different values of VE affect the estimates, we did not take into account other factors that have been found to influence VE, such as the vaccine type [19]. Finally, concurrent with the start of the vaccination roll-out, various non-pharmaceutical interventions were introduced to control the spread of the virus. Both the measures and the vaccination uptake are likely to have had an impact on the incidence of COVID-19 cases, hospitalisations, ICU admissions and deaths.

Conclusion
Our findings show a positive impact of the COVID-19 vaccination programme in Italy, and suggest that the rapid vaccination of high-risk groups has prevented a considerable number of severe COVID-19 outcomes. Averted hospitalisations and ICU admissions ranged between 53,299 and 148,756 and 6,434 and 16,276, respectively, and for deaths averted the range was 13,571–68,026. Geographical areas that achieved high vaccination rates faster were able to prevent a larger number of hospitalisations, ICU admissions and deaths over the summer months.

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Conflict of interest
None declared.

Authors’ contributions
PP, FR; AMU and CS designed the paper. AB, MDG, MFM and MB retrieved and linked databases. CS, supported by DP and MS, carried out the analysis. CS, AMU, MF, and PP wrote the manuscript, which was then reviewed and approved by the other authors.

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