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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

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ABSTRACT

Background: A first-dose of various vaccines provides acceptable protection against infections by SARS-CoV-2 and evolution to the most severe forms of COVID-19. The recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), was proven efficacious but information about effectiveness in the real-world setting is lacking. The aim of our study was to investigate the association between the rollout of the first component (rAd26) of Gam-COVID-Vac and PCR-positive tests, hospitalisations and deaths.

Methods: We conducted a retrospective cohort study which analyzed individuals aged 60-79 who self-registered in the online vaccination system of the Province of Buenos Aires, Argentina, from December 29, 2020 to March 21, 2021. Exclusion criteria were having a previous positive RT-PCR or antigen tests for SARS-CoV-2, having received other vaccines, or two doses of any vaccine.

Proportions of new laboratory-confirmed SARS-CoV-2 infections, hospitalisations and deaths until 83 days of vaccination were compared between vaccinated and unvaccinated subjects. Vaccine effectiveness for the three outcomes was calculated as $(1-OR) \times 100$. Kaplan-Meier cumulative incidence curves were constructed.

Findings: During the study period 415995 registered subjects received the first component of Gam-COVID-Vac; 40387 belonged to the 60-79 age group, and were compared to 38978 unvaccinated. Vaccine effectiveness for preventing laboratory-confirmed infections was 78•6% [$CI_{95\%}$ 74·8 - 81·7]; and for reducing hospitalizations and deaths was, respectively, 87·6% [$CI_{95\%}$ 80·3 - 92·2] and 84·8% [$CI_{95\%}$ 75·0 - 90·7]. Effectiveness was high across all subgroups.

Interpretation: Similarly to other vaccines, the administration of one dose of Gam-COVID-Vac was effective for a wide range of COVID-19–related outcomes.

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1. Introduction

The coronavirus disease 2019 (COVID-2019), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China in December 2020; and has since rapidly spread worldwide. The World Health Organisation declared COVID-2019 a pandemic on March 11, 2020 [1]. It soon became evident that only a massive vaccination campaign would effectively end the pandemic, and many countries started an unprecedented effort directed at vaccine development. Publication of phase 2 and 3 studies demonstrating safety and efficacy of the different vaccines occurred thereafter and were followed by Emergency Use authorization (EUA) [2-7].

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Research in context

Evidence before this study

While ChAdOx1 nCoV-19 (AZD1222) (Astra Zeneca) vaccine against SARS-CoV-2 were approved with a schedule of administration of two doses 28 days apart, a post-hoc analysis of 4 clinical trials demonstrated an increased efficacy with extended intervals between doses. This prompted UK, Canada and then Argentina to postpone the second dose of available vaccines, in an international context of vaccine shortage and increasing COVID-19 cases.

We searched PubMed, medRxiv, and SSRN for observational studies, with no language restrictions, using the term "COVID-19 OR Sars-CoV-2" AND "vaccine effectiveness" OR "vaccine impact" published between Dec 1, 2020, and June 1, 2021. We found 8 studies which included individuals that had received one dose of any of the available vaccines. Reported effectiveness in preventing symptomatic infection was between 51-76%, hospitalisations 66•9-91%, and deaths 85-91% for BNT162b2 mRNA (Pfizer-BioNTech), ChAdOx1 nCoV-19, mRNA-1273 (Moderna) and Ad26•COV2•S vaccines.

Added value of this study

At present, there is no published study on the effectiveness of the first component of Gam-COVID-Vac (Sputnik V) from Gamaleya National Research Centre for Epidemiology and Microbiology in real life settings. This study shows that Gam-COVID-Vac prevents 78•6% of laboratory-confirmed SARS-CoV-2 infections, 87•6% of hospitalisations and 84•8% of deaths at 21−83 40 days after vaccination, in a population from 60 to 79 years of age. These Gam-COVID-Vac effects were consistent across all subgroups.

Implications of all the available evidence

Our results might provide evidence for delaying the second dose of the Gam-COVID-Vac in countries facing vaccine shortages to allow broader population coverage with a single dose. In addition, this study might offers support for expanding the pool of vaccines the world has to offer.

As of May 28 2021, Argentina has reported more than 3.6 million cases of COVID-19 with 76,135 associated deaths [8]. While the country participated in phase 3 trials of the BNT162b2 mRNA (Pfizer-BioNTech) vaccine, its availability for massive utilization could not be secured [2]. Furthermore the establishment of a partnership with AstraZeneca for the synthesis of some elements of ChAdOx1 nCoV-19 (AZD1222) did not provide enough vaccination doses, although some were delivered via the Covax mechanism [9]. An important amount of doses of the inactivated Sinopharm vaccine were available on February 28, 2021. Undoubtedly, the mass roll-out of vaccination began after the recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), from Gamaleya National Research Centre for Epidemiology and Microbiology, became available on December 29, 2020. The Gam-COVID-Vac vaccine was proven efficacious in phase 2 and 3 trials, but there is scarce information about its performance (effectiveness) in the real-world setting [6,7]. At that moment, the availability of authorized vaccines for individuals older than 60 years was limited. It have recently been demonstrated that the first-dose of various vaccines provided acceptable immunity and protection against developing the most severe forms of COVID-19 [10-18]. Thus, in a context of increasing number of COVID-19 cases and low availability of vaccines, and following recommendations about prioritisation of the first dose to enhance vaccine supply in the short term, the Ministry of Health of Argentina decided to delay administration of second doses [19,20]. Our hypothesis was that Gam-COVID-Vac vaccine could be associated with a decrease in PCR-positive tests, hospitalisations and deaths in subjects at 21-40 days after vaccination with the first component (rAd26) compared to unvaccinated subjects, after a massive administration in the Province of Buenos Aires, Argentina.

2. Methods

2.1. Study design and participants

This is a retrospective cohort study aiming at determining the effectiveness of the first component of Gam-COVID-Vac in a population between 60 and 79 years of age in the province of Buenos Aires, Argentina. Buenos Aires Province has developed its own registration system (Vacunate PBA) to address the vaccination campaign against COVID-19 in which voluntary registration can be carried out via Android and IOS applications or via the specially designed website [22]. This database catalogues age, gender, occupation, and underlying conditions in a self-declared registration statement by provincial residents who enter their information into the system to receive a vaccine. Registration started on December 15st, 2020.

Additional information on subsequent laboratory-confirmed SARS-CoV-2 infections by RT-PCR or antigen test was obtained until May 1st, 2021. Importantly, those laboratory-confirmed SARS-CoV-2 infections corresponded mainly to symptomatic cases due to the testing policy of Buenos Province in that period of time. Information about hospitalisations and deaths of any of these subjects was recorded until May 15, 2021. Laboratory-confirmed SARS-CoV-2 infections, hospitalisations and deaths were obtained from the National System of Health Surveillance.

All these data were further validated with information from the Bed Management System, a province-level monitoring system for hospital admissions, discharges, and deaths.

Both vaccinated and unvaccinated subjects analyzed in this study had self-registered in the Vacunate PBA system.

The rollout of Gam-COVID-Vac began on December 29, 2020 and by March 21 2021, 513432 of 4791075 subjects registered had received the first dose of one of three vaccines approved for emergency use in Argentina: ChAdOx1 nCoV-19 (AZD1222) from the University of Oxford/AstraZeneca, Gam-COVID-Vac (Sputnik V) from Gamaleya National Research Centre for Epidemiology and Microbiology, and Sinopharm/BBIBP of Beijing Institute of Biological Products). From those, only 203334 subjects (39·6% of those vaccinated with the first dose in the province of Buenos Aires) had received the first component of Gam-COVID-Vac before March 21, 2021. In this study, only the subjects older than 60 were considered, as they were prioritized for vaccination in the guidelines proposed by the Argentine National Ministry of Health due to the increased risk of severe forms and mortality demonstrated in this age group [23-25]. The inclusion criteria were: (1) Age between 60 and 79 years; (2) Vaccination before March 21, 2021 and not having received the second component of Gam-COVID-Vac (rAd5) as of May 1, 2021; (3) Not having a previous positive RT-PCR or antigen tests for SARS-Cov2 and (4) Residence in the municipalities pertaining to the Greater Buenos Aires, Province of Buenos Aires, the most inhabited area of the country with a population of 17·7 million inhabitants.

For the unvaccinated population, the inclusion criteria was: (1) An age between 60 and 79, (2) Not having received any vaccine against COVID-19 up to May 1, 2021 (3) Not having a previous positive RT-PCR or antigen tests for SARS-Cov2 and (4) residence in the municipalities pertaining to Greater Buenos Aires, Province of Buenos Aires.

The population ≥80 years was not included in this study because by May 1, 2021 over 95% of this age group had already been vaccinated, leaving an insufficient number of unvaccinated subjects to

compare with, which would defeat the purpose of the study. In the vaccinated group, the monitoring begins at the vaccination date. However, the unvaccinated group cannot be assigned a precise date for the onset of monitoring. We sought to homogenize exposure time among vaccinated and unvaccinated individuals. First, for that purpose, we created a fictional vaccination date which acted as the starting date of monitoring for the unvaccinated group [13,26]. This fictional vaccination date was randomly assigned after sampling from the first-dose application date distribution of the vaccinated group. All patients had up to 40 days of monitoring to search for a positive SARS-CoV-2 test, hospital admission and/or death caused by COVID-19.

Data recorded were age, gender, and presence or absence of comorbidities. The date of confirmed-laboratory SARS-CoV-2 infections was identified by the symptom-onset date or, if not available, the date of the sample collected for either COVID-19 test. We also registered the date of hospitalisations and deaths.

The 60-79 age group was further split into two subgroups of 60-69 and 70-79. Since vaccination rollout prioritized subjects with higher risk of COVID-19, the campaign began targeting individuals $\geq$80, and followed with the 60-79 subgroup. To account for possible imbalances between vaccinated:unvaccinated ratios in the two age subgroups at the end of the study (May 1, 2021) that could act as confounders in the analysis, we generated an matched 60-79 subgroup with around 1:1 vaccinated-unvaccinated ratio. This approach was selected to deal with the higher proportion of comorbidities that was to be expected in the vaccinated group, given that the vaccination rollout usually began targeting older age subgroups, and then individuals with comorbidities within all age subgroups. A similar matching strategy has been used by other researchers [26,27].

The matched group was obtained following the next steps: (1) Vaccinated individuals were grouped by exact age, gender and comorbidities and the number for each group was registered (n). (2) For each combination of age, gender and comorbidities, n individuals matching exact values in the considered parameters were selected from the unvaccinated group. (3) In cases where the n of unvaccinated was not enough, all the unvaccinated individuals from this subgroup were selected (less than n). This step could lead to a slight difference between two groups leaving a not exactly 1:1 ratio between vaccinated and unvaccinated groups.

Patients were followed at least for 40 days from the vaccination date or fictional date for the unvaccinated.

3. Outcomes

The primary outcome measure was the proportion of participants with confirmed-laboratory SARS-CoV-2 infections at 21-40 days after vaccination. This period of time was selected based on previous studies about antibody generation and effectiveness after the first component of Gam-COVID-Vac, which increases significantly after day 21 of vaccination [28]. Secondary outcomes were proportions of hospitalisations and deaths, also obtained from those infected between day 21 up to day 40. The three outcomes were independently recorded in the database. We also estimated proportion of participants with confirmed-laboratory SARS-CoV-2 infection, hospitalisations and deaths, for age subgroups (60-69 and 70−79 years), sex and comorbidities. For each end-point analysis, all laboratory confirmed cases before day 21 were excluded.

4. Statistical analysis

For the main analysis, we calculated Odds ratios (OR) and their respective $CI_{95\%}$ of confirmed-laboratory SARS-CoV-2 infections, hospitalisations and deaths between vaccinated and unvaccinated individuals.

Vaccine effectiveness was defined as infection relative risk reduction (RRR) and calculated as: $(1 - OR) \times 100$.

Age, gender, age category, and presence of comorbid conditions in general were compared between vaccinated and unvaccinated groups. All analyses were performed with Chi^2 or t-tests, according to the nature of the variable. A P value $< 0{\cdot}05$ was considered significant.

All these analyses were calculated in the matched cohort and also in the entire cohort.

Additionally, OR between vaccinated and matched unvaccinated groups were calculated at days 0-6, 7-13, 14-20, 21-27, 28-34, and after 35 days of follow-up. Stratification per week was the strategy selected to account for the changing background dynamics of the pandemic throughout the study observation period.

Cumulative incidence curves comparing infections, hospitalisations and deaths between vaccinated and matched unvaccinated groups were constructed.

Analyses were done with statistical software R (version 3·6·1) and python (version 3·9·0). All developed codes are freely available on github (https://github·com/MarsicoFL/Health-Data-Analysis/).

Missing values were not imputed.

5. Ethics

Gam-COVID-Vac (Sputnik V) was approved for emergency utilization by the National Ministry of Health on December 24, 2020 (report number 2020-2784-APN-MS) after recommendation of the National Administration for Drugs, Food and Technology (Administración Nacional para Drogas, Alimentos y Tecnología, ANMAT).

The Central Ethics Committee of the Ministry of Health of the Province of Buenos Aires evaluated and approved the protocol of the present study on June 9, 2021. The report number IF-2021-14225454-GDEBA-CECMSALGP. This study was exempted of informed consent due to its retrospective nature and given it is a public health-related official programme.

Data were anonymized by the following procedure: The personal ID number was used to link the databases of follow-up and vaccination. After this process, we removed the personal ID number and created an ID reference number for each individual. This reference number is not associated with any personal information.

SG and FM had full access to the dataset. All authors decided to submit the manuscript.

6. Role of Funding

This study did not receive any funding.

7. Results

From December 20, 2020 to March 21, 2021, 4791075 subjects registered in VACUNATE-PBA. The mass roll-out of vaccination began on December 29, 2020. As the study period corresponded to summer months, there were no lockdown restrictions. Daily cases of SARS-CoV-2 infections increased in December and peaked in the third week of January 2021. A second peak in the last week of April prompted the implementation of new restrictions, limiting nocturnal circulation and social gatherings.

By March 21, 2021, 203334 subjects had received the first component of Gam-COVID-Vac (Figure 1, flowchart of the study). Of these, 40387 belonged to the 60-79 age group and live in the Greater Buenos Aires, Province of Buenos Aires, whereas in the same age segment there were 146194 unvaccinated subjects.

In the 60-69 age subgroup, 12195 subjects had been vaccinated and 119561 remained unvaccinated. By contrast, in the 70-79 age subgroup, 28192 were vaccinated and 26633 remained unvaccinated. This analysis provides a ratio near 1:3 vaccinated:unvaccinated

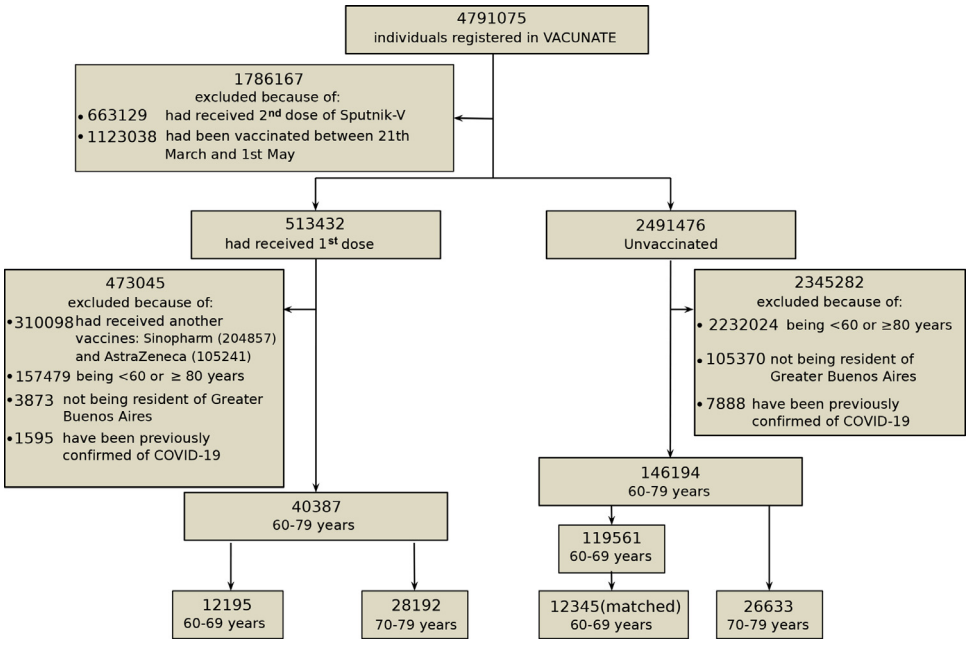

Figure 1. Flowchart of the study.

subjects for the entire study group aged 60-79, 1:10 for the 60-69 subgroup, and approximately 1:1 for the 70-79 subgroup. As expected, a strong imbalance between vaccinated and unvaccinated groups with respect to age was evident: 30% (12195/40387) of the vaccinated group and 80% (119561/146194) of the unvaccinated belonged to the 60-69 subgroup. Therefore a matched 60-79 subgroup (60-79m) with a 1:0·97 vaccinated-unvaccinated ratio was generated. A 1:1 perfect match could not be achieved because the number of unvaccinated individuals in the 70-79 subgroup was slightly lower than the vaccinated.

Characteristics of the entire group and comparisons between vaccinated and unvaccinated individuals are shown in Table 1, and in Table A1 for the entire, unmatched population. Briefly, gender distribution is similar for all groups. However, vaccinated individuals were older and had more comorbidities in the unmatched group. After matching, these differences disappeared. These characteristics are also shown in Figure 2, A-C.

Follow-up distributions showed the same probability density function between both groups indicating similar time-dependent epidemiological context (Figure 2D) and exposure time, which was extended to 82 days (Figure 2E) Being the median exposure time 44 days [95% CI 43-45].

Effectiveness for confirmed-laboratory SARS-CoV-2 infections between 21 and 40 days of vaccination, the main outcome measure of the study, was 78·6%[74·8 - 81·7]; for hospitalisations was 87·6% [80·3 - 92·2]; and for mortality 84·8% [75·0 - 90·7], considering the 60-79m group (Table 2, and Table A2 for the entire, unmatched population).

We found that vaccine effectiveness at 14-20 days post-vaccination for laboratory-confirmed COVID-19 infections among those receiving the first component of the vaccine Gam-Covid-Vac was 87% [95% CI 81-91]. With respect to hospitalisations, maximal effectiveness of 94% [75-99] was evident at 21-27 and 28-34 days . Prevention of deaths was higher at 28-34 days (93% [81-98]) compared to previous periods. After 35 days, effectiveness for laboratory-confirmed infections was 78% [95% CI 71-82], for hospitalisation was 90 % [95% CI 77-95, and for deaths was XXX. All these results are shown in Table 3.

Effectiveness for subgroups of age, sex and presence or not of comorbidities is shown in Table 4.

Effectiveness for prevention of infections, hospitalizations and deaths was similar across the sex, age and comorbidities subgroups (Figure 3).

Cumulative-incidence curves of confirmed-laboratory SARS-CoV-2 infections, hospitalisations and deaths, split after two weeks (Figure 4, A-C). Consistently, effectiveness calculated per week indicated high values from the beginning in confirmed cases, deaths and hospitalisations (Table 3).

Table 1
Epidemiological characteristics of the entire population and of the vaccinated and unvaccinated matched groups.Variables are expressed as n (%), or mean ± standard deviation.

Age group	60-79 years	60-79 years (matched)		
Group	All (n=186581)	Vaccinated (n = 40387)	Unvaccinated (n = 38978)	P value
Age (years)	67 ± 5	71 ± 5	71 ± 5	1
Gender (Female)	102735 (55%)	22357 (55%)	21255 (55%)	0·25
Presence of any comorbidity	59407 (32%)	17877 (44%)	17439 (45%)	0·18

8. Discussion

The results of this study carried out in real life settings indicate that the first component of Gam-COVID-Vac vaccine prevents 78·6% % of laboratory-confirmed SARS-CoV-2 infections, 87·6% of hospitalisations and 84·8% of deaths at 21−83 days after vaccination in a population from 60 to 79 years of age; this data is consistent with previous knowledge on the issue [10-18].

Undoubtedly, the complete schedule of vaccination should be the standard of care since it confers maximum effectiveness. However, if the first dose has an acceptable performance in decreasing infections, hospitalisations and deaths due to COVID-19, delaying the second dose will allow vaccination of a higher proportion of the population in a panorama of vaccine scarcity. This beneficial effect will also extend to the entire community indirectly, given that it helps to build population immunity to COVID-19. Results of the Phase-III study of AZ-ChAdOx1 nCoV-19 evidenced increased efficacy in prevention of

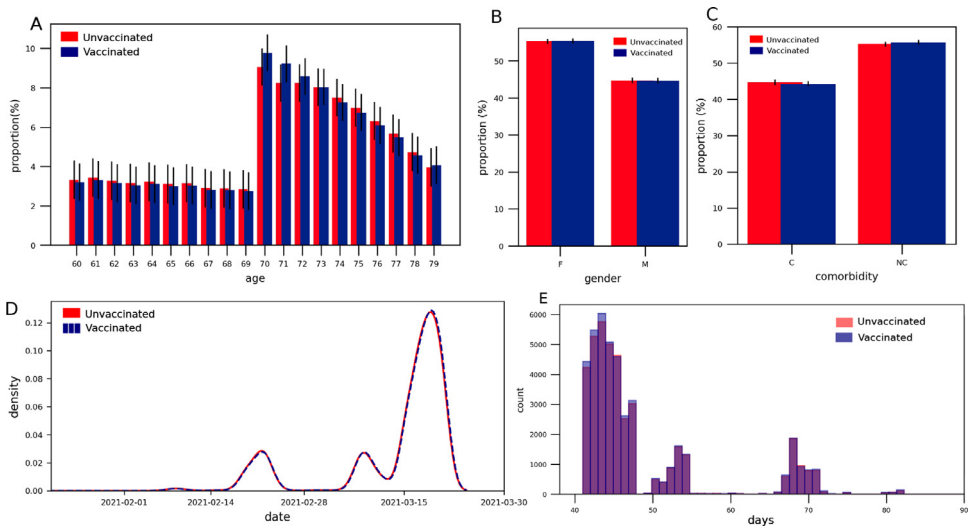

Figure 2. For 60 to 79 matched group, distribution between vaccinated and unvaccinated individuals for age (Panel A); gender (F, female; M, Male) (Panel B); presence of comorbidity (Panel C); vaccination date and follow-update for the unvaccinated) (Panel D); and distribution of the exposure time (Panel E). Error bars indicate the %[$CI_{95\%}$].

infection in a subgroup that received the second dose of the vaccine after a time interval which was longer than originally planned. Thus, first-dose efficacy was 55%, 69% and 81·3% in subjects who received the second dose 4-8, 9-12, and ≥12 weeks after the first one, respectively [10]. These encouraging results supported implementation of a delayed second dose in the context of a rapidly deteriorating epidemiological situation and/or low availability of vaccines in some regions. The UK and Canada adapted their vaccination campaigns to the new evidence and modified the schedule originally established by the manufacturers by postponing the second dose of their authorized vaccines for 3-4 months [19-21]. On March 26, 2021, the Ministry of Health in Argentina decided to prioritise the administration of the first dose to vulnerable populations in order to decrease COVID-19-related hospitalisations and deaths [21].

The earliest data about effectiveness in real life were provided by researchers from Israel, who reported a 51% relative risk reduction against SARS-CoV-2 infection 13-24 days after the first dose of the BNT162b2 mRNA [11]. In another study carried out in a cohort of 9,109 healthcare workers in Israel's largest hospital, adjusted relative rate reduction for SARS-CoV-2 infections were 30% and 75% for the 1−14-day period and 15−28-day period, respectively, after the first dose of the BNT162b2 mRNA vaccine [12]. This information was followed by similar data about first dose effectiveness reported by researchers from Scotland, who found that both BNT162b2 mRNA and ChAdOx1 nCoV-19 gave 89% protection against hospital admissions at 28-34 days post-vaccination· [13] In subjects over 80, researchers from England reported about 80% effectiveness against severe forms of the disease and hospital admissions for both vaccines. Moreover, a single dose of BNT162b2 mRNA was 85% effective at preventing death from COVID-19 [14].

With respect to Sputnik V, data provided by a phase III study showed efficacy of 91·6% for prevention of symptomatic infection in a 2-dose schedule, and of 87·4% at 14 days post vaccination with one dose. From 15 to 21 days after the first dose, efficacy against moderate/severe COVID-19 was 73·6%. Remarkably, in participants older than 60 years, vaccine efficacy was 91·8% [7].

Whilst the two-dose schedule continues to be the main strategy in Russia, the use of Sputnik Light has been approved for emergency use. To our knowledge, this is the first study reporting on the effectiveness of Sputnik V in the real-world; and the information provided on its prevention of 78·6% of laboratory-confirmed SARS-CoV-2 infections, 87·6% of hospitalisations and 84·8% of deaths from COVID-19 with one dose is in line with the results of studies of other vaccines [10-18].

A study carried out in Canada, where the second dose of BNT162b2 and mRNA-1273 COVID-19 vaccines was postponed for 4 months, showed first-dose effectiveness of 48% and 71% for prevention of symptomatic infection after 14−20 days and 35−41 days from administration, respectively. With regard to prevention against severe forms of COVID-19, including hospitalisation and death, effectiveness was 62% and 91%, after 14−20 days and beyond 35 days from administration, respectively [18].

Recently, in a real-life study, it was reported that a single dose of Ad26·COV2·S vaccine (Johnson & Johnson) which is similar to component I of Sputnik V (rAdn26), had 76·7% effectiveness for preventing SARS-CoV-2 infections after 14 days from administration. However there had not been enough hospitalisations, ICU admissions or deaths up to the time of the publication of the study to calculate effectiveness in preventing severe COVID-19 or deaths [16]. This figure is comparable to t our own results. A phase 3 trial of Ad26.COV2.S demonstrated 66.9% efficacy against moderate to severe-critical COVID-19, with onset at least 14 days after vaccination, and 66.1% after 28 days. Efficacy for preventing severe-critical COVID-19 was 76·7% for disease

Table 2
Laboratory-confirmed infections, hospitalisations, and deaths. Analysis of effectiveness (%) in vaccinated (n= 40387) and matched unvaccinated (n = 38978) individuals. Data are presented as n (%). Effectiveness is presented as %[$CI_{95\%}$]

	Vaccinated	Unvaccinated matched	OR*	Effectiveness
Laboratory-confirmed infections¶	180 (0·446%)	810 (2·078%)	0·21 [0·18-0·25]	78·6% [74·8-81·7]
Hospitalisations	20 (0·050%)	156 (0·400%)	0·12 [0·08-0·20]	87·6% [80·3-92·2]
Deaths	18 (0·045%)	114 (0·292%)	0·15 [0·09-0·25]	84·8% [75·0-90·7]

* Odds Ratio
¶ This includes asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19).

Table 3
Vaccine OR and RRR of laboratory confirmed-cases, hospitalisations and deaths per week and number of events for vaccinated (n= 40539) and unvaccinated (n= 39439) groups. Data are presented as n (%). Effectiveness is presented as %[$CI_{95\%}$]

	Laboratory-confirmed cases¶				Hospitalisations				Deaths			
Days after vaccination	N° events vaccinated	N° events unvaccinated	OR*	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness
(0-6)	55 (0·136%)	189 (0·479%)	0·28 [0·21-0·38]	71·7 [61·8-79·0]	4 (0·010%)	19 (0·048%)	0·21 [0·07-0·60]	79·5 [39·8-93·0]	2 (0·005%)	9 (0·023%)	0·22 [0·05-1]	87·3 [58·0-96·2]
(7-13)	56 (0·138%)	215 (0·545%)	0·25 [0·19-0·34]	74·7 [66·0-81·1]	8 (0·020%)	37 (0·094%)	0·21 [0·10-0·45]	79·0 [54·8-90·2]	3 (0·007%)	13 (0·033%)	0·23 [0·06-0·79]	85·1 [74·3-91·3]
(14-20)	32 (0·079%)	239 (0·606%)	0·13 [0·09-0·19]	87·0 [81·2-91·0]	4 (0·010%)	15 (0·038%)	0·26 [0·09-0·78]	74·1 [21·8-91·4]	4 (0·010%)	17 (0·043%)	0·23 [0·08-0·68]	89·4 [75·5-95·5]
(21-27)	58 (0·143%)	297 (0·753%)	0·19 [0·14-0·25]	81·0 [74·8-85·7]	2 (0·005%)	33 (0·084%)	0·06 [0·01-0·25]	94·1 [75·4-98·6]	3 (0·007%)	25 (0·063%)	0·12 [0·04-0·39]	81·9 [66·4-90·2]
(28-34)	77 (0·190%)	333 (0·844%)	0·23 [0·18-0·29]	77·5 [71·2-82·4]	6 (0·015%)	61 (0·155%)	0·10 [0·04-0·22]	90·4 [77·9-95·9]	4 (0·010%)	57 (0·145%)	0·07 [0·02-0·19]	87·5 [75·9-93·5]
35 - end)	113 (0·280%)	429 (1,088%)	0·26 [0·21-0·32]	74·4 [68·5-79·2]	16 (0·039%)	131 (0·332%)	0·12 [0·07-0·20]	88·1 [80·0-92·9]	24 (0·059%)	165 (0·418%)	0·14 [0·09-0·22]	81·3 [60·2-91·2]

¶ This includes asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19).
* Odds Ratio

Table 4
Effectiveness in preventing laboratory confirmed cases, hospitalisations and deaths for each subgroup of age, sex and comorbidities from day 21 to 42 of vaccination. Data are presented as n (%). Effectiveness is presented as %[$CI_{95\%}$]

	Total		Laboratory confirmed cases¶				Hospitalisations				Deaths			
	Vaccinated (n = 40387)	Unvaccinated (n=38978)	N° events vaccinated	N° events unvaccinated	OR*	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness
60-69 years	12195 (30%)	12345 (32%)	68 (0·558%)	403 (3·264%)	0·17 [0·13-0·22]	82·9 [77·9-86·8]	5 (0·041%)	37 (0·300%)	0·14 [0·05-0·35]	86·3 [65·2-94·6]	3 (0·025%)	24 (0·194%)	0·13 [0·04-0·42]	87·3 [58·0-96·2]
70-79 years	28192 (70%)	26633 (68%)	116 (0·411%)	433 (1·626%)	0·25 [0·20-0·31]	74·7 [69·0-79·4]	15 (0·053%)	121 (0·454%)	0·12 [0·07-0·20]	88·3 [80·0-93·1]	15 (0·053%)	95 (0·357%)	0·15 [0·09-0·26]	85·1 [74·3-91·3]
Female	22357 (55%)	21255 (55%)	84 (0·376%)	417 (1·962%)	0·19 [0·15-0·24]	80·8 [75·8-84·8]	7 (0·031%)	75 (0·353%)	0·09 [0·04-0·19]	91·1 [80·8-96·0]	6 (0·027%)	54 (0·254%)	0·11 [0·05-0·25]	89·4 [75·5-95·5]
Male	18030 (45%)	17723 (45%)	100 (0·555%)	419 (2·364%)	0·23 [0·19-0·29]	76·5 [70·9-81·1]	13 (0·072%)	83 (0·468%)	0·15 [0·09-0·18]	84·6 [72·4-91·4]	12 (0·067%)	65 (0·367%)	0·18 [0·10-0·34]	81·9 [66·4-90·2]
Comorbidities	17877 (44%)	17439 (45%)	94 (0·526%)	428 (2·454%)	0·21 [0·17-0·26]	78·6 [73·2-82·8]	13 (0·073%)	98 (0·562%)	0·13 [0·07-0·23]	87·1 [76·9-92·7]	10 (0·056%)	78 (0·447%)	0·12 [0·06-0·24]	87·5 [75·9-93·5]
Without comorbidities	22510 (56%)	21539 (55%)	90 (0·400%)	408 (1·894%)	0·21 [0·17-0·26]	78·9 [73·5-83·2]	7 (0·031%)	60 (0·279%)	0·11 [0·05-0·24]	88·8 [75·6-94·9]	8 (0·036%)	41 (0·190%)	0·19 [0·09-0·40]	81·3 [60·2-91·2]

¶ This includes asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19).
* Odds Ratio

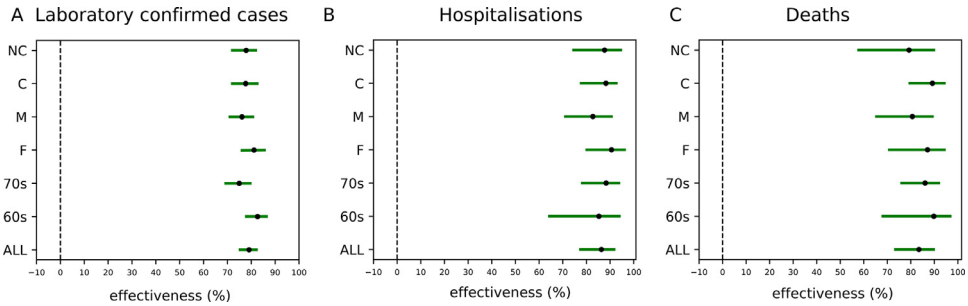

Figure 3. Vaccine effectiveness for different categories: 60-69 and 70-79 age subgroups, Females (F), Males (M), individuals with comorbidities (C) and without them (NC), between days 21 and 40 of follow-up days. Laboratory confirmed cases include asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19). Error bars indicate the %[$CI_{95\%}$].

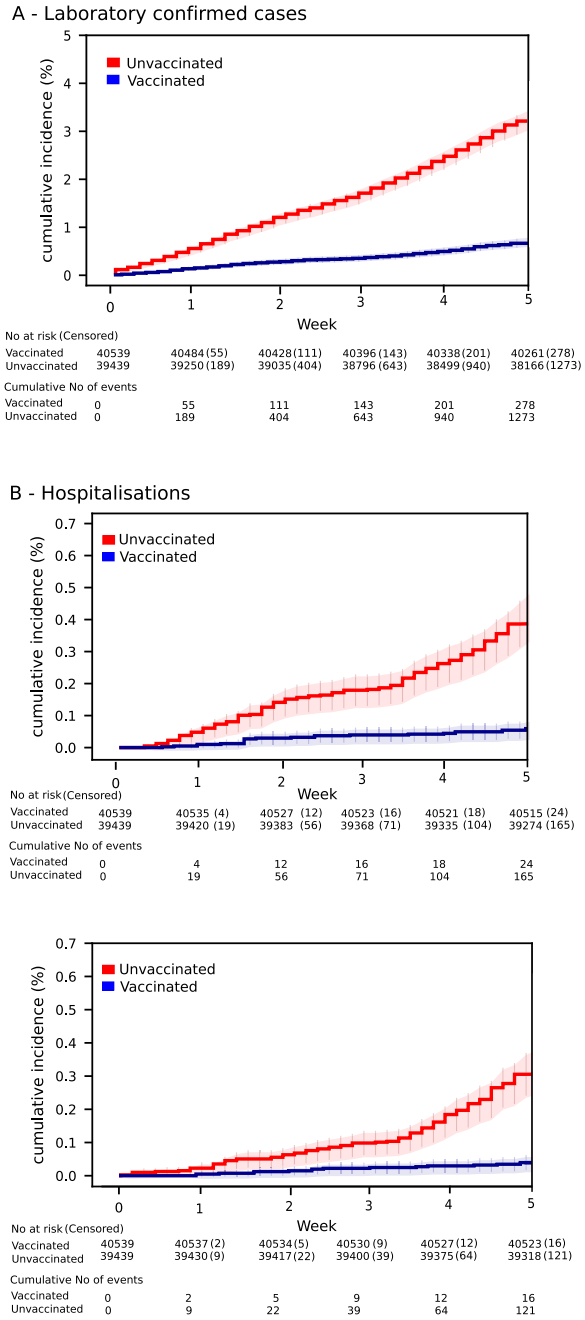

Figure 4. Cumulative incidence of laboratory confirmed-cases, hospitalisations and deaths for vaccinated and unvaccinated (matched) groups. Laboratory confirmed cases include asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19). Error bars indicate the %[$CI_{95\%}$].

onset after 14 days of vaccine administration, and 85·4% after 28 days [29].

In previous phase III studies of vaccines against COVID-19 cumulative incidence curves of COVID-19 cases in vaccinated vs. placebo began to diverge at 12 (BNT162b2 mRNA) or 16–18 days after the first immunisation (Gam-COVID-Vac) [2,7]. However, we observed an early effect of decreasing symptomatic infections at 7-14 days from vaccine administration, which cannot be ascribed to the biological effect of the vaccine. These unexpected findings have been observed in real life studies. Possible underlying mechanisms might be due to different causes. For example, the appearance of COVID-19 symptoms during the post-vaccination period might have been attributed to adverse effects of the vaccine and thus the vaccinated were not tested for COVID-19, while they actually might have had COVID-19. This could have led to an underestimation of COVID-19 cases in the vaccinated group. In the vaccination program of the Province of Buenos Aires, registered individuals were contacted at least one week before the vaccination date, and were instructed not to show up if they had had symptoms or if they were isolated due to close contact with a confirmed COVID-19 case. Moreover, individuals who were vaccinated received additional instructions to comply with prevention measures at the time of the procedure, compared to the unvaccinated. This could have reinforced aspects of self-care and made them less prone to developing infections within the first two weeks. These procedures differ from those of phase III vaccination studies in which patients from both arms of the study are subjected to similar procedures, which includes receiving similar information. . Finally, in patients that could have had previous asymptomatic infections with SARS-CoV-2, a genuine early immunological response could have occurred [13].

Other researchers have also described an earlier decrease of COVID-19 cases in vaccinated individuals, as we did. For example, for prevention of infections, an effectiveness of 47% has been described within 1-14 days, of 50·6% within 0-7 days, of 65·5% within 8-14 days, and of 47% within 1-14 days of vaccination [12,16,17]. Likewise, an effectiveness of 75% 0-6 days post-administration for decreasing hospitalizations has been reported [13]. To prevent this distortions, some studies have eliminated the first 14 days post-vaccination for the calculation of effectiveness [.26]

In conclusion, the effectiveness of Gam-COVID-Vac in preventing infections, hospitalisations and deaths was comparable across age subgroups with or without comorbidities, consistent with phase III and some real life studies [6,7,11].

The first limitation of this study lies in the observational nature of the study design. Cohort studies differ from clinical trials in several aspects; as the unvaccinated population does not receive a placebo any behavioral change in the vaccinated population, such as modifying prevention measures and social distancing, might act as a source of systematic uncertainty. However, observational studies are complementary to clinical trials and give valuable real-life information. Second, other outcomes of relevance such as emergency department

consultations and intensive care unit admissions were not measured. Third, non-vaccine measures, which might affect vaccine effectiveness like lockdowns or new restrictions, might be implemented during the period of the study. Nevertheless, this study was carried out over the summer months when restrictions are usually eased. Anyway, we adjusted for time to decrease for any putative effect of these interventions on vaccine effectiveness. Fourth, a lack of active laboratory surveillance in the cohort might have resulted in the underestimation of asymptomatic cases. Fifth, since registration was voluntary, there is a clear chance of non-response bias: we cannot assure that those individuals who were included in the study were similar to those who did not register. Sixth, information about comorbidities was provided by the individuals themselves, which might be inaccurate and therefore induce a self-reporting bias. Seventh, relevant epidemiological data such as ethnicity and body mass index were not collected. Eighth, our results might not be applicable to new variants, such as the delta variant; this highlights the need to continuously monitor the effectiveness of current vaccines. Ninth, we did not impute missing data; however the registration in VACUNATE required filling obligatory fields, such as age, gender and comorbidities. Besides, infections by SARS-CoV2, hospitalizations and deaths are of mandatory report therefore it is possible that degree of missingness was scarce. Tenth, we did not include vaccinated individuals younger than 60 years. At the time of the study, most of them belonged to the health care and other essential workforce, whose exposure time and risk were different to that of the general population. Finally, we could only assess the effectiveness of a single dose for a short period of 21-83 days post vaccination. Longer follow-up period than the 83 days tested in our study will be crucial to identifying the most appropriate length of time the second dose can be delayed.

The study results indicate that in real life the first component of the Sputnik V vaccine confers high protection against laboratory-confirmed SARS-CoV-2 infections, COVID-19 hospitalisations and deaths in a population of 60-79 years of age. This effect was consistent in all subgroups tested. Our results could provide support for delaying the second dose in countries facing vaccine shortages to allow for higher population coverage with a single dose. Assessing the effectiveness of a single dose for a longer follow-up period than the 83 days tested in this study could be crucial to identifying the most appropriate length of time the second dose can be delayed.

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Authors contribution

Soledad González: Writing – original draft, Writing – review & editing, Methodology, Conceptualization, Project administration. Santiago Olszevicki: Software, Data curation, Validation, Writing – original draft, Writing – review & editing, Methodology. Martín Salazar: Writing – original draft, Writing – review & editing, Methodology, Project administration, Conceptualization. Ana Calabria: Writing – original draft, Writing – review & editing, Conceptualization. Lorena Regairaz: Writing – original draft, Writing – review & editing, Conceptualization. Lupe Marín: Software, Data curation, Validation. Patricia Campos: Conceptualization. Teresa Varela: Conceptualization. Veronica V. González Martínez: Conceptualization. Leticia Ceriani: Conceptualization, Resources. Enio Garcia: Conceptualization, Resources. Nicolás Kreplak: Conceptualization, Resources. Marina Pifano: Conceptualization, Methodology, Writing – review & editing. Elisa Estenssoro: Writing – original draft, Writing – review & editing, Methodology, Project administration, Conceptualization. Franco Marsico: Software, Writing – original draft, Writing – review & editing, Methodology, Project administration.

Data sharing statement

The confidentiality of the data obtained through the VacunatePBA and Bed Management System records was guaranteed. The use of the data was exclusively for the purposes of this research, preserving the anonymity of the persons included. Data will be available for researchers who provide a methodologically sound proposal after it is approved. The data that could be shared is Individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures, and appendices). Proposals should be directed to franco.lmarsico@gmail.com; to gain access, data requestors will need to sign a data access agreement

Declaration of Competing Interest

NK, LC, TV and PC declared being involved in the decision making process of the vaccination campaign in the Province of Buenos Aires, Argentina. All other authors report no competing interests.

Appendix

Tables A1 and A2.

Table A1
Epidemiological characteristics of the entire population and of the vaccinated and unmatched unvaccinated groups. Data are presented as mean ± standard deviation (SD) or n (%), unless specified.

	All (n=186581)	Vaccinated (n = 40387)	Unvaccinated (n = 146194)	P value
Age	67 ± 5	71 ± 5	66 ± 4	0·0001
Gender (Females)	102735 (55%)	22357 (55%)	80378 (55%)	0·18
Presence of any comorbidity	59407 (32%)	17877 (44%)	41530 (28%)	0·00001

Table A2
Laboratory-confirmed infections, hospitalisations and deaths. Analysis of effectiveness in vaccinated and unmatched unvaccinated individuals. Data are presented as n (%). Effectiveness is presented as %[$CI_{95\%}$]

	Total		Laboratory confirmed cases*				Hospitalisations				Deaths			
	Vaccinated	Unvaccinated	N° events vaccinated	N° events unvaccinated	OR	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness	N° events vaccinated	N° events unvaccinated	OR	Effectiveness
60-79 years	40387 (100%)	146194 (100%)	180 (0·446%)	4005 (2·740%)	0·16 [0·13-0·19]	83·7 [81·1-86·0]	20 (0·050%)	405 (0·277%)	0·18 [0·12-0·24]	82·1 [72·0-88·6]	18 (0·045%)	372 (0·254%)	0·16 [0·09-0·23]	82·5 [71·9-89·0]
60-69 years	12195 (30%)	119561 (82%)	68 (0·057%)	3572 (2·990%)	0·19 [0·15-0·24]	81·3 [76·3-85·3]	5 (0·004%)	284 (0·207%)	0·20 [0·08-0·48]	80·2 [52·1-91·8]	3 (0·003%)	277 (0·232%)	0·11 [0·03-0·33]	89·4 [66·9-96·6]
70-79 years	28192 (70%)	26633 (18%)	116 (0·411%)	433 (1·626%)	0·25 [0·20-0·31]	74·7 [69·0-79·4]	15 (0·053%)	121 (0·454%)	0·12 [0·07-0·20]	88·3 [80·0-93·1]	15 (0·053%)	95 (0·357%)	0·15 [0·09-0·26]	85·1 [74·3-91·3]

* This includes asymptomatic infections by SARS-CoV2 and symptomatic infections (COVID-19).

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