Impact of COVID-19 vaccination on the risk of SARS-CoV-2 infection and hospitalization and death in Italy (27.12.2020 - 14.07.2021)

Combined analysis of data from the National Vaccination Registry and the COVID-19 Integrated Surveillance System

English version

Key Points

- This is the third report on the combined analysis of data from the Italian National Vaccination Registry and the COVID-19 integrated surveillance system. This activity is pursuant to Decree-law No. 2 of 14 January 2021 regulating the information systems that are instrumental to implementing the national strategic vaccination plan for the prevention of SARS-CoV-2 infections (Art. 3, Paragraph 7).
- The aim of the assessment is to analyse the impact of COVID-19 vaccination on the risk of being infected, hospitalized, admitted to an Intensive Care Unit, or dying from SARS-CoV-2, and the persistence of vaccine-induced protection over time. The data contained in this report are complementary to the vaccine efficacy estimates obtained with different methods and reported in the weekly bulletin "COVID19 Epidemic. National Update" available on the ISS website (www.iss.it).
- This report takes into consideration over 27 million people (representing half of the Italian population ≥12 years of age) who received at least one dose of a COVID-19 vaccine. The risk of being diagnosed with a SARS-CoV-2 infection is assessed after over 170 days since the first vaccine dose administration.
- In the study period, the incidence of a COVID-19 diagnosis decreases from 1.2 per 10,000 person-days in the first 14 days after the first dose (reference period, during which risk is comparable to non-vaccinated individuals) to 0.6 in incompletely vaccinated persons and to 0.3 in those that are completely vaccinated. The risk of receiving a COVID-19 diagnosis decreases progressively starting two weeks after the first dose administration, reaching a risk reduction rate greater than 95% at the end of the observation period. The risk of a Covid diagnosis continues to remain very low over 170 days after receiving a first dose.
- The incidence rate of hospitalization in persons vaccinated before 16 May 2021 decreases from 0.27 (per 10,000 person-days) in the first 14 days after the first dose, to 0.09 in incompletely vaccinated persons and to 0.03 in those completely vaccinated. In the first 14 days after the first dose of vaccine, a higher incidence is observed in the ≥80 years age group compared to people aged below 40 (respectively 0.70 versus 0.05/10,000 person days); this difference narrows down in those fully vaccinated (0.06 vs 0.01).
- The incidence rate of mortality following a COVID-19 diagnosis among people vaccinated before 16 May 2021 decreases from 0.08 per 10,000 person-days in the first 14 days after receipt of a first dose, to 0.01 in completely vaccinated individuals. In the latter group, the incidence does not differ substantially in terms of age, gender, geographical area, calendar period and brand, and always remains below 0.02 per 10,000 person-days.
- Vaccines are confirmed to be beneficial in all age groups, in both males and females, also over the longer observation period (170 days).
- The stratified analysis by brand suggests, for all vaccines, a reduction of the risk of infection, hospitalization, admission to an intensive care unit, and of mortality, starting from the second week after the first or -single dose administration; in case of a two-dose vaccine schedule, a further risk reduction is observed after administration of the second dose, and no loss of efficacy over time was observed.
- The report includes estimations of incidence rates per brand, however, it is not possible, methodologically, to compare vaccines, because the different products were used in different periods of time, with different circulation of the virus, and in populations with heterogeneous risk rates.

This report was produced by the ISS Working Group and the "*COVID-19 vaccine surveillance system*" of the Ministry of Health

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Introduction

In Italy, the COVID-19 vaccination campaign was launched on 27 December 2020. To date, four vaccines have been authorized by the European Medicines Agency (EMA) and the Italian Medicines Agency (AIFA): Comirnaty (Pfizer-BioNtech), Spikevax (Moderna), Vaxzevria (AstraZeneca) and COVID-19 Vaccine Janssen (Johnson&Johnson). All except for COVID-19 Vaccine Janssen require a two-dose vaccination schedule, each at different time intervals. **Table 1** shows the dates in which each of the four vaccines were first authorized and administered.

Table 1. Date of authorization and first administration of COVID-19 vaccines in Italy

Vaccine	Date of authorization	First administration
Comirnaty (Pfizer-BioNtech)	22/12/2020	27/12/2020
Spikevax (Moderna)	07/01/2021	14/01/2021
Vaxzevria (AstraZeneca)	29/01/2021	01/02/2021
COVID-19 Vaccine Janssen (Johnson&Johnson)	11/03/2021	22/04/2021

Our preceding report published in June 2021 assessed the nationwide impact of COVID-19 vaccination against Sars-CoV-2 infections, subsequent hospitalizations and deaths (1), and showed that, compared to the first two weeks after the first dose, the risk of SARS-CoV-2 infection, hospitalization or dying from SARS-CoV-2, declines gradually and substantially in vaccinated people. Results suggest that the vaccination campaign has the capacity of significantly reducing the rates of morbidity and mortality from COVID-19 when high vaccine coverage are achieved.

The present report expands on the previous study to analyse the impact of COVID-19 vaccination according to vaccination status of reported cases. A case is considered "**completely vaccinated**" after at least 14 days the second or single dose administration (COVID-19 Vaccine Janssen), or "**incompletely vaccinated**" after at least 14 days the first dose and within 15 days from the second dose of a two-dose vaccination schedule.

Real world data on the risk-benefit profile of the approved vaccines have started to emerge as the vaccination campaigns proceed. Several studies conducted in Europe (2-5), North America (6-7) and Israel (8-9) support the effectiveness of mRNA and viral vector COVID-19 vaccines, both in the general population (4, 6, 7, 9) and in specific categories at risk such as the elderly, healthcare workers, long- term care residents, pregnant women, etc. (2, 3, 5, 10, 11). In Italy, available evidence suggests that in the general population, vaccines are effective in reducing the risk of SARS-CoV-2 infections, and of COVID-19- related hospitalizations and death (12-13), although so far, no specific study has been published on single brand of vaccine. Consequently, this report aims to verify the effectiveness of the different COVID-19 vaccines authorized in Italy, taking into consideration the vaccination strategy that established priority groups on the basis of vaccine availability and results of preregistration trials.

There are three additional factors that may have an impact on the effectiveness of vaccines: the different time intervals between the administration of the first and second vaccine doses; the use of mixed schedule; the Delta variant spreading in Europe.

In Italy, the vaccination strategy has been revised over time (**Table 2**): for example, extending the timing between vaccine doses (for Comirnaty and Spikevax), replacing the second dose of Vaxzevria with an mRNA vaccine in persons aged below 60 years (mixed schedule). To date, this report, although of great interest, does not assess the effectiveness of these different vaccination strategies, because at the time of the analyses (13/06/2021 for diagnoses and 16/05/2021 for hospitalizations, admissions to an intensive care unit (ICU) and deaths) there was not a sufficiently large number of vaccinated persons.

Present data, which were collected up to mid-June (and up to mid-May for hospitalizations, ICU admission and deaths), does not allow to evaluated the impact of the current spread of the Delta variant in Italy, that recently reached a higher rate of transmissibility and for which only a few studies assessed the effectiveness of vaccines.

Table 2. Main measures concerning anti SARS-CoV-2 vaccines adopted nationally (updated at 23/07/2021)

24/12/2020	**Law Decree**: Recommendations for the organization of the vaccination campaign against SARS-CoV-2/COVID-19 and vaccination procedures.
02/01/2021	**Ministry of health (MoH):** Adoption of the national strategic plan for the prevention of SARS-CoV-2 infections (statement of the Minister of Health to Parliament, 2nd December 2020; updated on 12th December 2020; Decree of 2nd January 2021)
22/02/2021	**MoH:** Update COVID-19 AstraZeneca **v**accine allocation and interim recommendations on vaccination target groups.
08/03/2021	**MoH:** use of the COVID-19 AstraZeneca **v**accine in persons aged 65 years and older.
13/03/2021	**MoH /ISS:** COVID-19 n. 4/2021 report by ISS "Interim recommendations on prevention and control measures for SARS-CoV-2 infections (variants and vaccination against COVID-19)".
13/03/2021	**Presidency of the Council of Ministers:** Vaccination plan by the Extraordinary Commissioner for the COVID-19 emergency national vaccination campaign.
15/03/2021	**Italian Medicines Agency (AIFA):** AstraZeneca vaccine discontinuation as a precaution.
19/03/2021	**MoH: Note of the Italian medicine Agency (AIFA)** on the advice of discontinuation and withdrawal of ban of Astrazenca vaccine.
24/03/2021	**MoH:** Interim recommendations on vaccination target groups, 10th March 2021.
01/04/2021	**MoH:** Ordinance on urgent measures for the containment and management of the COVID-19 pandemic emergency: anti SARS-CoV-2 vaccination, justice and public tenders.
07/04/2021	**MoH:** 7th April 2021 - AIFA note on the advice of discontinuation and withdrawal of ban for AstraZeneca vaccine. *Vaxzevria is approved in people aged 18 years and older; based on current evidence and taking into account the low risk of adverse reactions of thromboembolic events compared to high COVID-19 mortality in the elderly, it is recommended that the vaccine be used preferentially in persons* **over** *60 years of age.*
09/04/2021	**MoH:** In line with the National Plan of the Ministry of Health (law decree, 12nd March 2021), the following priority groups have been identified: persons aged 80 years and older; persons with high frailty and, as per the specific indications of Category 1, Table 1 and 2 of Interim recommendations, their household members, caregivers, parents/guardians/foster carers; - persons aged between 70 and 79 years and, subsequently, those aged between 60 and 69 years, using mainly Vaxzevria vaccines (previously called COVID-19 Vaccine AstraZeneca) as recently indicated by AIFA.
15/04/2021	**AIFA**: Instructions for the correct handling, storage and administration of the Comirnaty - BioNTech / Pfizer vaccine (updated as of 15th April 2021).
05/05/2021	**MoH: S**cientific advice/opinion of the Technical Scientific Committee regarding the extension of the interval between the two doses of the mRNA vaccines and the second dose of Vaxzevria vaccine.
03/06/2021	**AB, EMA, AIFA:** Information note of the 3rd June 2021, VAXZEVRIA/COVID-19 Vaccine AstraZeneca: Risk of thrombosis in combination with thrombocytopenia.
04/06/2021	**MoH**: Extension of indication for the use of COVID-19 vaccine Comirnaty (BioNTech/Pfizer) in children aged 12-15 years. (Decision of 31st May, 2021)
11/06/2021	**MoH:** Updated opinion of Vaccine Technical Scientific Committee. *Vaxzevria vaccine should be offered only to persons aged 60 years and older (complete vaccination series).*
13/06/2021	**MoH:** Updated information on Moderna vaccine (related to Annex 3 of General Directorate for Prevention of 11st June 2021)
14/06/2021	**MoH:** Vaccination anti-SARS-CoV2/COVID-19. Transmission of AIFA opinion and decision on use of different mRNA vaccines to complete vaccination series (mixed schedule).
18/06/2021	**MoH:** Completion of vaccination series in persons below 60 years of age who have received a first dose of Vaxzevria vaccine, and explanations/clarification on use of COVID-19 Vaccine Janssen.
23/06/2021	**AIFA**: VAXZEVRIA/COVID-19 AstraZeneca vaccine: contraindication in individuals with a history of capillary leak syndrome (Information note of the 3rd June, 2021)
25/06/2021	**MoH**: Update tof the classification, transmission and strengthening of surveillance of SARS-CoV-2 variants in Italy, with special reference to the Delta variant (Circular letter of the MoH n. 28537 of the 6th June, 2021)
09/07/2021	**European Medicnes Agency (EMA):** Comirnaty e Spikevax: possible link to very rare cases of myocarditis and pericarditis
19/07/2021	**AIFA:** Information note on COVID-19 Vaccine Janssen: Contraindication in individuals with a history of capillary leak syndrome and update on thrombosis with thrombocytopenia syndrome
20/07/2021	Commissioner's Office: completing COVID-19 vaccination - "hesitant" population
23/07/2021	**EMA:** COVID-19 vaccine Spikevax approved for children aged 12-17 years in EU
23/07/2021	**EMA**: COVID-19 Vaccine Janssen: Guillain-Barré syndrome listed as a very rare side effect

MoH: Ministry of Health; ISS: Istituto Superiore di Sanità (National Institute of Health); AIFA: Agenzia Italiana del Farmaco (Italian Medicine Agency); AB: Astrazeneca AB; EMA: European Medicine Agency

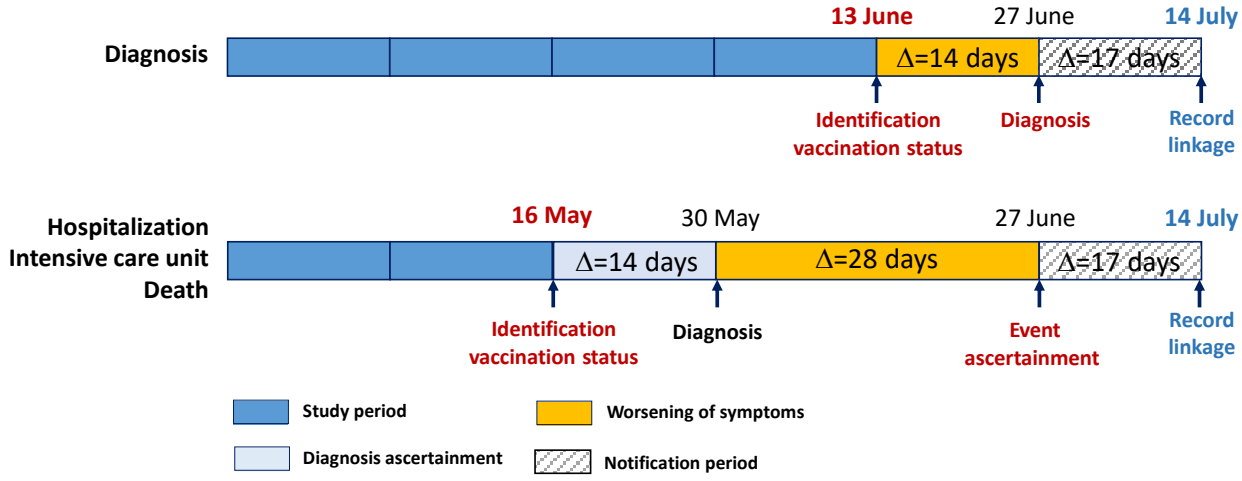
Methodological note

Data are obtained by linking COVID-19 vaccinated persons listed in the National Vaccination Registry [1] of the Ministry of Health with data on SARS-CoV-2 infections notified to the National COVID-19 Integrated Surveillance System[2]. This activity was realised according to the Decree Law No. 2 of 14 January 2021, which regulates the information systems for the implementation of the National Strategic Vaccination Plan for the Prevention of SARS-CoV-2 Infections[3] and that, under Art. 3, Para. 7 reads: *"In order to carry out immunological and pharmaco-epidemiological surveillance activities, the Ministry of Health transfers individual data of anti-SARS-CoV-2 vaccinated persons, recorded in the National Vaccination Registry, to the Italian National Institute of Health."*

The study population includes all Italian persons who have received at least one dose of any authorized COVID-19 vaccine from 27 December 2020. COVID-19 diagnoses was obtained through a record linkage between the National Vaccination Registry of the Ministry of Health (updated at 14.07.2021) and the National COVID-19 Integrated Surveillance System coordinated by the Italian National Institute of Health (updated as of 14.07.2021). The study assesses the incidence rate of SARS-CoV-2 infection and subsequent hospitalizations, admission to an ICU and death.

All persons who were diagnosed with a SARS-CoV-2 infection prior to the date of their first vaccination dose were excluded. Moreover, persons who were vaccinated but who had not been subjected to a sufficiently long observation period (follow-up) to be able to develop the events under study and for such events to be notified to the surveillance system were also excluded. **Figure 1** shows the timeline at which the study populations were selected.

Figure 1. Timeline of selection of the study populations for the ascertainment of each study event.



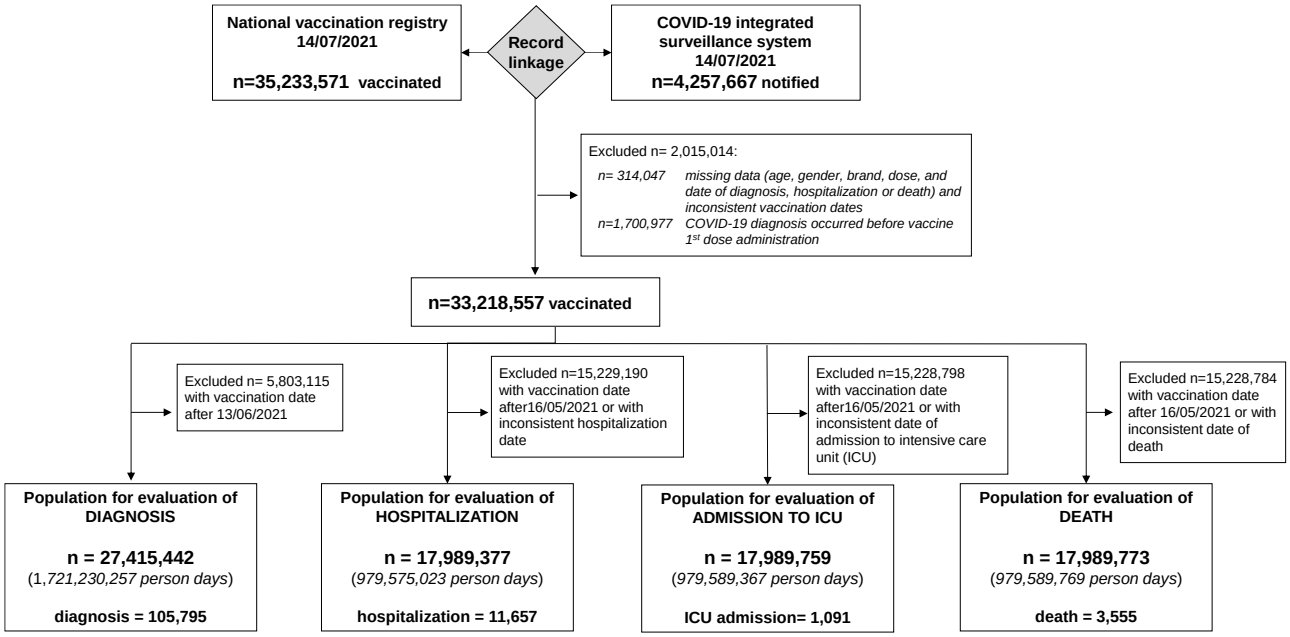
The rate of diagnosis of SARS-CoV-2 infection was estimated in persons receiving their first dose of vaccine by 13 June 2021 and who had been diagnosed before 27 June 2021, in order to take into account a follow-up period of at least 14 days from vaccine administration, and an adequate time for diagnostic assessment (including the incubation period) and for post-diagnosis notification to the surveillance system (another 17

[1] http://www.salute.gov.it/portale/vaccinazioni/dettaglioContenutiVaccinazioni.jsp?lingua=italiano&id=5067&area=vaccinazioni&menu=vuoto
[2] https://www.epicentro.iss.it/coronavirus/sars-cov-2-sorveglianza
[3] http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioContenutiNuovoCoronavirus.jsp?lingua=italiano&id=5452&area=nuovoCoronavirus&menu=vuoto

days after 27 June 2021). Hospitalization, ICU admission and mortality rates were ascertained in those had receiving a first dose of vaccine by 16 May 2021, to allow for a minimum diagnostic assessment follow-up period and notification time and for an another 28 days to observe a possible worsening of clinical conditions up to hospitalization/death.

The details of the inclusion and exclusion criteria are described in **Figure 2**.

Figure 2. Flow chart of the study population from the National Vaccination Registry and the COVID-19 Integrated Surveillance System for assessment of the study events



The incidence rates of diagnoses, hospitalizations, ICU admissions and mortality were calculated as ratio between the number of study events and the total observation period (person-time in days) in vaccinated persons: a) who received the first dose from 14 days or less (**reference**); b) who received only the first dose of a two-dose vaccine (Comirnaty, Spikevax and Vaxzevria vaccines) after 14 days, or who received the second dose from ≤14 days (**incompletely vaccinated**); c) who received the second dose (Comirnaty, Moderna and Vaxzevria) or single dose (COVID-19 Vaccine Janssen) after at least 14 days (**completed vaccinated**).

Incidence rates were also stratified by age group, gender, geographic area, calendar period of the administration of the first dose and brand. Each individual record was split to consider the exposure time of the three vaccination status of reported cases (reference, incomplete vaccination and complete vaccination). Follow-up period ended at the date of SARS-CoV-2 infection for those who experienced the study events.

Multivariate analyses was carried out to estimate the reduction of risk of diagnoses, hospitalization, ICU admission and death at different time intervals after the administration of the first dose of vaccine compared to the 0–14-day interval after the first dose (reference period). In order to consider only the associated COVID-19 events, a conservative approach was applied including hospitalizations and deaths occurring within 28 days of the diagnosis (representing region98% and 87% of those recorded in the Integrated Surveillance System, respectively).

The multivariate analyses were carried out through negative binomial models with a robust variance estimator including the following covariates: gender, age group (<40 years, 40-59 years, 60-79 years and ≥80 years), region of vaccination, vaccine brand and vaccination priority groups (healthcare workers, school

employees, nursing home residents, individuals with comorbidity, and other priority groups). The analysis was also adjusted for calendar week of the first dose administration (to take into account the different chronological vaccination for each vaccination priority group, e.g.: healthcare personnel working in ICU were probably vaccinated before those working in other departments) and for regional weekly incidence in the general population (to take into account that the risk of infection varied according to the level of virus circulation within the community in different calendar periods).

For each of the study events (diagnosis, hospitalization, ICU admission, death), the impact of vaccination at different weeks from administration of the first dose was measured as a relative risk comparing to the incidence rate in the first two weeks after vaccination, with 95% confidence intervals (CI 95%). The reduction of risk of diagnosis, at different time intervals after the administration of the first dose of vaccine, was calculated by age groups. The results of the analysis by vaccination priority group and gender are not presented in this report because are in line with those already presented in the previous report.

The reduction of the risk of diagnosis, hospitalization, ICU admission, and death at different time intervals since administration of the first and second doses was estimated by vaccine brand.

Results

As of **14 July 2021,** the National Vaccination Registry recorded 35,233,571 persons who had received at least one dose of COVID-19 vaccine (56,689,937 doses), of whom 314,047 (0.9%) were excluded from this analysis because of lack of information on age, gender and vaccine dose and/or inconsistency between vaccine administration dates (e.g., date of the first dose > date of the second dose). After record linkage with the COVID-19 Integrated Surveillance System, 1,700,977 (4.8%) persons who were infected before being vaccinated were excluded (**Figure 2**). The remaining 33,218,557 persons had received either at least one dose of Comirnaty (N=22,921,983; 69.0%), Spikevax (N=3,048,534; 9.2%), or Vaxzevria vaccines (N= 6,051,773; 18.2%), or the single dose of the Janssen vaccine (N= 1,196,267; 3.6%) (**Figures 3, 4**).

Of the 27,415,442 persons vaccinated by 13 June 2021 (included in the analysis of the impact of the vaccination, hereinafter "study population"), 65% received at least one dose of Comirnaty vaccine (N=17,857,894), 21% at least one dose of Vaxzevria vaccine (N= 5,748,848), 9% at least one dose of Spikevax vaccine (N=2,441,629), 4% had completed the vaccination series with Janssen vaccine (N=1,083,364) (**Figure 3**); 86% had completed the vaccination schedule with Comirnaty , 87% with Spikevax and 60% with Vaxzevria (**Figure 4**).

Figure 3. Distribution of vaccinated persons by vaccine brand; study population and overall population

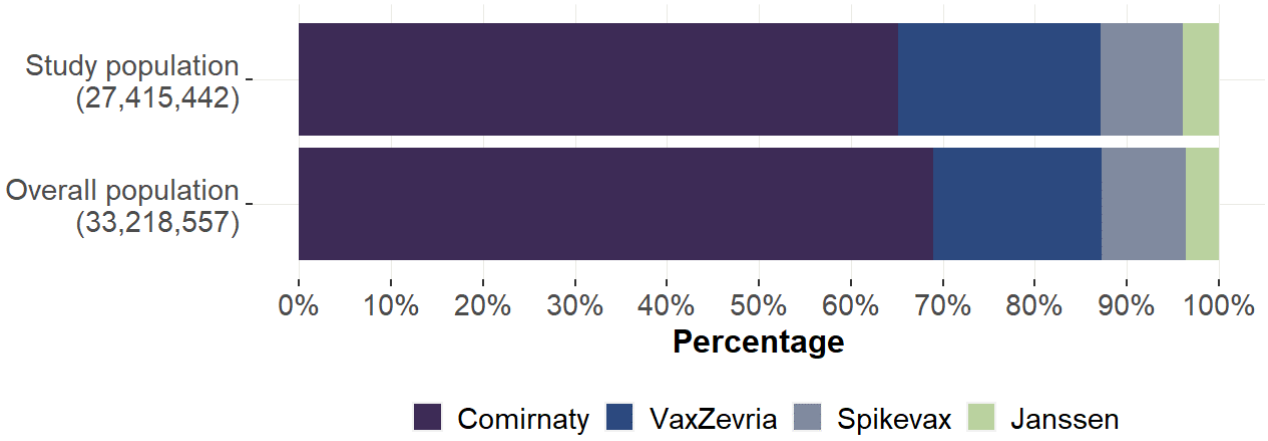
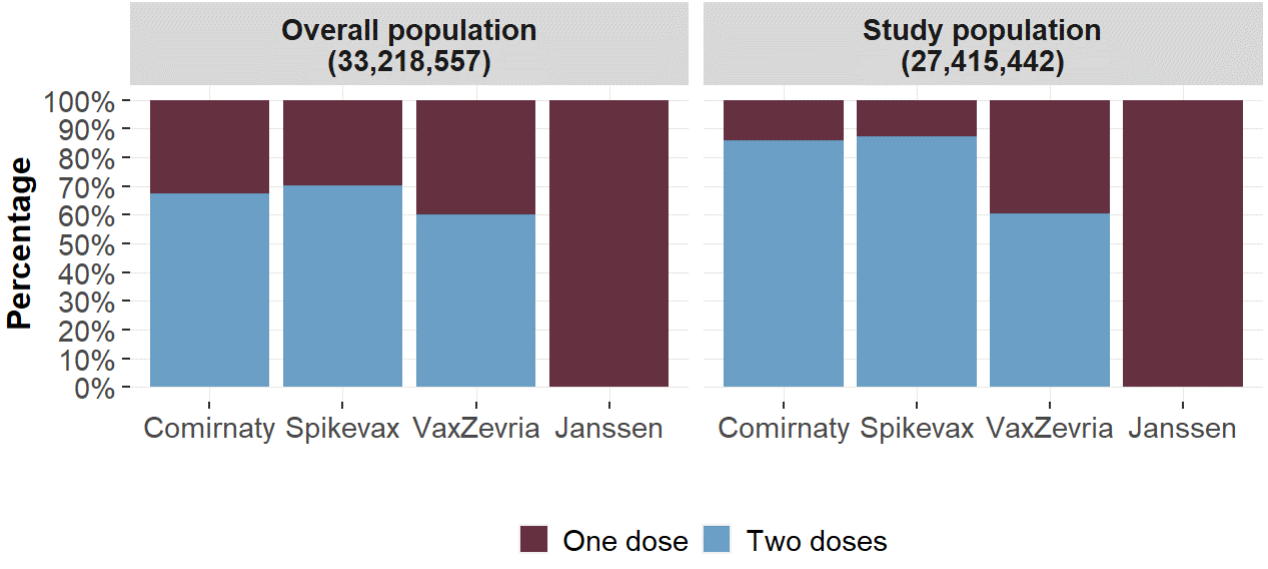
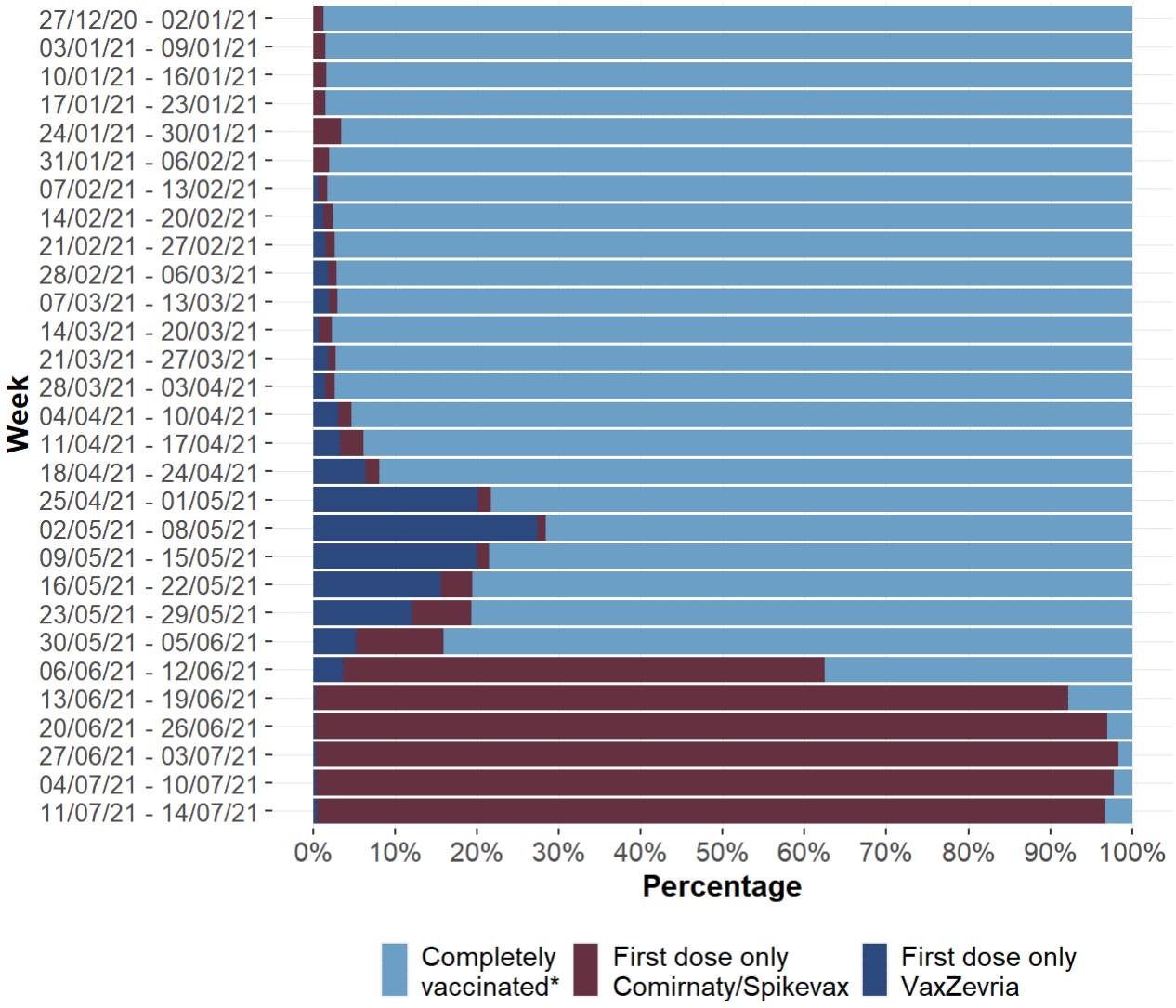


Figure 4. Percentage of persons vaccinated with one or two doses by vaccine brand



The proportion of individuals who completed the vaccination series is higher among those who received the first dose between January and March compared to those vaccinated in later months. The observed weekly variation may be explained by the availability of different vaccine brand and the different time intervals between doses (**Figure 5**).

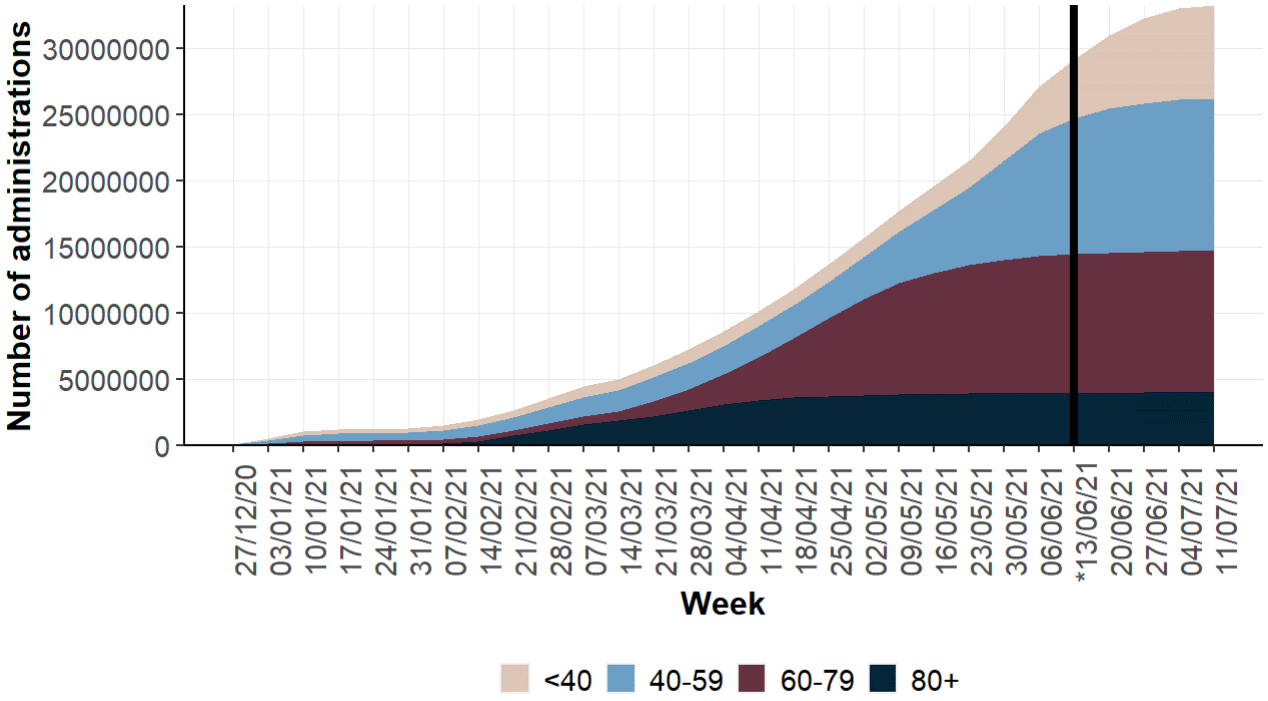
Figure 5. Percentage of completely and incompletely vaccinated persons by week of administration of the first dose and vaccine brand (overall population N=33,218,557)



*two doses Comirnaty/Spikevax/VaxZevria, one dose Janssen

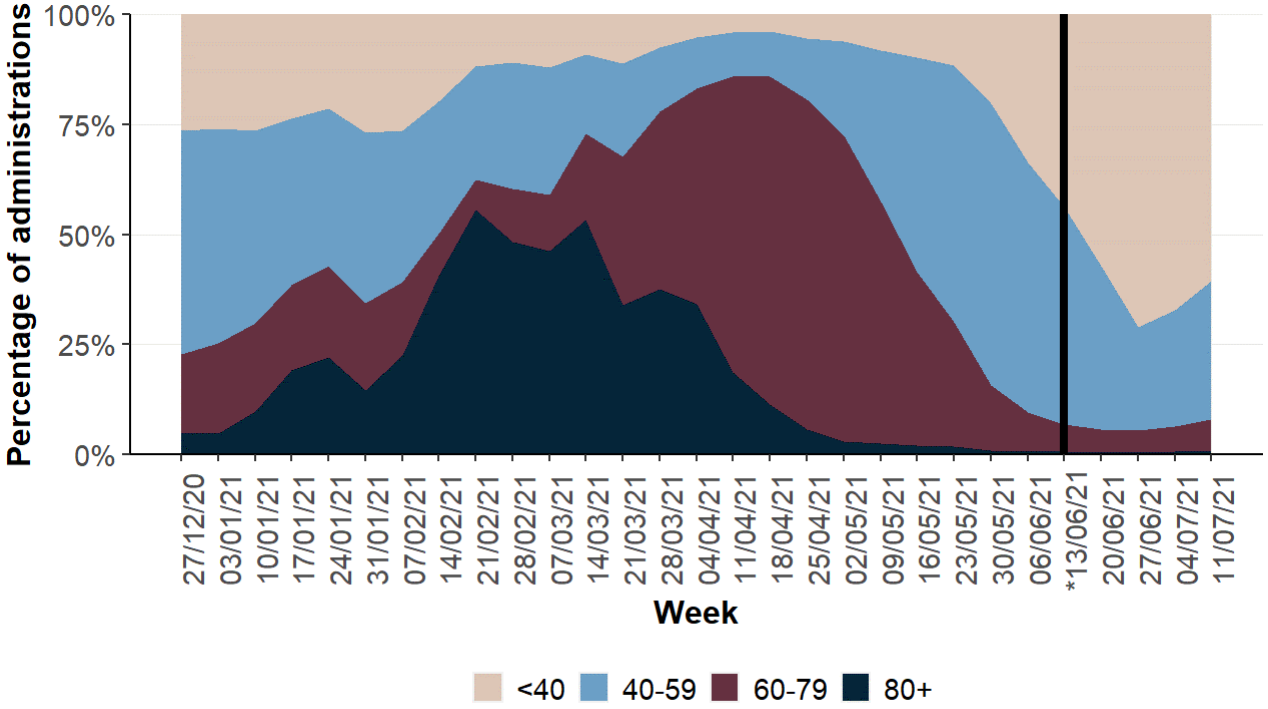
Age distribution of vaccinated persons varies over the weeks reflecting the revision over time of the National Strategic COVID-19 Vaccination Plan. As expected, the number of vaccinated persons aged below 40 years has increased over the last weeks, while the number of vaccinated persons aged 60 years or older has decreased (**Figures 6 and 7**).

Figure 6. Cumulative number of administrations of first/single dose by vaccination week and age group (overall population N=33,218,557)



*latest vaccination date included in the study

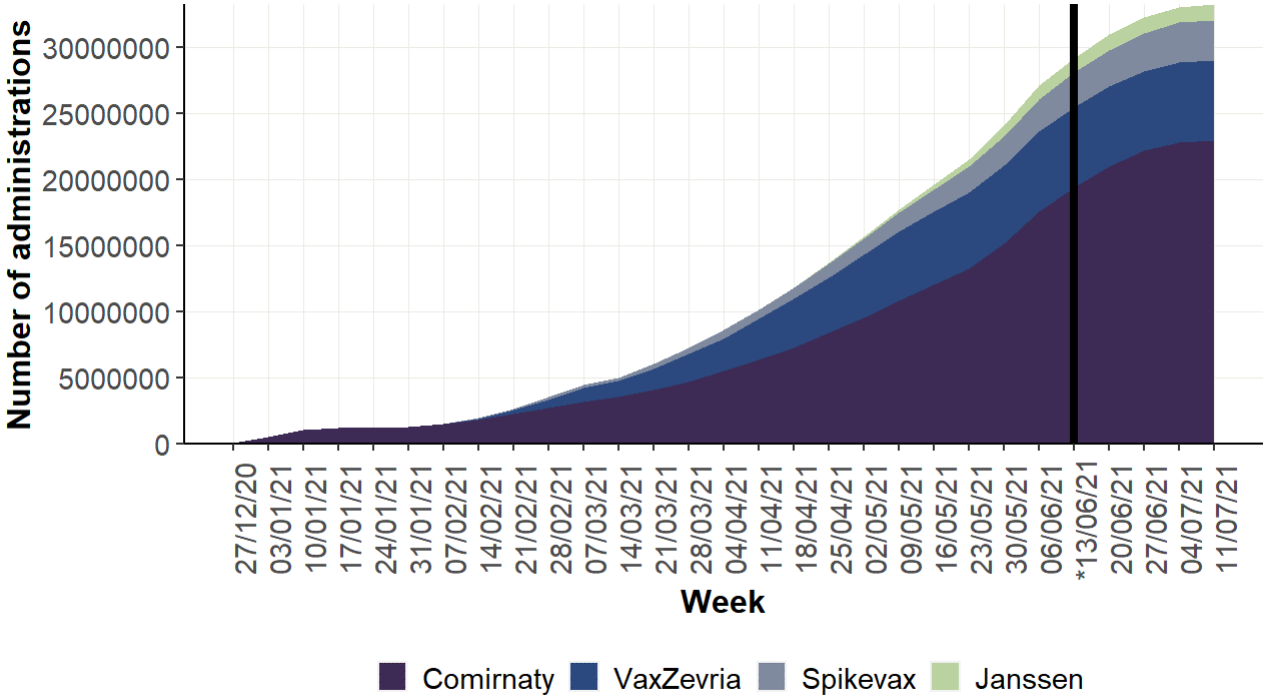
Figure 7. Percentage distribution of administrations of first/single dose by vaccination week and age group (overall population N=33,218,557)



*latest vaccination date included in the study

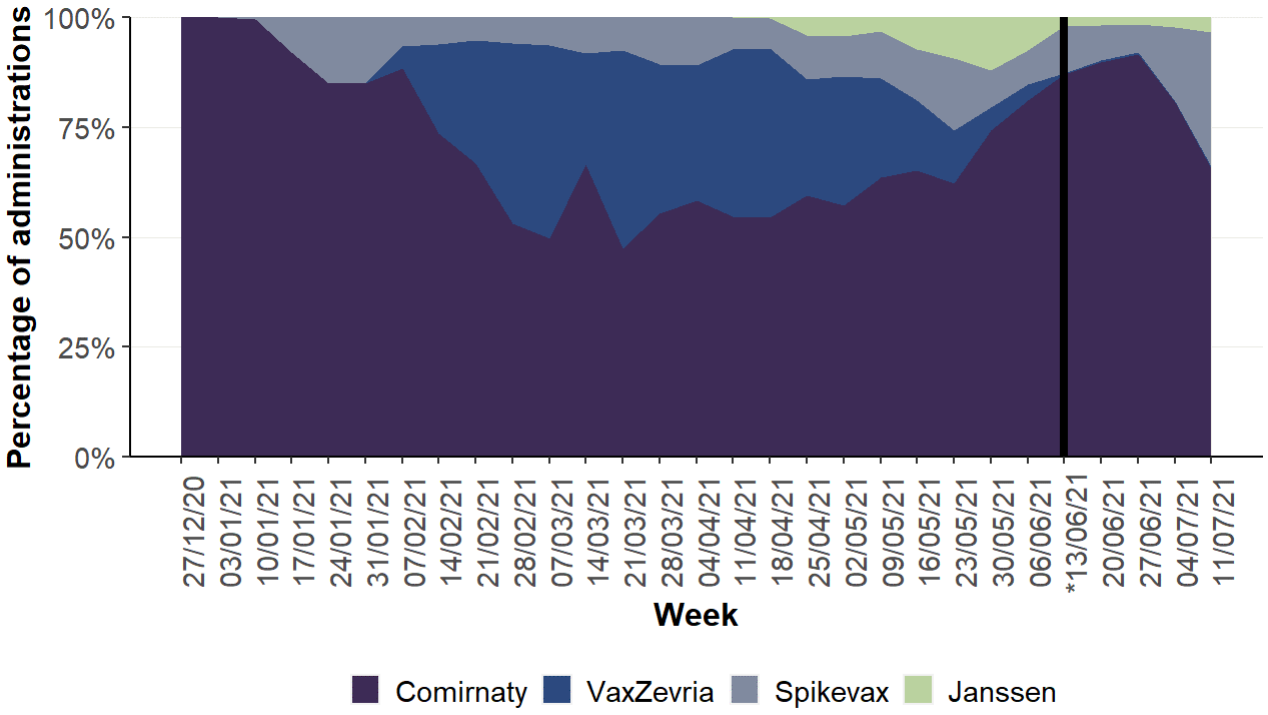
Figures 8 and 9 show an increasing number of doses of Comirnaty and Spikevax administered and a decreasing number of doses of Janssen and Vaxzevria administered.

Figure 8. Number of administration of first/single dose by vaccination week and vaccine brand (overall population N=33,218,557)



*latest vaccination date included in the study

Figure 9. Percentage distribution of administration of first/single dose by vaccination week and vaccine brand (overall population N=33,218,557)



*latest vaccination date included in the study

The incidence of COVID-19 diagnoses declines from 1.19 per 10,000 person-days in the first 14 days after the first dose to 0.60 in incompletely vaccinated persons and to 0.28 in completely vaccinated persons. A similar decrease is also observed when stratified by age, gender, geographic area, calendar period and vaccine brand (**Table 3**). It should be noted the drastic reduction of the incidence of diagnoses during the first 14 days after the first dose administration by calendar period (5.76 in January 2021 and 0.20 in the period 24 May - 13 June 2021), probably due to a progressive increase of the vaccination coverage and a consequent decrease of viral circulation. The median age of vaccinated individuals with COVID-19 diagnosis is 60 years (interquartile range, IQR 46-80), 82 years (IQR 73-87) for hospitalized cases, 78 years (IQR 70-84) for those admitted to ICU, and 86 years (IQR 81-91) for deceased cases.

The hospitalization rate in vaccinated persons before 16 May 2021 decreased from 0.27 per 10,000 person-days in the first 14 days after the first dose to 0.09 in incompletely vaccinated persons and to 0.03 in those completely vaccinated. An higher incidence in the first 14 days after the first dose of vaccine is observed in person aged over 80 year or older compared to person aged under 40 years (0.70 *vs* 0.05); the gap narrows in completely vaccinated persons (0.06 *vs* 0.01) (**Table 4**). The rate of admission to ICU shows a similar trend (**Table 5**).

The mortality rate in vaccinated persons before 16 May 2021 varies from 0.08 per 10,000 person-days in the first 14 days after the first dose to 0.01 in completely vaccinated persons. In the latter group, the mortality rate does not differ considerably by age, gender, geographical area, calendar period and vaccine brand (**Table 6**).

Table 3. Incidence rate of COVID-19 diagnoses in vaccinated persons before 13 June 2021

		Dose 1 ≤ 14 days			Incompletely vaccinated (1)			Completely Vaccinated (2)		
	Total people vaccinated	**Diagnosis**	**Person-time** (in days)	**Incidence x 10,000 person-days***	**Diagnosis**	**Person-time** (in days)	**Incidence x 10,000 person-days***	**Diagnosis**	**Person-time** (in days)	**Incidence x 10,000 person-days***
Total	27,415,442	45,632	383,524,845	1.19	42,186	706,632,220	0.60	17,977	631,073,192	0.28
Age group (years)										
<40	3,694,693	6,820	51,679,707	1.32	6,135	76,145,658	0.81	3,590	82,421,664	0.44
40-59	9,407,981	14,197	131,618,574	1.08	14,114	202,986,569	0.70	6,412	155,713,696	0.41
60-79	10,354,684	13,120	144,882,695	0.91	11,193	331,951,941	0.34	2,716	165,212,524	0.16
≥80	3,958,084	11,495	55,343,869	2.08	10,744	95,548,053	1.12	5,259	227,725,308	0.23
Gender										
Women	14,697,550	25,704	205,602,302	1.25	24,703	389,741,539	0.63	11,428	364,374,928	0.31
Men	12,717,892	19,928	177,922,488	1.12	17,483	316,890,447	0.55	6,549	266,698,195	0.25
Geographical Area										
North	14,210,196	26,801	198,766,869	1.35	21,954	367,503,310	0.60	10,311	344,861,328	0.30
Centre	3,844,695	5,669	53,790,273	1.05	5,737	101,139,616	0.57	2,669	88,533,808	0.30
South and islands	9,360,551	13,162	130,967,703	1.00	14,495	237,989,294	0,61	4,997	197,678,056	0.25
Calendar Period (first dose)										
27/12/2020-31/01/2021	1,235,239	9,915	17,226,156	5.76	5,349	27,700,032	1.93	10,871	158,477,165	0.69
01/02/2021-28/02/2021	1,501,683	5,407	20,991,716	2.58	8,055	52,604,582	1.53	3,262	116,343,993	0.28
01/03/2021-28/03/2021	3,439,673	11,606	48,083,885	2.41	15,653	154,751,917	1.01	2,326	151,458,776	0.15
29/03/2021-25/04/2021	5,829,271	10,535	81,544,043	1.29	9,266	212,204,245	0.44	1,154	141,998,765	0.08
26/04/2021-23/05/2021	7,840,158	6,027	109,721,984	0.55	3,277	199,335,537	0.16	299	55,880,894	0.05
24/05/2021-13/06/2021	7,569,418	2,142	105,957,063	0.20	586	60,035,908	0.10	65	6,913,599	0.09
Brand										
Cominarty	17,857,894	30,978	249,810,167	1.24	21,347	326,190,751	0.65	17,049	540,809,537	0.32
Spikevax	2,441,629	3,182	34,161,814	0.93	2,211	54,949,627	0.40	500	44,811,202	0.11
Vaxzevria	5,748,848	10,820	80,418,362	1.35	18,491	306,324,564	0.60	196	25,401,038	0.08
Janssen	1,083,364	473	15,163,881	0.31	-	-	-	232	20,041,813	0.12
Vaxzevria+Cominarty	241,285	156	3,376,858	0.46	115	16,345,921	0.07	0	9,147	0.00
Vaxzevria+Spikevax	42,422	23	593,764	0.39	22	2,821,358	0.08	0	455	0.00

(1) Vaccinated persons who received only the first dose of a two-dose vaccine (Comirnaty, Spikevax and Vaxzevria vaccines) after 14 days, or who received the second dose from ≤14 days

(2) Vaccinated persons who received the second dose (Comirnaty, Moderna and Vaxzevria) or single dose (COVID-19 Vaccine Janssen) after at least 14 days

* Number of diagnoses/person-time

Table 4. Incidence rate of hospitalization in vaccinated persons before 16 May 2021

		Dose 1 ≤ 14 days			Incompletely Vaccinated (1)			Completely Vaccinated (2)		
	Total people vaccinated	**Hospitalizations**	**Person-time** (in days)	**Incidence x 10,000 person-days***	**Hospitalizations**	**Person-time** (in days)	**Incidenza x 10.000 giorni persona***	**Hospitalizations**	**Person-time** (in days)	**Incidence x 10,000 person-days***
Total	17,989,377	6,891	251,581,513	0.27	3,721	403,765,573	0.09	1,045	324,227,937	0.03
Age groups (years)										
<40	1,638,021	115	22,891,109	0.05	47	46,813,520	0.01	32	49,844,252	0.01
40-59	3,982,477	619	55,673,477	0.11	233	103,090,380	0.02	104	84,753,017	0.01
60-79	8,524,867	2,416	119,269,577	0.20	937	167,856,528	0.06	142	61,561,059	0.02
≥80	3,844,012	3,741	53,747,350	0.70	2,504	86,005,146	0.29	767	128,069,609	0.06
Gender										
Women	9,968,006	3,152	139,398,932	0.23	1,788	229,013,880	0.08	568	192,219,953	0.03
Men	8,021,371	3,739	112,182,539	0,33	1,933	174,751,528	0.11	477	132,007,967	0.04
Geographical Area										
North	9,647,154	4,693	134,894,777	0.35	2,443	212,781,855	0.11	674	179,575,130	0.04
Centre	2,467,779	765	34,516,440	0.22	523	58,533,126	0.09	181	46,231,618	0.04
South and islands	5,874,444	1,433	82,170,297	0.17	755	132,450,593	0.06	190	98,421,189	0.02
Calendar Period (first dose)										
27/12/2020-31/01/2021	1,235,109	733	17,224,606	0.43	338	27,405,376	0.12	363	124,904,092	0.03
01/02/2021-28/02/2021	1,501,623	783	20,990,953	0.37	615	50,562,738	0.12	249	75,815,021	0.03
01/03/2021-28/03/2021	3,439,566	2,235	48,082,544	0.46	1,469	130,001,758	0.11	329	79,792,112	0.04
29/03/2021-25/04/2021	5,829,192	2,369	81,543,079	0.29	1,165	150,980,659	0.08	99	41,374,912	0.02
26/04/2021-23/05/2021	5,983,887	771	83,740,332	0.09	134	44,815,043	0.03	5	2,341,800	0.02
Brand										
Cominarty	10,978,265	5,065	153,510,995	0.33	2,851	184,762,069	0.15	985	302,245,863	0.03
Spikevax	1,452,881	727	20,321,601	0.36	364	28,434,132	0.13	54	18,006,191	0.03
Vaxzevria	5,026,433	1,069	70,306,243	0.15	501	177,693,336	0.03	0	1,375,704	0.00
Janssen	248,223	28	3,473,902	0.08	-	-	-	6	2,600,179	0.02
Vaxzevria+Cominarty	241,174	2	3,375,304	0.01	5	10,989,210	<0.01			
Vaxzevria+Spikevax	42,401	0	593,470	0.00	0	1,886,827	0.00			

(1) Vaccinated persons who received only the first dose of a two-dose vaccine (Comirnaty, Spikevax and Vaxzevria vaccines) after 14 days, or who received the second dose from ≤14 days

(2) Vaccinated persons who received the second dose (Comirnaty, Moderna and Vaxzevria) or single dose (COVID-19 Vaccine Janssen) after at least 14 days

* Number of diagnoses/person-time

Table 5. Incidence rate of admission in ICU in vaccinated persons before 16 May 2021

		Dose 1 ≤ 14 days			Incompletely Vaccinated (1)			Completely Vaccinated (2)		
	Total people vaccinated	**Admissions in ICU**	**Person-time** (in days)	**Incidence x 10,000 person-days**	**Admissions in ICU**	**Person-time** (in days)	**Incidence x 10,000 person-days**	**Admissions in ICU**	**Person-time** (in days)	**Incidence x 10,000 person-days**
Total	17,989,759	763	251,586,192	0.03	278	403,770,679	0.01	50	324,232,496	<0.01
Age group (years)										
<40	1,638,049	4	22,891,408	<0.01	1	46,813,764	<0.01	0	49,844,701	0.00
40-59	3,982,546	64	55,674,344	0.01	17	103,091,251	<0.01	7	84,754,367	<0.01
60-79	8,524,946	387	119,270,506	0.03	102	167,857,553	0.01	9	61,561,667	<0.01
≥80	3,844,218	308	53,749,934	0.06	158	86,008,112	0.02	34	128,071,761	<0.01
Gender										
Women	9,968,219	257	139,401,609	0.02	115	229,016,762	0.01	25	192,222,896	<0.01
Men	8,021,540	506	112,184,541	0.05	163	174,753,752	0.01	25	132,009,583	<0.01
Geographical Area										
North	9,647,441	522	134,898,285	0.04	186	212,785,516	0.01	19	179,579,127	<0.01
Centre	2,467,845	96	34,517,206	0.03	46	58,533,994	0.01	17	46,232,147	<0.01
South and islands	5,874,473	145	82,170,702	0.02	46	132,451,170	<0.01	14	98,421,222	<0.01
Calendar Period (first dose)										
27/12/2020-31/01/2021	1,235,238	56	17,226,068	0.03	23	27,406,885	0.01	17	124,907,249	<0.01
01/02/2021-28/02/2021	1,501,683	96	20,991,688	0.05	54	50,563,812	0.01	9	75,815,653	<0.01
01/03/2021-28/03/2021	3,439,673	262	48,083,843	0.05	98	130,003,137	0.01	17	79,792,688	<0.01
29/03/2021-25/04/2021	5,829,271	245	81,544,026	0.03	85	150,981,723	0.01	7	41,375,106	<0.01
26/04/2021-23/05/2021	5,983,908	104	83,740,568	0.01	18	44,815,124	<0.01	0	2,341,800	0.00
Brand										
Cominarty	10,978,595	537	153,514,998	0.03	209	184,766,270	0.01	47	302,250,295	<0.01
Spikevax	1,452,912	58	20,322,004	0.03	19	28,434,637	0.01	3	18,006,318	<0.01
Vaxzevria	5,026,454	162	70,306,516	0.02	50	177,693,736	<0.01	0	1,375,704	0.00
Janssen	248,223	6	3,473,902	0.02				0	2,600,179	0.00
Vaxzevria+Cominarty	241,174	0	3,375,304	0.00	0	10,989,210	0.00			
Vaxzevria+Spikevax	42,401	0	593,470	0.00	0	1,886,827	0.00			

(1) Vaccinated persons who received only the first dose of a two-dose vaccine (Comirnaty, Spikevax and Vaxzevria vaccines) after 14 days, or who received the second dose from ≤14 days

(2) Vaccinated persons who received the second dose (Comirnaty, Moderna and Vaxzevria) or single dose (COVID-19 Vaccine Janssen) after at least 14 days

* Number of diagnoses/person-time

Table 6. Mortality rate in vaccinated persons before 16 May 2021

		Dose 1 ≤ 14 giorni			Incompletely Vaccinated(1)			Completely Vaccinated(2)		
	Total people vaccinated	**Deaths**	**Person-time** (in days)	**Incidence x 10,000 person-days**	**Deaths**	**person-time** (in days)	**Incidence x 10,000 person-days**	**Deaths**	**Person-time** (in days)	**Incidence x 10,000 person-days**
Total	17,989,773	2,046	251,586,353	0.08	1,188	403,770,813	0.03	321	324,232,603	0.01
Age group (years)										
<40	1,638,049	1	22,891,408	<0.01	2	46,813,764	<0.01	1	49,844,701	<0.01
40-59	3,982,548	21	55,674,364	<0.01	18	103,091,262	<0.01	5	84,754,367	<0.01
60-79	8,524,949	424	119,270,532	0.04	174	167,857,559	0.01	28	61,561,667	<0.01
≥80	3,844,227	1,600	53,750,049	0.30	994	86,008,229	0.12	287	128,071,868	0.02
Gender										
Women	9,968,227	922	139,401,710	0.07	561	229,016,847	0.02	154	192,222,958	0.01
Men	8,021,546	1,124	112,184,601	0.10	627	174,753,801	0.04	167	132,009,628	0.01
Geographical Area										
North	9,647,454	1,358	134,898,443	0.10	755	212,785,650	0.04	211	179,579,234	0.01
Centre	2,467,845	228	34,517,206	0.07	154	58,533,994	0.03	55	46,232,147	0.01
South and islands	5,874,474	460	82,170,705	0.06	279	132,451,170	0.02	55	98,421,222	0.01
Calendar Period (first dose)										
27/12/2020-31/01/2021	1,235,238	441	17,226,142	0.26	198	27,406,939	0.07	128	124,907,323	0.01
01/02/2021-28/02/2021	1,501,683	281	20,991,716	0.13	217	50,563,866	0.04	75	75,815,686	0.01
01/03/2021-28/03/2021	3,439,673	667	48,083,885	0.14	452	130,003,157	0.03	97	79,792,688	0.01
29/03/2021-25/04/2021	5,829,271	564	81,544,043	0.07	301	150,981,729	0.02	21	41,375,106	0.01
26/04/2021-23/05/2021	5,983,908	93	83,740,568	0.01	20	44,815,124	<0.01	0	2,341,800	0.00
Brand										
Cominarty	10,978,607	1,683	153,515,142	0.11	987	184,766,369	0.05	303	302,250,369	0.01
Spikevax	1,452,913	253	20,322,018	0.12	150	28,434,672	0.05	18	18,006,351	0.01
Vaxzevria	5,026,455	109	70,306,519	0.02	51	177,693,736	<0.01	0	1,375,704	0.00
Janssen	248,223	1	3,473,902	<0.01				0	2,600,179	0.00
Vaxzevria+Cominarty	241,174	0	3,375,304	0.00	0	10,989,210	0.00			
Vaxzevria+Spikevax	42,401	0	593,470	0.00	0	1,886,827	0.00			

(1) Vaccinated persons who received only the first dose of a two-dose vaccine (Comirnaty, Spikevax and Vaxzevria vaccines) after 14 days, or who received the second dose from ≤14 days

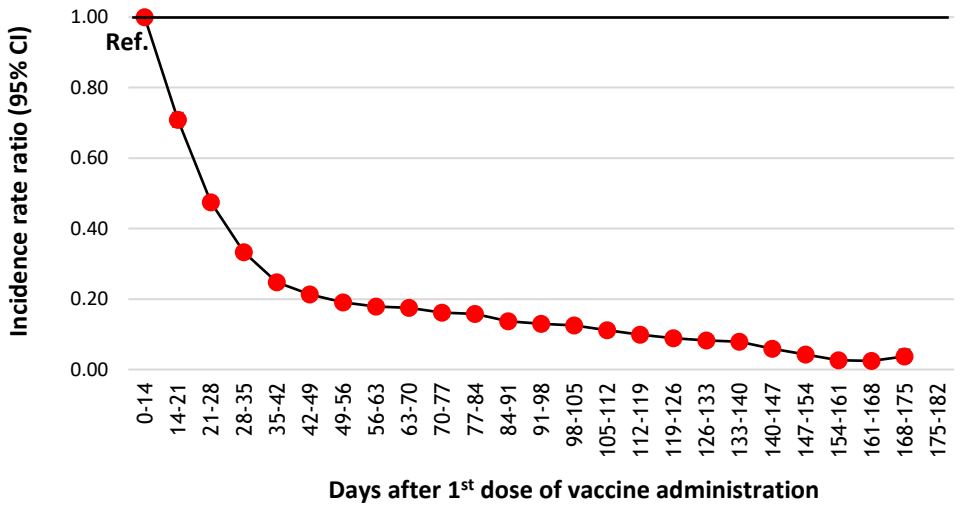
(2) Vaccinated persons who received the second dose (Comirnaty, Moderna and Vaxzevria) or single dose (COVID-19 Vaccine Janssen) after at least 14 days

* Number of diagnoses/person-time

Figures 11-19 present the results of the multivariate analyses, conducted using negative binomial models with robust variance estimator, to assess adjusted estimates of the Incidence Rate Ratio (IRR) of diagnosis, hospitalization, admission in ICU and death at different time intervals after the administration of the first and second dose of the vaccine, compared to the 0-14-day interval after the administration of the first dose (reference period). The models include the following variables: gender, age group, region of vaccination, priority vaccination group (healthcare personnel, school employees, nursing home residents, disease-affected individuals, and other priority groups), vaccine brand (Comirnaty, Spikevax, Vaxzevria and COVID-19 Vaccine Janssen), calendar week of the first dose administration and regional weekly incidence in the general population .

Figure 11 shows the estimates of the adjusted IRR of COVID-19 diagnosis in the weeks after the administration of the first dose. It should be noted that, from the 14-21-day period after the administration of the first dose, there is a progressive reduction of the IRRs reaching an adjusted IRR equal to 0.03 after 175 days.

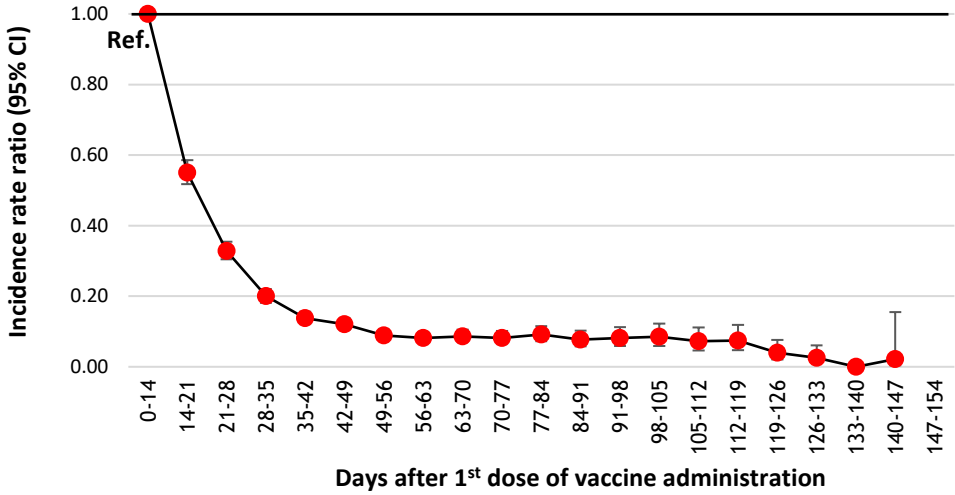
Figure 11. Adjusted estimates of the Incidence Rate Ratio of diagnosis at different time intervals from the administration of the first dose compared to the reference period (0-14 days from the first dose) (N=27,415,442)



Note: The model takes into account the following: weeks elapsed from vaccination, weekly incidence rate in local population, age group, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g., intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to the viral circulation within the community.

Figure 12, similarly to **Figure 11**, shows the estimates of the adjusted IRR of hospitalization in the weeks after the administration of the first dose. There is a progressive reduction of the IRRs from the 14-21-day period after the administration of the first dose, reaching an IRR equal to 0.02 after 147 days.

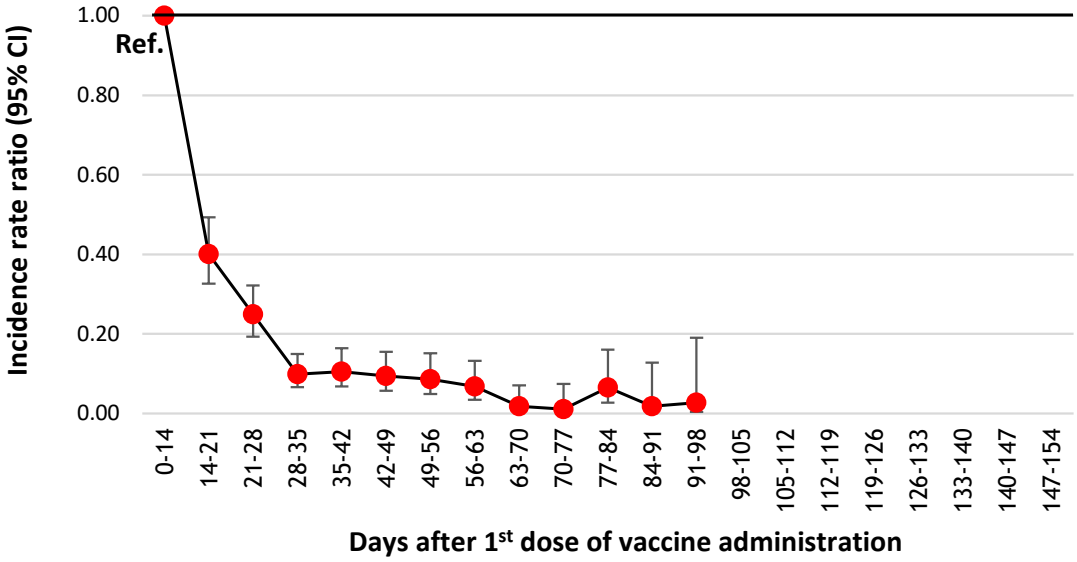
Figure 12. Adjusted estimates of the Incidence Rate Ratio of hospitalization at different time intervals from the administration of the first dose compared to the reference period (0-14 days from the first dose) (N=17,989,377)



Note: The model takes into account: weeks elapsed from vaccination, weekly incidence rate in local population, age group, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g., intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to the viral circulation within the community.

Figure 13 shows the relative risks of admission into intensive care in the weeks following the inoculation with the first dose. A swift reduction can be observed 14 days after the administration of the first dose, which reaches a value of 0.03 after 98 days.

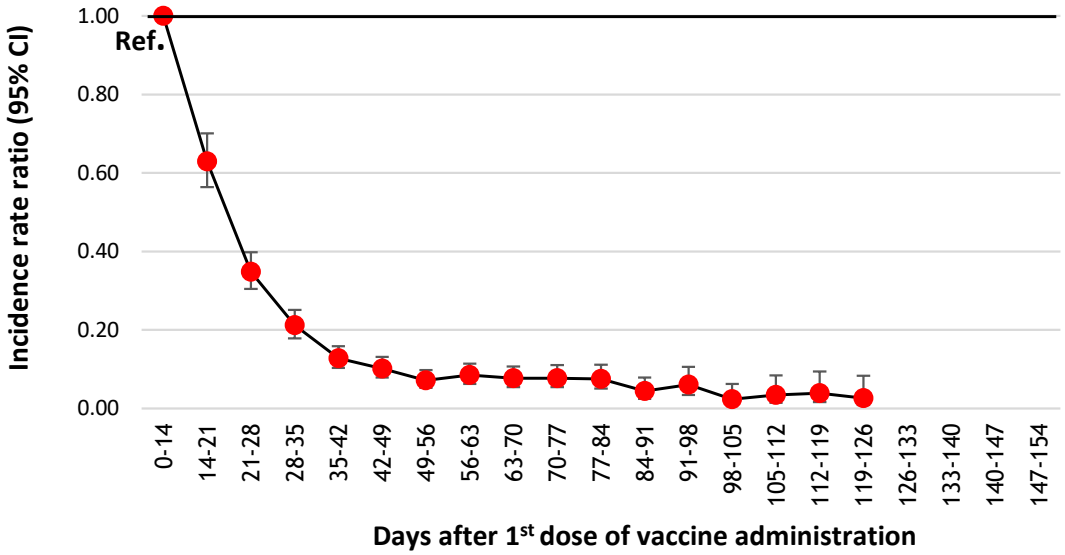
Figure 13. Adjusted estimates of the Incidence Rate Ratio of admission in ICU at different time intervals from the administration of the first dose compared to the reference period (0-14 days from the first dose) (N=17,989,759)



Note- *The model takes into account: weeks elapsed from vaccination, weekly incidence rate in local population, age group, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.*
** The risk reduction recorded from 98 to 147 days after the inoculation with the first dose has not been estimated since the data related to this time interval were not sufficiently consolidated.*

Figure 14 shows the relative risks of death in the weeks following the inoculation with the first dose. The trend is basically in line with the results shown in **Figures 11-13** with an incidence rate ratio which starts decreasing in the second week from the administration of the first dose, reaching a value of 0.03 after 126 days.

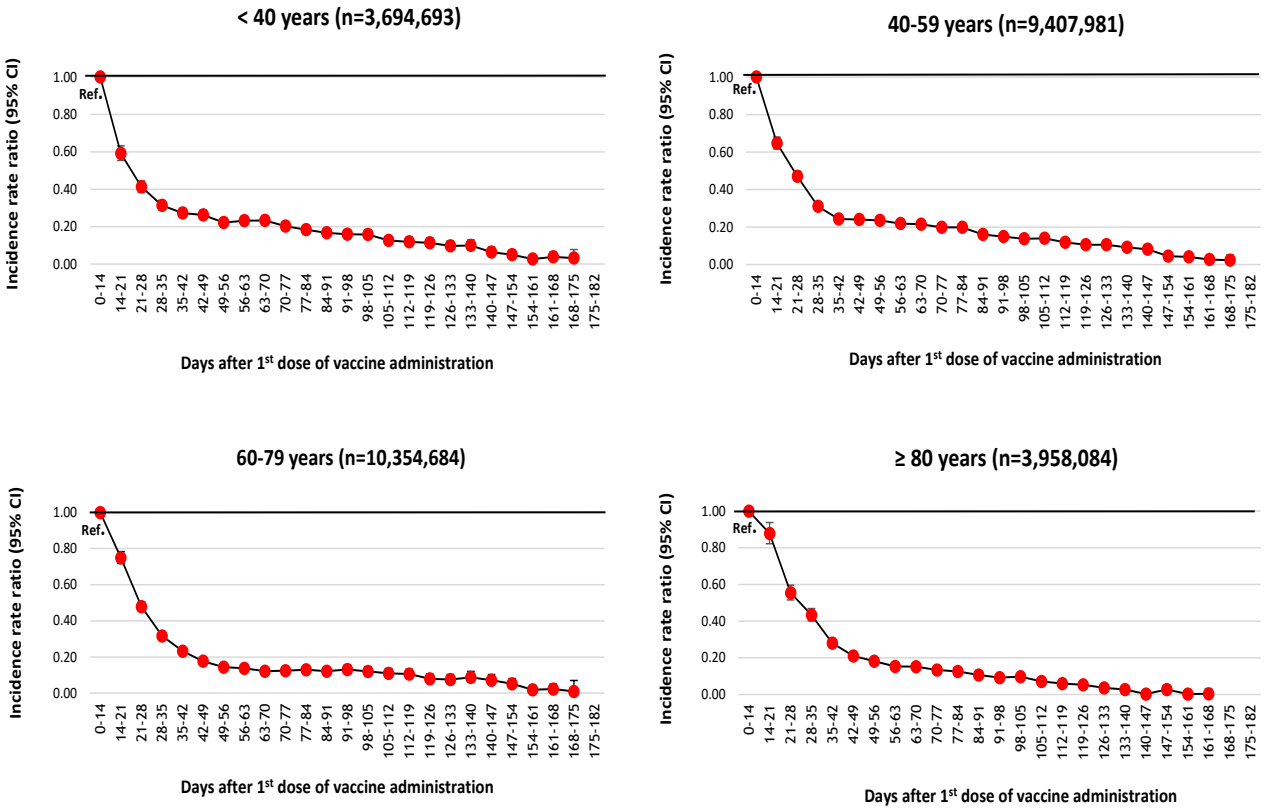
Figure 14. Adjusted estimates of the Incidence Rate Ratio of death at different time intervals from the administration of the first dose compared to the reference period (0-14 days from the first dose) (N=19,989,773)



Note - *The model takes into account: weeks elapsed from vaccination, weekly incidence rate in local population, age group, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.*
* The risk reduction recorded from 126 to 147 days after the inoculation with the first dose has not been estimated since the data related to this time interval were not sufficiently consolidated.

The stratified analysis by age group shows a similar trend in all age groups with the incidence rate ratio of diagnosis reaching a value of ≤0.03 at about 170 days from the first dose administration in all age groups (**Figure 15**).

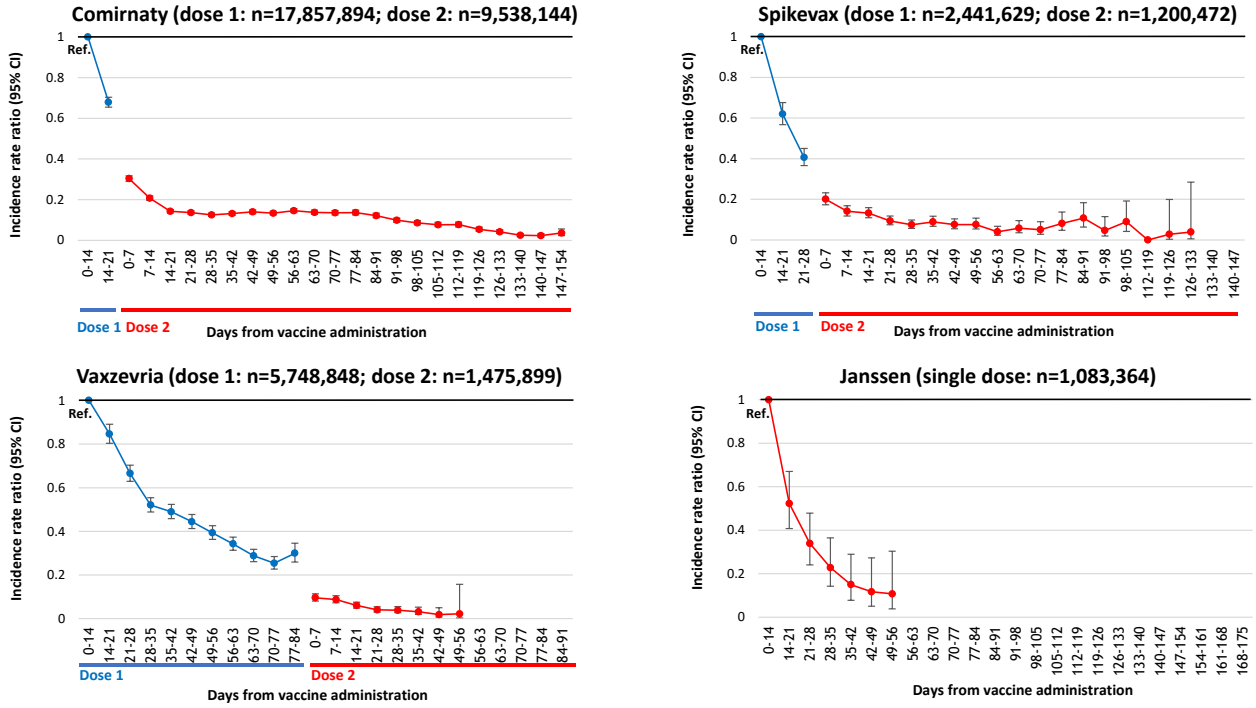
Figure 15. Adjusted estimates of the Incidence Rate Ratio of diagnosis at different time intervals from the administration of the first dose compared to the reference period (0-14 days from the first dose) by age group



Note: The model takes into account: weeks elapsed from vaccination, weekly incidence rate in local population, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.

The analysis by vaccine brand and dose shows, for all vaccines, a reduced IRR of diagnosis from the second week after the first dose or single dose administration. IRR decreases substantially after the second dose administration reaching a value of about 0.05 at the end of the observation period, without a relevant loss of efficacy over time (**Figure 16**).

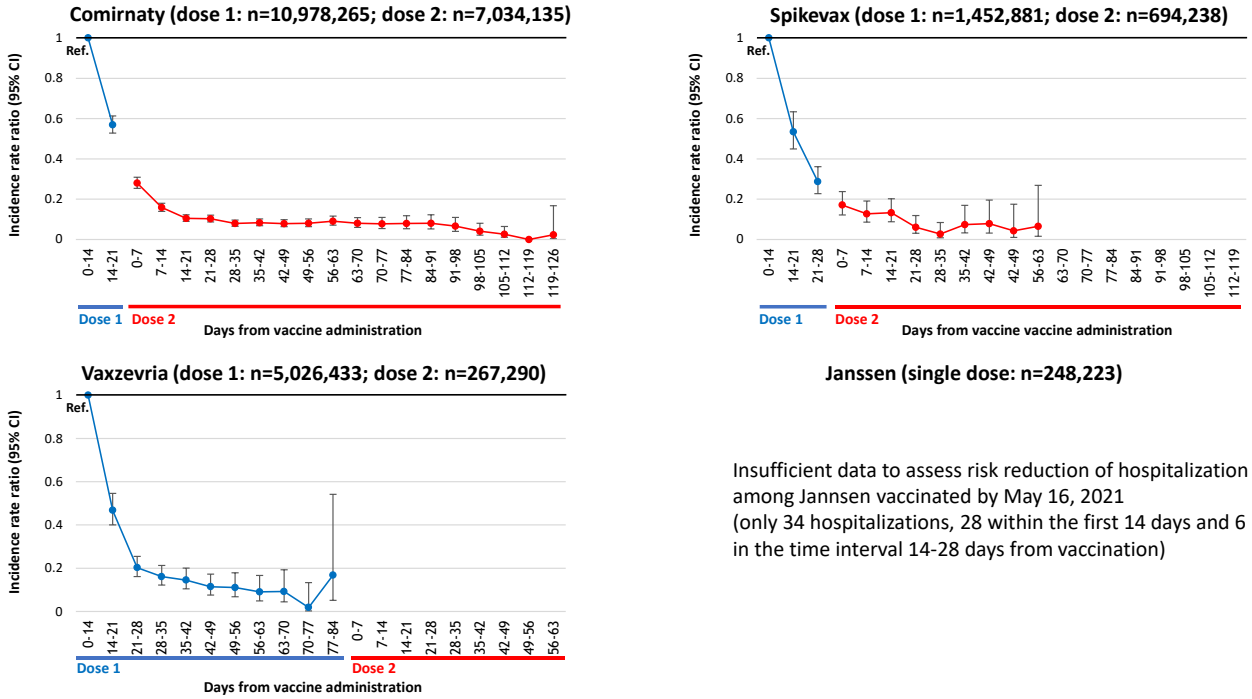
Figure 16. Adjusted estimates of the Incidence Rate Ratio of diagnosis at different time intervals from the administration of the first and second dose compared to the reference period (0-14 days from the first dose) by vaccine brand



Note: The model takes into account the following: weeks elapsed from vaccination, weekly incidence rate in local population, gender,region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.
The end of the observation period on the x-axis reflects the maximum number of days elapsed from the start of the vaccination campaign, according to the selection criteria of the study population presented in Figure1 (considering the total number of days elapsed from the first and second dose). The early truncation of the observation period for Spikevax, Vaxzevria and Janssen vaccines depends on the fact that they were authorized and then used after the launching of the vaccination campaign, which started with the Comirnaty vaccine alone.

The analysis of the IRR of hospitalization for Comirnaty and Spikevax vaccines shows similar results to those presented in Figure 16 (**Figure 17**). The IRR for the Vaxzevria vaccine, due to short observation period available after the administration of the second dose, was estimated only in the weeks after the first dose (IRR< 0.20 after 21 days from the administration).

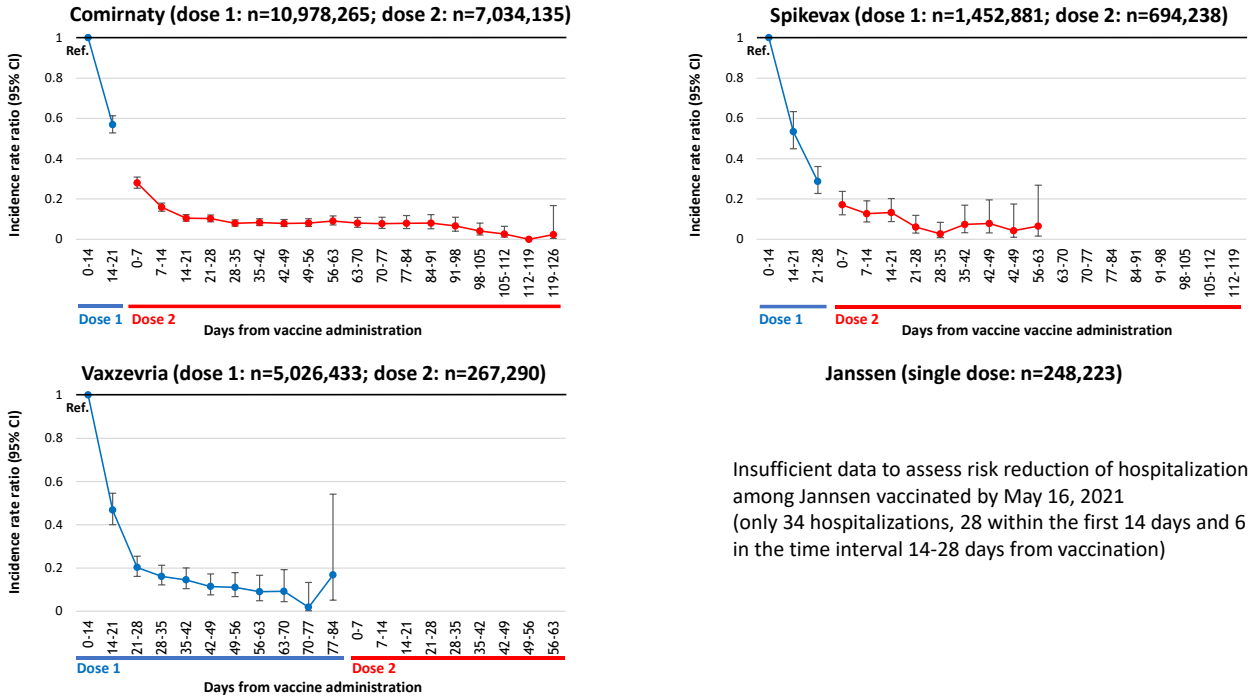
Figure 17. Adjusted estimates of the Incidence Rate Ratio of hospitalization at different time intervals from the administration of the first and second dose compared to the reference period (0-14 days from the first dose) by vaccine brand



Note: The model takes into account the following: weeks elapsed from vaccination, weekly incidence rate in local population, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.
The end of the observation period (as shown on the x-axis) reflects on the maximum number of days passed from the start of the vaccination campaign, according to the selection criteria of the study population presented in Figure1 (considering the total number of days elapsed from the first and second dose).The early truncation of the observation period for Spikevax, Vaxzevria and Janssen vaccines is due to the fact that they were authorized and then used after the launching of the vaccination campaign which started with the Comirnaty vaccine alone (in addition to that, data were not sufficiently consolidated for some of the last weeks to allow for an estimate to be made).

The analysis regarding the Comirnaty vaccine shows a reduction in the IRR of admission in ICU of more than 90% after 7 days from the administration with the second dose (**Figure 18**). A similar trend was also observed for the Spikevax and Vaxzevria vaccines, however it must be noted that estimates are uncertain due to the low number of study events and the short observation period, which also made it impossible to estimate the IRR after the second dose of the Vaxzevria vaccine or the first dose of the Janssen vaccine.

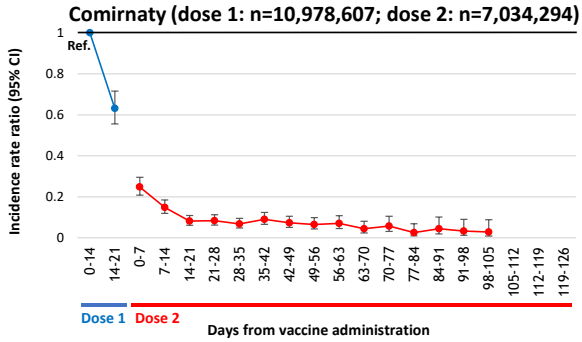
Figure 18. Adjusted estimates of the Incidence Rate Ratio of admission in intensive care at different time intervals from the administration of the first and second dose compared to the reference period (0-14 days from the first dose) by vaccine brand

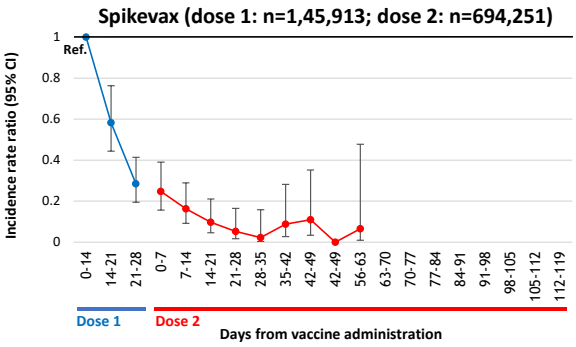


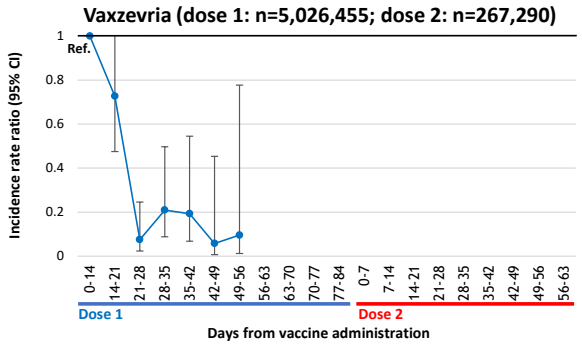
Note: The model takes into account the following: weeks elapsed from vaccination, weekly incidence rate in local population, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.
The end of the observation period (as shown on the x-axis) reflects the maximum number of days passed from the start of the vaccination campaign, according to the selection criteria of the study population presented in Figure1 (considering the total number of days elapsed from the first and second dose). The early truncation of the observation period for the Spikevax, Vaxzevria and Janssen vaccines is due to the fact that they were authorized and then used after the launching of the vaccination campaign which started with the Comirnaty vaccine alone (in addition to that, data were not sufficiently consolidated for some of the las weeks to allow for an estimate to be made).

Finally, the analysis regarding Comirnaty and Spikevax shows a reduction of the risk of death higher than 90% after 14 days from the second dose administration (**Figure 19**). Regarding Spikevax and Vaxzevria, although we observed an overall reduction in the risk of death after vaccination, it must be noted that the estimates are uncertain due to the low number of study events and the short observation period, which, as for the analysis of hospitalizations and admissions to ICU, made it impossible to estimate the IRR after the second dose of the Vaxzevria vaccine or the first dose of the Janssen vaccine.

Figure 19. Adjusted estimates of the Incidence Rate Ratio of deaths at different time intervals from the administration of the first and second dose compared to the reference period (0-14 days from the first dose) by vaccine brand







Janssen (unica dose: n=248,223)

Insufficient data to assess risk reduction of death among Jannsen vaccinated by May 16, 2021
(only 1 death within the first 14 days from vaccination)

Note: The model takes into account the following: weeks elapsed from vaccination, weekly incidence rate in local population, gender, region of vaccination, vaccination priority group, and brand. The week-from-administration adjustment assumes that within every group, a chronological order was followed in the administration of vaccines for those with higher levels of exposure (e.g. intensive care healthcare professionals were vaccinated before those employed in other departments). The adjustment by weekly incidence rate in the local population takes into consideration that in different calendar periods the risk of infection varies according to viral circulation within the community.
The end of the observation period (as shown on the x-axis) reflects the maximum number of days passed from the start of the vaccination campaign, according to the selection criteria of the study population presented in Figure1 (considering the total number of days elapsed from the first and second dose). The early truncation of the observation period for the Spikevax, Vaxzevria and Janssen vaccines is due to the fact that they were authorized and then used after the launching of the vaccination campaign which started with the Comirnaty vaccine alone (in addition to that, data were not sufficiently consolidated for some of the las weeks to allow for an estimate to be made).

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Further notes for a correct interpretation of the results

To properly understand the timeline of the events described in the report, it is important to consider that the time intervals do not exactly reflect the time elapsed between vaccination and the moment when the infection was contracted. These intervals do not take into account the incubation period of the disease (5 days on average; IQR: 3-7, based on literature data), possible delays in accessing diagnostic tests after the onset of symptoms (2 days on average; IQR: 1-4 for symptomatic cases in the January-February 2021 period), and the time needed to make the diagnosis (1 day on average; IQR: 0-1 for cases in the January-February 2021 period).

It should also be pointed out that because of prevention departments being subject to strong pressure, there may have been delays in the notification and timely updating of the data regarding the cases entered in the integrated surveillance system, as well as possible errors while recording the vaccinations into the National Vaccination Registry of the Ministry of Health thus underestimating the most recent data. It is for this reason that the analyses have been carried out only the events observed up until mid-May.

Any inconsistent data at the time of extraction were excluded from the analyses of this report (e.g. vaccination dates prior to the start of the vaccination campaign, vaccination dates after the data extraction date, doses other than the first or second dose, second doses without a first dose, etc.). Furthermore, since the data contained in this report are the result of a deterministic record linkage between the National Vaccination Registry and the SARS-CoV-2 positive case database by means of a unique identifier, any errors present in the identifier may not allow the linkage between some of the records contained in the two datasets.

The data contained in the National Vaccination Registry and in the integrated surveillance system are constantly being consolidated, and as expected in an emergency situation, some information may be incomplete. As a result, the number of vaccinated individuals and the number of COVID-19 cases relating to the most recent period must be considered as provisional.

When reading the results of this report, it is proper to consider that the different vaccines were made available at different times. Consequently, the vaccines which were used last may not have just as yet a sufficiently ample time to observe a given event.