Original Article

The impact of COVID-19 vaccination programme in the Republic of San Marino: Focus on effectiveness of Gam-Covid-Vac

Giuseppe Tonnara [1], Pierluca Piselli [2, *], Claudia Cimaglia [2], Massimo Arlotti [1], Elena Sacchini [1], Samanta Manoni [1], Antonio Zani [1], Fausto Muccioli [1], Anna Laderchi [1], Sergio Rabini [1], Andrea Antinori [2], Francesco Vaia [2], Emanuele Nicastri [2], Enrico Girardi [2]

[1] Istituto per la Sicurezza Sociale, San Marino
[2] Istituto Nazionale per le Malattie Infettive "L. Spallanzani", IRCCS, Rome, Italy

ABSTRACT

Objective: The adenovirus-based vaccine Gam-COVID-Vac (Sputnik V) showed promising effectiveness in a phase 3 clinical trial; however, data concerning its impact at a population level are scarce. The Republic of San Marino (RSM) conducted a SARS-CoV-2 vaccination programme mainly based (>80%) on Gam-COVID-Vac. Our aims were to investigate the impact of Gam-COVID-Vac vaccination programme and its effectiveness in a retrospective observational study based on the entire RSM population aged ≥12 years.
Methods: We calculated the incidence rate and the vaccine effectiveness (VE) in the entire RSM population not previously infected, against SARS-CoV-2 infection and COVID-19—related hospitalization, from 25 February to 1 October 2021, considering any vaccine and separately according to the vaccine used. Vaccine effectiveness was calculated using a multivariable negative binomial regression model as 1-Incidence Rate Ratio.
Results: During the study period, 21 568/28 791 (74.9%) not previously infected subjects received at least one dose of the Gam-COVID-Vac (84%) or BNT162b2, vaccines with 98% completing the vaccination schedule. Overall, 1634 SARS-CoV-2 infections and 166 COVID-19-related hospitalizations were observed with 17 COVID-19-related deaths reported. Incidence rates of SARS-CoV-2 infection and COVID-19-related hospitalization were 7.11 and 0.49/100 000 person-days in the fully vaccinated population, respectively. The adjusted overall VE was 67.6% (95% CI: 61.8—72.5) against SARS-CoV-2 infection and 87.9% (95% CI: 77.4—93.5) against COVID-19-related hospitalizations.
Gam-COVID-Vac against SARS-CoV-2 infection VE peaked 91.8% (95% CI: 86.3—95.1) in the first bimester from the second dose, declining to 57.8% (95% CI: 42.2—69.2) at 6 months. Protection against hospitalization with COVID-19 was overall 91.6% (95% CI: 81.5—96.2), with no relevant waning trend over time.
Discussion: Our study demonstrated the effectiveness of overall vaccination (Gam-COVID-Vac [84%] and BNT162b2 [16%]) in the prevention SARS-CoV-2 infection (pre-*Omicron* variant), waning over time but still with sustainable effectiveness against COVID-19-related hospitalization in the Republic of San Marino. **Giuseppe Tonnara, Clin Microbiol Infect 2022;■:1**

Introduction

Vaccine development against SARS-CoV-2 received unprecedented efforts since the early stages of the COVID-19 pandemic [1].

As of May 2022, >11 billion vaccine doses were administered worldwide [2], and several observational studies have analysed real world effectiveness of vaccines against SARS-CoV-2 [3].

Gam-COVID-Vac (also referred to as Sputnik V, Gamaleya Research Institute) is a vaccine based on two recombinant adenovirus (rAd26-S and rAd5-S) vectors, both carrying the gene for full-length SARS-CoV-2 spike protein, administered intramuscularly 21 days apart [4], which showed 91.6% efficacy with a reassuring

* Corresponding author. Pierluca Piselli, Dipartimento di Epidemiologia e Ricerca Pre-Clinica, Istituto Nazionale per le Malattie Infettive "L. Spallanzani," Via Portuense, 292, 00149 Rome, Italy.
E-mail address: pierluca.piselli@inmi.it (P. Piselli).

safety profile in phase 3 trial [5]. Gam-COVID-Vac is still under review by WHO and EMA; nonetheless, it has been used in >70 countries [6]. However, data concerning the impact of vaccination programs in which Gam-COVID-Vac has been used are still scarce [7].

The Republic of San Marino (RSM) is a small landlocked state located in the north-central Italian peninsula, with a population of 33 909 inhabitants [8]. Its public and universalistic Health System assists all RSM residents. On 25 February 2021, RSM started the COVID-19 vaccination campaign. BNT162b2 (Comirnaty; Pfizer-BioNTech, Mainz, Germany) vaccine was administered to selected population groups, whereas Gam-COVID-Vac was offered to the general population and was administered to >80% of vaccinated persons.

The present study was conducted to assess the impact of this vaccination campaign until the initiation of booster campaign in late October 2021 and its effectiveness, in terms of protection from SARS-CoV-2 infection and COVID-19-related hospitalization.

Methods

A retrospective observational study was conducted using data on the entire RSM Health System assisted population aged ≥12 years. The study period spanned from 25 February 2021 to 1 October 2021.

The data on all enrolled individuals included information on demographics, vaccinations, documented SARS-CoV-2 infections, hospitalizations, and death. Data were fully deidentified to the researchers.

The details on vaccine rollout and public health measures adopted in RSM to contain the pandemics are provided in the Supplementary appendix.

The study was approved by the RSM Ethical Committee (decision n. 58/2021).

Vaccination exposure status definition

At baseline, all RSM Health System–assisted individuals aged ≥12 years were included in the unvaccinated cohort; we excluded those with a previous SARS-CoV-2-diagnosed infection, ascertained by PCR or validated antigen test on nasopharyngeal swabs, and those receiving any COVID vaccine before the start of RSM vaccination campaign.

The exposure status changed over time; according to vaccination received, subjects were dynamically categorized as unvaccinated (no doses received), within 13 days from first dose, partially vaccinated (≥14 days from first dose and up to 6 days from second dose), or fully vaccinated (≥7 days after second dose). Time at risk in each status was accrued according to the above defined classification.

Study endpoints (infection, hospitalization)

Each study subject was considered to be at risk of the outcome of interest (i.e. documented laboratory-confirmed SARS-CoV-2 infection, as well as any COVID-19-related hospitalizations) from the beginning of the study until the first occurrence of any of the following events: outcome of interest, death, 180 days from second dose, or end of study.

Among SARS-CoV-2-infected subjects, those who needed acute-care hospitalization within 30 days because SARS-CoV-2 infection were considered COVID-19-related hospitalizations. The COVID-19 hospitalizations were further classified as critical cases if admitted to an intensive care unit (ICU). The COVID-19-related deaths were defined as those occurring in a confirmed COVID-19 case unless there is a clear alternative cause of death (e.g. trauma). All of these classifications followed the World Health Organization guidelines [9,10], and assessments were made by trained medical personnel using individual chart reviews.

Statistical analysis

The continuous variables were expressed as medians and interquartile ranges. The categorical variables were summarized as counts and percentages. The comparisons between groups were performed using the Mann-Whitney U test for continuous variables or the χ^2 test for categorical variables.

The COVID-19 trends in incidence and hospitalization rate as well as mortality were analysed globally and by sex, age group, vaccine used, and vaccination status.

A negative binomial regression model (nbreg command in STATA), better suited for over-dispersion of variance than the traditional Poisson regression method, was used to derive incidence rate ratios (IRRs) with 95% CIs for each outcome, comparing incidence in those fully vaccinated (overall or with Gam-COVID-Vac only) with that observed in unvaccinated, using exposure command to account for varying patient days across strata. Vaccine effectiveness (VE) was calculated as (1 − IRR) and expressed as relative percentages [11].

In the multivariable model, IRRs were adjusted for sex, age group, and for calendar period (February–March, April–June, and July–September) to account for differences over time in COVID-19 incidence and public health restriction applied in Italy [12] and RSM, as detailed in the Supplementary material.

To assess the effectiveness of full vaccination, contributions of subjects in the partial vaccination status were excluded. Vaccine product–specific estimates excluded the contribution of those who received a different COVID-19 vaccine after the first dose of a given vaccine. Because Gam-COVID-Vac was not offered to persons aged 12 to 17, these subjects were excluded from Gam-COVID-Vac VE estimates.

The VE was calculated overall, according to age group and time from full vaccination (within 59 days, ≤119 days, and ≤180 days from second dose).

To compare our findings with data collected in other studies when the *Alpha* variant of concern (VoC), was prevalent (i.e. 25 February– 4 July 2021), we performed a subanalysis of VE limited to this period.

All statistical analyses were performed using STATA release 17 (StataCorp LLC, College Station, TX).

Results

Study population and cohorts

A total of 32 126 persons aged ≥12 years assisted by the RSM Health System as of 1 January 2021 were considered for inclusion in the study population. A total of 3335 (10.4%) individuals were excluded for the following reasons occurred before the study start: 3140 (9.8%) infected with SARS-CoV-2; 158 (0.5%) received a vaccine dose abroad; and 37 (0.1%) deceased (see flowchart in Fig. S1).

The final study population consisted of 28 791 individuals (51.2% females) with a median age of 50 years (IQR: 34–63). During the study period, 21 568 individuals (74.9%) received at least one vaccine dose: 18 109 (84.0%) received Gam-COVID-Vac and 3457

(16.0%) BNT162b2; 21 134 individuals (98.0%) completed the two-dose regimen. The median time from first to second dose was 21 days (IQR: 21−22 days), with 98.8% of individuals receiving their second dose ≤30 days after the first dose (Table S1).

Fig. 1 shows the time course of vaccine rollout, SARS-CoV-2 infection cases and corresponding incidence rates, as well as COVID-19-related hospitalization during the study period, showing a decreasing incidence of infections and hospitalizations along with increased vaccine coverage.

Overall, we registered 1634 laboratory-confirmed COVID-19 cases, 166 (10.1%) COVID-19-related hospitalizations, of which 37 (2.2%) needed access to ICU, and, overall, 17 (1.0%) COVID-19-related deaths.

Incidence of SARS-CoV-2 infection and related vaccine effectiveness

At the beginning of vaccination campaign, the weekly incidence of COVID-19 in the RSM general population was 800 per 100 000
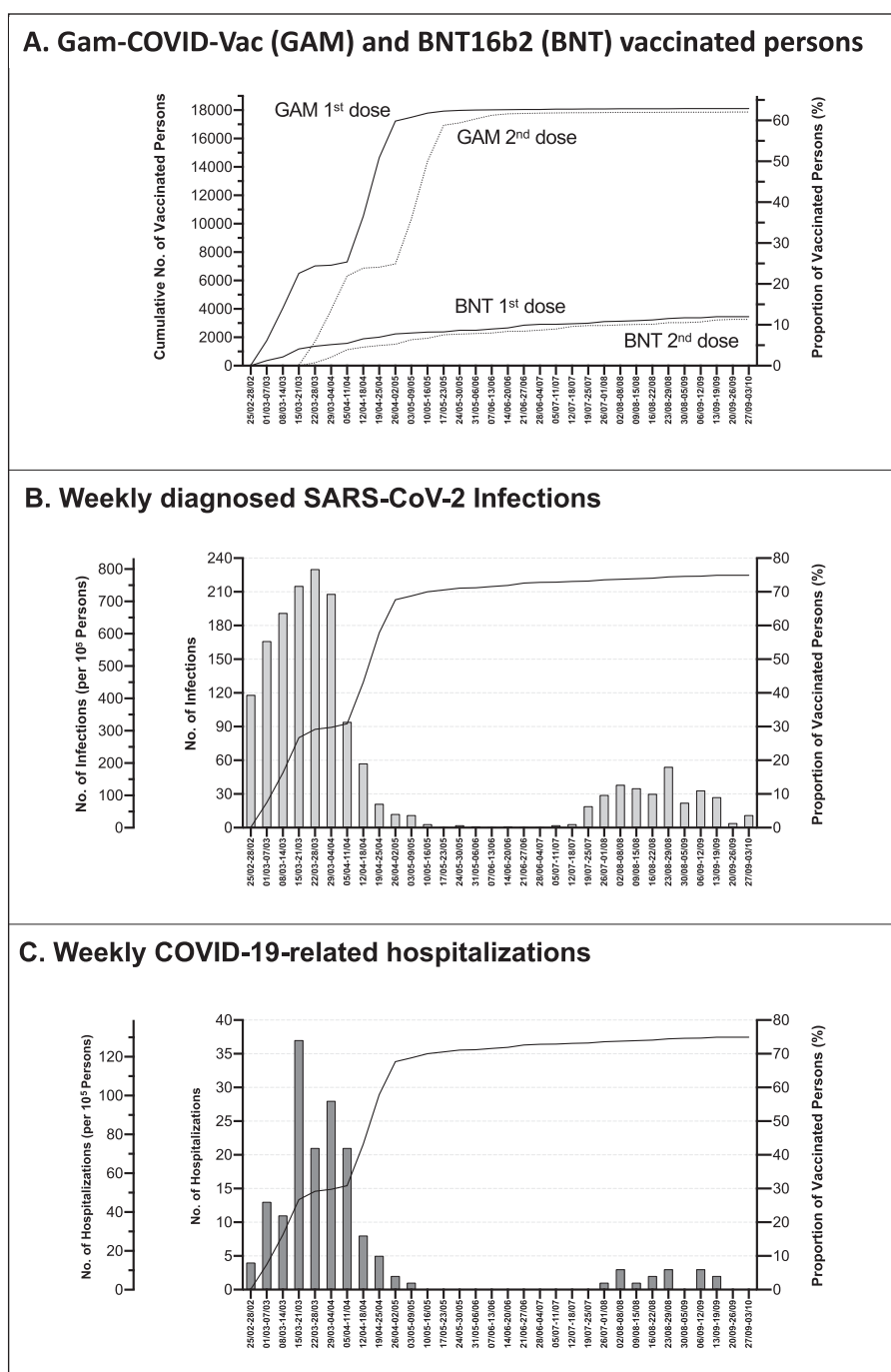
Fig. 1. Time trend of vaccinated persons (A), SARS-CoV-2 infections (B), and COVID-19-related hospitalizations (C) in Republic of San Marino. In panel A, the cumulative number of subjects who received first and second dose of any vaccine was indicated according to date. In panel B, the number of SARS-CoV-2 infections (and rate per 100 000 persons) was shown with the cumulative proportion of subjects receiving a first dose of any vaccine. Panel C similarly shows the number of COVID-19-related hospitalization (and the corresponding rate per 100 000 persons) with the cumulative proportion of subjects receiving a fist dose of any vaccine.

persons, remaining substantially stable for about a month, decreasing through April with no cases diagnosed during the second half of May, then increasing again in July.

The incidence rates of SARS-CoV-2-confirmed cases according to final vaccination status and age group are provided in Table 1, Table S2, and Fig. S2.

An adjusted vaccine effectiveness to prevent laboratory-confirmed SARS-CoV-2 infection of 67.6% was observed overall and 68.5% for those vaccinated with Gam-COVID-Vac. In the sub-analysis limited to the *Alpha*-VoC prevalent period, adjusted VE was 96.2% overall and 97.3% in those receiving Gam-COVID-Vac (Table S4).

The VE declined over time, being 88.7% within the first 60 days from the second dose (95% CI: 82.8–92.6), 51.6% (95% CI: 40.3–60.7) in the second 2-month period and 52.1% (95% CI: 36.7–63.8) in the third. Regarding Gam-COVID-Vac, adjusted VE declined from 91.8% to 57.8% (see Table 2 and Fig. 2). VE was lower in young adults, being always >70% for fully vaccinated subjects aged >60 years (overall and for those vaccinated with Gam-COVID-Vac; see Fig. 3[A]).

Incidence of COVID-19-related hospitalizations and related vaccine effectiveness

We recorded 69.46 COVID-19 hospitalizations per 100 000 persons weekly at the beginning of the study, peaking at 114.61 per 100 000 during the third week of March 2021, then declining through April, reaching zero cases during the second week of May and no further COVID-19-related hospitalizations until August.

Overall, we observed 166 (10.1%) COVID-19 cases in the study population needing hospitalization, of which 37 (2.2%) defined as critical.

The median age of inpatients was significantly higher than outpatients (71 vs 44, p < 0.001) with prevalence of male sex (60.2% vs 49.2%, p = 0.007), whereas the median age of the 37 critical inpatients was slightly lower (68 vs 72, p = 0.09).

Among 159 deaths observed during the study period, 22 were reported in SARS-CoV-2 cases (13.8%), of which 17/22 (77.3%) classified as COVID-19-related deaths: 9 observed in females

(52.9%), and all reported in inpatients. Fatal COVID-19 cases were significantly older than hospitalized who recovered (median age 88 vs 69 years, p < 0.001). Fourteen out of 17 COVID-19 related deaths (82.4%) occurred in subjects not previously vaccinated (5 admitted also in ICU), 2 in partially vaccinated individuals and 1 in a fully vaccinated subject (all of them with BNT162b2, none admitted to ICU) (see Figure S3).

Table 1 and Table S3 shows incidence of COVID-19 hospitalizations according to vaccination status.

The VE against hospitalization was overall 87.9% (95% CI: 77.4–93.5) with a limited change over time (Table 2 and Figs. 2 and 3). Similar results were observed in those vaccinated with Gam-COVID-Vac with VE = 91.6% (95% CI: 81.5–96.2).

During the *Alpha*-VoC prevalent period, VE against COVID-19-related hospitalizations was 94.2% overall and 96.9% for those vaccinated with Gam-COVID-Vac (Table S4). Overall, VE against hospitalization was <85% only for those in the 50- to 59-year-old age group (Fig. 3[B]).

Discussion

Our data described the impact of the campaign conducted with two COVID-19 vaccines in the RSM.

Like in most industrialized countries, the proportion of vaccinated people was high, reaching 70% of the eligible population in 2 months from 25 February 2021 with an excellent completion rate (98%). The progressive rollout of vaccination was accompanied by a concomitant decrease of overall SARS-CoV-2 incidence rate.

Overall, vaccination granted 67.6% effectiveness against SARS-CoV-2 infection and 87.9% reduction in COVID-19 severe clinical forms. The effectiveness against infection declined from 88.7% to 52.1% at 6 months, whereas protection against hospitalization was more robust, showing no significant waning trend over time and remaining after 120 days from full vaccination >75%.

Our study provided additional data on effectiveness of Gam-COVID-Vac, which was the most administered vaccine (84%) in RSM, with an overall 68.5% VE against SARS-CoV-2 infections and 91.6% against COVID-19-related hospitalizations.

Table 1
Incidence of SARS-CoV-2 confirmed cases according to final vaccination status during the study period (25 Feb–1 Oct 2021)

	Total cases	Unvaccinated			Fully vaccinated Any vaccine			Fully vaccinated Gam-COVID-vac		
		Cases	PDs x10^3	IR/10^5 PDs	Cases	PDs x10^3	IR/10^5 PDs	Cases	PDs x10^3	IR/10^5 PDs
SARS-CoV-2 infections										
Sex F	812	630	1147.28	54.91	102	1587.31	6.43	88	1341.74	6.56
M	822	628	1143.37	54.93	115	1463.78	7.86	98	1301.03	7.53
Age 12–17	122	116	335.97	34.53	5	81.5	6.14	—	—	—
18–49	817	650	1135.88	57.23	122	1151.26	10.6	114	1063.22	10.72
50–59	350	280	443.41	63.15	50	606.05	8.25	48	571.29	8.4
60–69	161	112	213.51	52.46	17	513.54	3.31	15	484.54	3.1
70-79	110	63	97.25	64.80	10	420.66	2.38	6	398.15	1.51
80+	74	37	64.63	57.26	13	278.09	4.67	3	125.56	2.39
Total	1634	1258	2290.65	54.92	217	3051.09	7.11	186	2642.77	7.04
COVID-19-related hospitalizations										
Sex F	66	48	1147.28	4.18	5	1587.31	0.32	1	1341.74	0.07
M	100	64	1143.37	5.60	10	1463.78	0.68	7	1301.03	0.54
Age 12–17	0	0	335.97	—	0	81.50	—	—	—	—
18–49	20	17	1135.88	1.50	1	1151.26	0.09	1	1063.22	0.09
50–59	31	25	443.41	5.64	4	606.05	0.66	4	571.29	0.70
60–69	27	18	213.51	8.43	3	513.54	0.58	2	484.54	0.41
70–79	44	28	97.25	28.79	2	420.66	0.48	0	398.15	—
80+	44	24	64.63	37.13	5	278.09	1.80	1	125.56	0.80
Total	166	112	2290.65	4.89	15	3051.09	0.49	8	2462.77	0.30

PDs x10^3 = person-days per 1000; IR/10^5 PDs = incidence rate per 100 000 person-days.

Table 2

Crude and adjusted VE% against SARS-CoV-2 infection and COVID-19 hospitalization of fully vaccination versus unvaccinated status, according to type of vaccine and age over time from vaccination
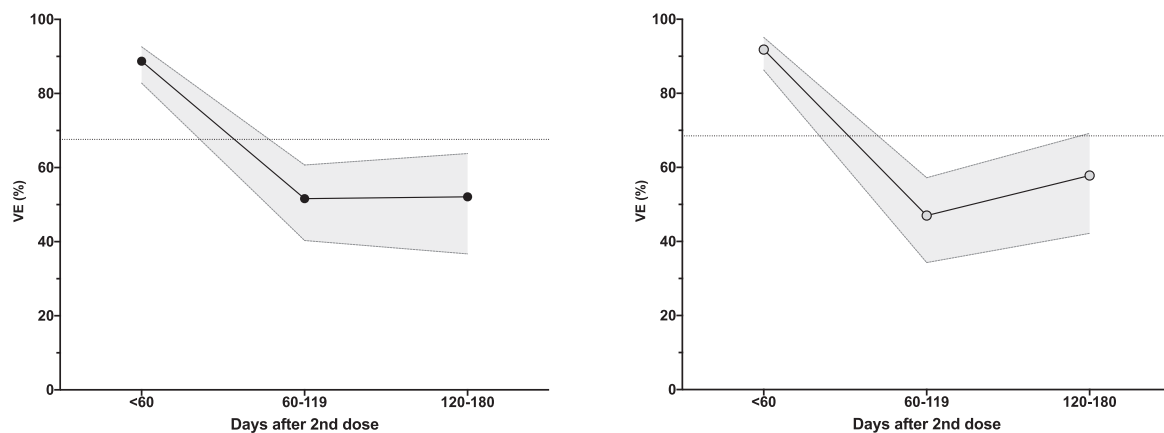
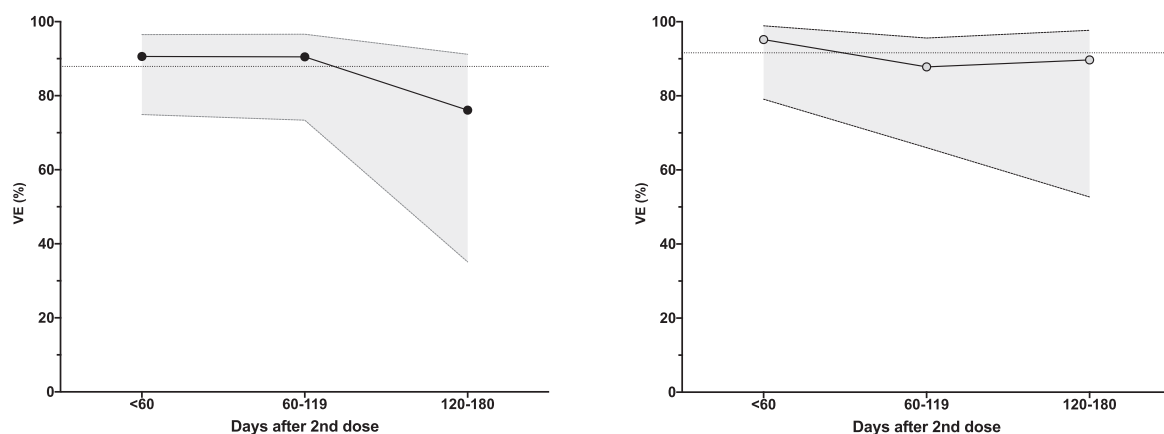|	Period	Any vaccine					Gam-COVID-vac				
		Cases*	Crude		Adjusted[a]		Cases*	Crude		Adjusted[a]	
			VE	95% CI	VE	95% CI		VE	95% CI	VE	95% CI
SARS-CoV-2 infections											
	<60 d	25	96.6	94.9–97.8	88.7	82.8–92.6	16	97.1	95.3–98.2	91.8	86.3–95.1
	60–119 d	122	84.7	81.0–87.7	51.6	40.3–60.7	117	81.1	77.1–84.4	47.0	34.3–57.2
	120+ d	70	85.5	81.1–88.9	52.1	36.7–63.8	53	85.8	81.3–89.2	57.8	42.2–69.2
	Total	217	89.3	87.2–91.0	67.6	61.8–72.5	186	89.9	87.7–91.6	68.5	62.5–73.6
COVID-19-related hospitalizations											
	<60 d	5	94.5	84.9–98.0	90.6	74.9–96.5	2	97.5	88.9–99.4	95.2	79.1–98.9
	60–119 d	4	96.2	88.4–98.7	90.5	73.4–96.6	4	95.5	86.5–98.5	87.8	66.0–95.6
	120+ d	6	89.3	71.5–95.9	76.1	35.1–91.2	2	96.2	82.5–99.2	89.7	52.7–97.7
	Total	15	94.0	88.1–97.0	87.9	77.4–93.5	8	96.4	91.6–98.4	91.6	81.5–96.2

VE, vaccine effectiveness.

*Cases reported are those observed in fully vaccinated people.

[a]Adjusted for age group, sex, calendar period (see Methods for further details).

A. Vaccine Efficacy (VE) against SARS-CoV-2 infections

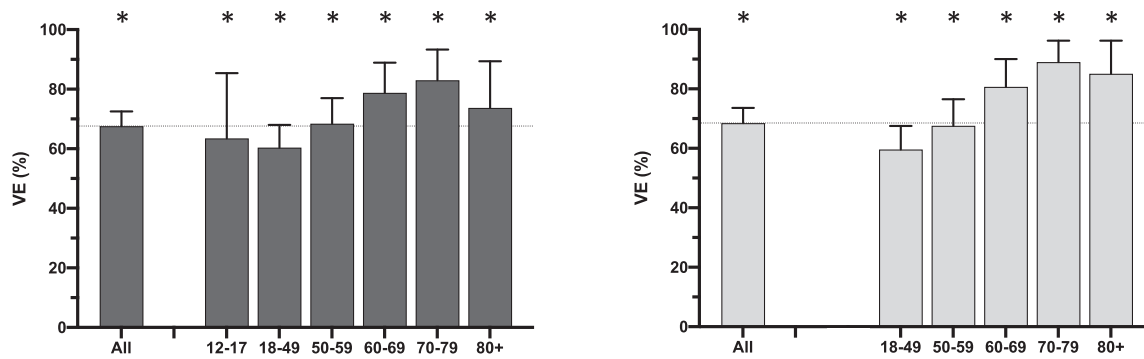## B. Vaccine Efficacy (VE) against COVID-19-related Hospitalizations

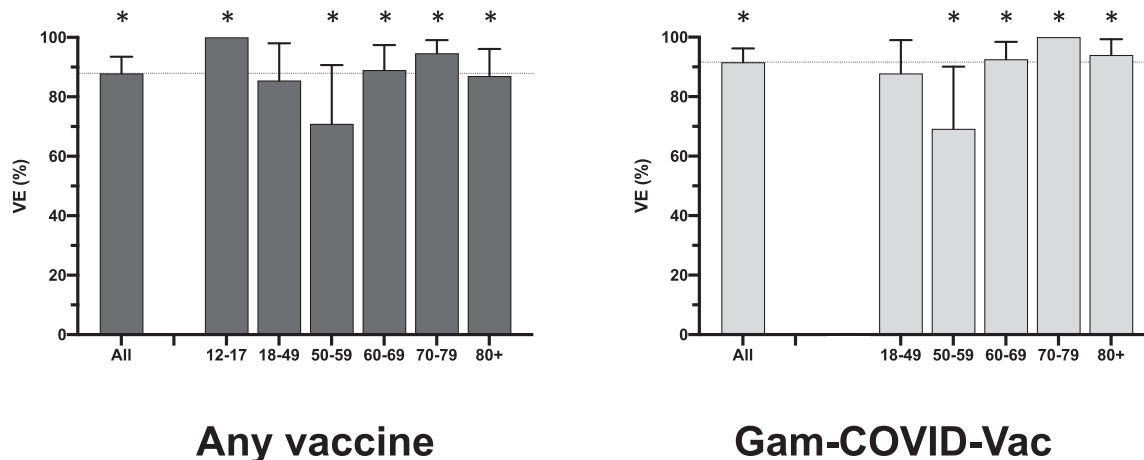**Any vaccine**   **Gam-COVID-Vac**

Fig. 2. Vaccine efficacy (VE; expressed as percentage VE%) in fully vaccinated persons versus unvaccinated individuals against SARS-CoV-2 infections (A) and COVID-19-related hospitalizations (B) in Republic of San Marino according to days from second dose (vaccine schedule completed). Left panels refer to the use of any vaccine, whereas right panels to the use of Gam-COVID-Vac. Dotted line reports the overall VE% for the specific group. The shaded areas show 95% CIs of VE.

A. Vaccine Efficacy (VE) against SARS-CoV-2 infections

B. Vaccine Efficacy (VE) against COVID-19-related Hospitalizations

Any vaccine   **Gam-COVID-Vac**

Fig. 3. Vaccine efficacy (expressed as percentage - VE% - and 95% confidence intervals) in fully vaccinated persons versus unvaccinated individuals against SARS-CoV-2 infections (A) and COVID-19-related hospitalizations (B) in Republic of San Marino according to age group. Left panels refer to the use of any vaccine, whereas right panels to the use of Gam-COVID-Vac (note that Gam-COVID-Vac was not offered for persons aged 12—17). *p < 0.05.

Our study covered a first period (February to June 2021) of *Alpha*-VoC predominant circulation, and a second period (July to September 2021) characterized by the spread of the *Delta*-VoC [13].

There are, up to now, only two population-based studies where VE of Gam-COVID-Vac was investigated. In a first study conducted in Argentina in the first trimester of 2021 [14], Gam-COVID-Vac effectiveness in preventing laboratory-confirmed infection was 78.6% and 87.6% in reducing COVID-19-related hospitalization, but the study was limited to persons aged 60 to 79.

A second nationwide study performed in Hungary [15] covering the period characterized by a high prevalence of *Alpha*-VoC (up to June 2021) estimated a Gam-COVID-Vac VE of 85.7% against SARS-CoV-2-confirmed infection and of 97.5% against fatal COVID-19.

To compare our findings with these studies, in a subanalysis limited to the period of *Alpha*-VoC circulation, VE was 97.3% against SARS-CoV-2 infection and >95% against hospitalization for those fully vaccinated with Gam-COVID-Vac consistently with the Hungarian study.

Our estimates of long-term effectiveness and waning of protection against SARS-CoV-2 infections were consistent with results

from similar studies [16—21], but no other population-based studies where Gam-COVID-Vac vaccine was used covering all populations for a longer period were conducted. A recent study from Argentina analysed risk of SARS-CoV-2 infection and of death in persons vaccinated with several vaccines including Gam-COVID-Vac with a similar trend, but the analysis, conducted with a different methodology, was limited to persons aged >60 years [22].

A study from Argentina observed that Gam-COVID-Vac elicited high titers of anti-receptor-binding domain antibodies beginning to decrease at 60 days, persisting in only 31% at 180 days [23].

The mutation occurred in the *Delta*-VoC and contributed to lower capacity of recognition by a primed immune system and a further decline of vaccine effectiveness [24,25]; in a study conducted in Russia, sera from Gam-COVID-Vac-vaccinated individuals showed a 2.5-fold significantly reduced virus-neutralizing activity against *Delta*-VoC compared to other VoCs [26].

The COVID vaccination could have induced changes in vaccinated people's behaviour, likely increasing social contacts and reducing adherence to prevention measures [27,28], and public health restrictions have been eased differently for vaccinated and

unvaccinated persons in RSM. It is likely that this phenomenon had a greater impact on young adults, explaining the reduced VE against SARS-CoV-2 infection observed in this age group.

The increased SARS-CoV-2 testing activity performed in RSM during the summer season has likely contributed to an increased identification of otherwise missed asymptomatic infections.

Despite the waning of protection against SARS-CoV-2 infection, the protection against severe forms of COVID-19 in Gam-COVID-Vac fully vaccinated peoples was >90% even 6 months from second dose, consistent with data reported for other vaccines [3].

Our study presented some limitations, such as the small size of the RSM population. Although this allowed excellent traceability of epidemiological and clinical data for all study subjects [29], we could not exclude some underreporting of SARS-CoV-2 infections diagnosed in Italy not notified to RSM.

In our analysis we excluded subjects with a confirmed SARS-CoV-2 infection diagnosed before the study period (roughly 10% of the original population). However, one can speculate that, given the high incidence of SARS-COV-2 infection in the RSM and Italy mainly in the early phases of the pandemic, the number of persons with naturally acquired immunity due to undiagnosed SARS-CoV-2 occurred before study start, and possibly vaccinated, was not negligible [30]. This could have affected the final VE estimates.

Moreover, the lower incidence observed as in many European countries in May to June 2021 could be explained not solely by the effect of vaccination but also by other factors such as warmer climate or more outdoor activity, though adjusting for calendar period was meant to deal with this possible limitation.

The available data did not include motivation of testing or the category of people being vaccinated (health care workers, other prioritized professional categories, or those with comorbidities). Accordingly, the adjustment performed based on available data cannot rule out residual confounding.

Another important limitation is that our study period does not cover the spread of the now ubiquitous *Omicron*-VoC.

Finally, the study was not designed to compare effectiveness between Gam-COVID-Vac and BNT162b2 vaccines, which was administered only in specific population groups (see Supplementary Appendix).

Regardless of these limitations, this study addressed a data gap on Gam-COVID-Vac effectiveness in real life. Vaccination with Gam-COVID-Vac generates similar results to that obtained with other vaccines and, despite an expected waning immunity against SARS-CoV-2 infections, generates a substantial protection against severe COVID-19 cases 6 months from full vaccination.

Transparency declaration

Author contributions

GT, PP, and CC contributed to conceptualization, methodology, formal analysis, validation, data curation, and writing the original draft, review, and editing. MA, EN, AA, FV, and EG contributed to conceptualization, methodology, investigation, and writing review and editing. GT performed the chart review of all hospitalizations and deaths that arose in SARS-CoV-2 infected subjects. ES, AL, SM, FM, and AZ contributed to data collection and final revision of the paper. MA and SR were involved in the decision-making process of the vaccination campaign in RSM, project administration, and paper validation. GT and PP contributed equally to this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.06.026.

References

[1] Le TT, Cramer JP, Chen R, Mayhew S. Evolution of the COVID-19 vaccine development landscape. Nat Rev Drug Discov 2020;19:667–8.

[2] Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, et al. A global database of COVID-19 vaccinations. Nat Hum Behav 2021;5:947–53.

[3] Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. Int J Infect Dis 2022;114:252.

[4] Logunov DY, Dolzhikova IV, Zubkova OV, Tukhvatullin AI, Shcheblyakov DV, Dzharullaeva AS, et al. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. Lancet 2020;396:887–97.

[5] Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. Lancet 2021;397:671–81.

[6] Nogrady B. Mounting evidence suggests Sputnik COVID vaccine is safe and effective. Nature 2021;595:339–40.

[7] Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clin Microbiol Infect 2022;28:202.

[8] Ufficio Informatica, Tecnologia, Dati e Statistica della Repubblica di San Marino. Popolazione Residente Per Castello [cited, https://www.statistica.sm/on-line/home/dati-statistici/popolazione/docCat.14000552.1.10.1.html?Categoria=Popolazione residente per castello. [Accessed 18 May 2020].

[9] World Health Organization. Living guidance for clinical management of COVID-19 [cited, https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2. [Accessed 13 May 2022].

[10] World Health Organization. International guidelines for certification and classification (coding) of COVID-19 as cause of death [cited, https://www.who.int/publications/m/item/international-guidelines-for-certification-and-classification-%28coding%29-of-covid-19-as-cause-of-death. [Accessed 23 May 2022].

[11] Zhang X, Mallick H, Tang Z, Zhang L, Cui X, Benson AK, et al. Negative binomial mixed models for analyzing microbiome count data. BMC Bioinformatics 2017;18:1–10.

[12] Gazzetta Ufficiale. Il presidente della Repubblica [cited, https://www.gazzettaufficiale.it/eli/id/2021/07/23/21G00117/sg. [Accessed 13 May 2022].

[13] Loconsole D, Centrone F, Morcavallo C, Campanella S, Accogli M, Sallustio A, et al. Changing features of COVID-19: characteristics of infections with the SARS-CoV-2 delta (B.1.617.2) and Alpha (B.1.1.7) variants in Southern Italy. Vaccines 2021;9:1354.

[14] González S, Olszevicki S, Salazar M, Calabria A, Regairaz L, Marín L, et al. Effectiveness of the first component of Gam-COVID-Vac (Sputnik V) on reduction of SARS-CoV-2 confirmed infections, hospitalisations and mortality in patients aged 60-79: a retrospective cohort study in Argentina. EClinicalMedicine 2021;40:101126.

[15] Vokó Z, Kiss Z, Surján G, Surján O, Barcza Z, Pályi B, et al. Nationwide effectiveness of five SARS-CoV-2 vaccines in Hungary—the HUN-VE study. Clin Microbiol Infect 2022;28:398–404.

[16] Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman L, Haas EJ, et al. Waning immunity after the BNT162b2 vaccine in Israel. N Engl J Med 2021;385:e85.

[17] Rosenberg ES, Dorabawila V, Easton D, Bauer UE, Kumar J, Hoen R, et al. Covid-19 vaccine effectiveness in New York State. N Engl J Med 2021;386:116–27.

[18] Chemaitelly H, Tang P, Hasan MR, AlMukdad S, Yassine HM, Benslimane FM, et al. Waning of BNT162b2 vaccine protection against SARS-CoV-2 infection in Qatar. N Engl J Med 2021;385:e83.

[19] Andrews N, Tessier E, Stowe J, Gower C, Kirsebom F, Simmons R, et al. Duration of protection against mild and severe disease by Covid-19 vaccines. N Engl J Med 2022;386:340–50.

[20] Lin D-Y, Gu Y, Wheeler B, Young H, Holloway S, Sunny S-K, et al. Effectiveness of Covid-19 vaccines over a 9-month period in North Carolina. N Engl J Med 2022;386:933–41.

[21] Fabiani M, Puopolo M, Morciano C, Spuri M, Spila Alegiani S, Filia A, et al. Effectiveness of mRNA vaccines and waning of protection against SARS-CoV-2 infection and severe covid-19 during predominant circulation of the delta variant in Italy: retrospective cohort study. BMJ 2022:376.

[22] Rearte A, Castelli JM, Rearte R, Fuentes N, Pennini V, Pesce M, et al. Effectiveness of rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines for risk of infection with SARS-CoV-2 and death due to COVID-19 in people older than 60 years in Argentina: a test-negative, case-control, and retrospective longitudinal study. Lancet 2022;399:1254—64.

[23] Chahla RE, Tomas-Grau RH, Cazorla SI, Ploper D, Pingitore EV, López MA, et al. Long-term analysis of antibodies elicited by SPUTNIK V: a prospective cohort study in Tucumán, Argentina. Lancet Reg Heal Am 2022;6:100123.

[24] Mlcochova P, Kemp S, Dhar MS, Papa G, Meng B, Ferreira IATM, et al. SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion. Nature 2021;599:114—9.

[25] Collier AY, Yu J, McMahan K, Liu J, Chandrashekar A, Maron JS, et al. Differential kinetics of immune responses elicited by Covid-19 vaccines. N Engl J Med 2021;385:2010. —2.

[26] Gushchin VA, Dolzhikova IV, Shchetinin AM, Odintsova AS, Siniavin AE, Nikiforova MA, et al. Neutralizing activity of sera from sputnik v-vaccinated people against variants of concern (VOC: B.1.1.7, B.1.351, P.1, B.1.617.2, B.1.617.3) and Moscow endemic SARS-CoV-2 variants. Vaccines 2021;9:779.

[27] Usherwood T, LaJoie Z, Srivastava V. A model and predictions for COVID-19 considering population behavior and vaccination. Sci Rep 2021;11:1—11.

[28] Andersson O, Campos-Mercade P, Meier AN, Wengström E. Anticipation of COVID-19 vaccines reduces willingness to socially distance. J Health Econ 2021;80:102530.

[29] Montalti M, Soldà G, Valerio Z Di, Salussolia A, Lenzi J, Forcellini M, et al. ROCCA observational study: early results on safety of Sputnik V vaccine (Gam-COVID-Vac) in the Republic of San Marino using active surveillance. EClinicalMedicine 2021;38:101027.

[30] Shariati M, Mesgari T, Kasraee M, Jahangiri-rad M. Spatiotemporal analysis and hotspots detection of COVID-19 using geographic information system (March and April, 2020). J Environ Heal Sci Eng 2020;18:1499.