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Brand-specific vaccine effectiveness against SARS-CoV-2 infection, hospitalization and mortality, in people aged 50-59 years in Spain

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Efectividad de las vacunas frente a SARS-CoV-2 utilizadas en España: infección, hospitalización y mortalidad en personas de cincuenta a cincuenta y nueve años

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ABSTRACT

We compared brand-specific vaccine effectiveness during August 2021 in people born between 1962 and 1971, vaccinated during June. For symptomatic infection, protection was lower for Janssen (56%;53-59) or Astra Zeneca (68%;65-70), compared to Pfizer (78%;77-78), AZ/Pfizer (86%;80-90) or Moderna (89%;88-90). VE against hospitalization ranged 86% for Janssen to 97-98% for other vaccines.

KEYWORDS // COVID-19; SARS-CoV-2; Vaccine effectiveness; Janssen; AstraZeneca.

RESUMEN

En este trabajo se comparó la efectividad de la vacuna contra la COVID-19 (EV) durante agosto de 2021, en personas nacidas entre 1962 y 1971 y vacunadas durante junio, según la marca utilizada. La protección frente a infección por SARS-CoV-2 sintomática fue menor para la vacuna de Janssen (56%; IC95%: 53-59) y AstraZeneca [Vaxzevria] (68%; IC95%: 65-70), en comparación con Pfizer [Comirnaty] (78%; IC95%: 77-78), AZ/Pfizer (86%; IC95%: 80-90) y Moderna [Spikevax] (89%; IC95%: 88-90). La EV contra la hospitalización osciló entre el 86% de Janssen y el 97%-98% de las demás vacunas.

PALABRAS CLAVE // COVID-19; SARS-CoV-2; Efectividad de la vacuna; Janssen; AstraZeneca.

SARS-COV-2 VARIANT B.1.617.2 (DELTA) HAS rapidly become dominant in Europe, and shows reduced sensitivity to neutralizing antibodies (1). Estimating COVID-19 vaccine effectiveness (VE) is challenged by the high correlation between age, date of vaccination and type of vaccine, due to the design of vaccination programs. Our objective is to compare VE against different COVID-19 end-points, in the current Delta-dominant scenario, for vaccine-brands used in Europe. For that, we studied age cohorts (50-59 years) in which distinct vaccines were used in the general population at the same calendar time.

In Spain, the first vaccinated were frontline healthcare workers, nursing home residents and staff, and those over 70 years, who received mRNA vaccines, followed by those aged 60-69 years, who received mostly Astra Zeneca. Cohorts born 1962-1971 (aged 50-59 years) were vaccinated later and indistinctly with Pfizer, Moderna or Janssen. Second-line healthcare workers and other essential workers, like the education sector, received Astra Zeneca regardless of age (with Pfizer as second dose, optionally) while Janssen was prioritized for people with dependencies, mobile and hard-to-reach populations and prison inmates.

We used the screening method, similarly to previously reported (2), with aggregated vaccine coverage and individual cases notified to the national epidemiological surveillance network (RENAVE). We selected persons born 1962-1971 who were not residents of care-homes or institutions, and who achieved complete vaccination during weeks 23 to 26, removing those vaccinated earlier as part of specific risk groups, and those vaccinated later that could correspond to people with past infection, who were asked to delay vaccination. We selected cases with symptom onset, or diagnosis if asymptomatic, during August. The proportion of cases fully vaccinated during weeks 23-26 with different brands vs. those who did not receive any vaccine dose up to end of August was compared with the proportion of the population in the same categories in REGVACU with similar sex and autonomous community. Details on the methods are provided in **Appendix I**. We estimated VE against infection, symptomatic infection, hospitalization, and death.

Results are shown in **Figure 1** and additional Tables and Figures can be found in **Appendix II-VII**. VE was highest for Moderna against infection and symptomatic COVID-19, of 87% (95%CI: 86-88) and 89% (88-90) respectively, followed by Pfizer, with corresponding VE of 77% (76-78) and 78% (77-78). VE against these outcomes was lower for Astra Zeneca, of 68% (66-70) and 68% (65-70), and Janssen, with 64% (62-66) and 56% (53-59). Interestingly, VE against hospitalization was high for all vaccines, although lower for Janssen, from: 98% (97-99) Moderna, 97% (97-98) Pfizer, 97% (95-98) Astra Zeneca and 86% (83-89) Janssen. Estimations for AZ/mRNA were similar to those for mRNA vaccines, with wider confidence intervals. VE for mortality could only be estimated for Janssen (89%; 64-97), Moderna (94%; 76-99) and Pfizer (97%; 93-99). In the sensitivity analysis removing healthcare workers **[Appendix V-VI]**, estimates for Astra Zeneca decreased to 59% (56-61) for infection and 59% (55-62) for symptomatic COVID-19 but remained unchanged for hospitalization.

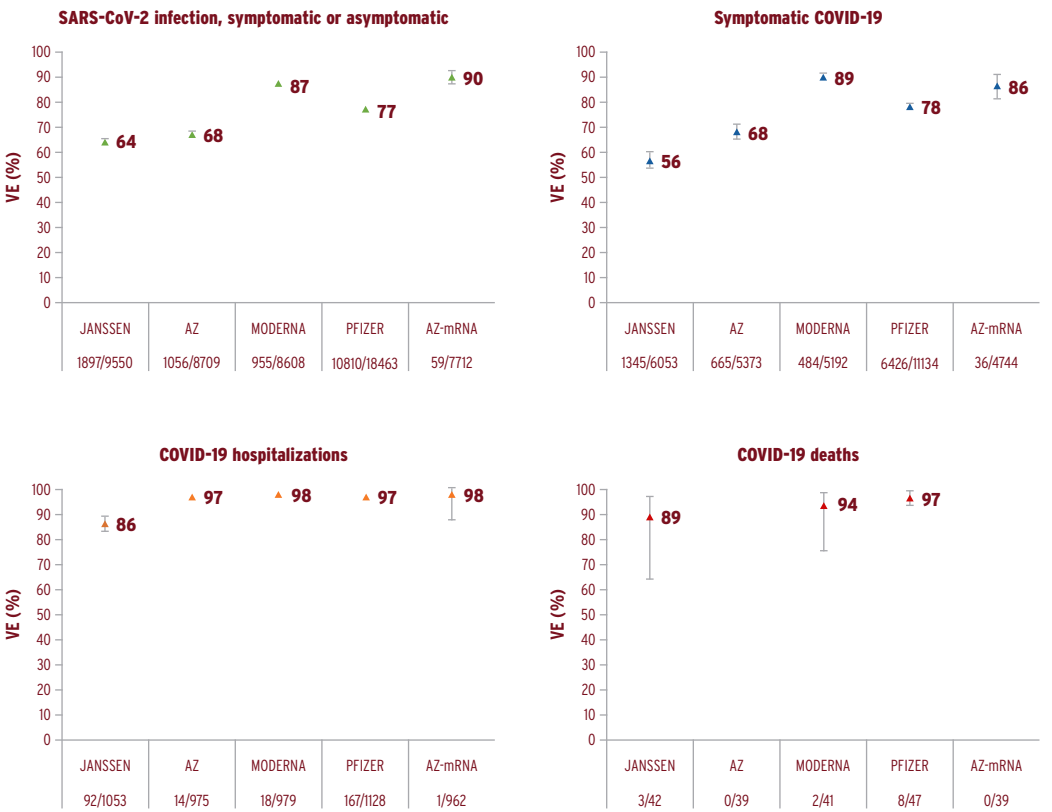
VE of complete mRNA vaccination against infection and symptomatic infection is lower than previous observational studies in the USA, Canada and England (3,4,5) but higher than estimates from Qatar (6). VE against hospitalization are higher than those from the USA (of 84-93% (7)), but similar to those reported in England and the UK, of 90%-99% against hospitalization and 90-95% against mortality (8,9). Like in the UK and Navarre (Spain) (9,10), Moderna showed higher VE than Pfizer, although mostly for the infection outcomes, and not for hospitalization. However, we included individuals aged 50-59 years, not fully comparable with age-categories in other studies.

VE for Astra Zeneca was similar in our study to that reported in England against infection (67%) **(4)** and, against hospitalization, higher (≈90%), or similar (90-99%) **(8,9)**. Similar to the UK and Navarre **(9,10)**, we found lower VE for Astra Zeneca compared to Pfizer for infection, but not for hospitalization.

Our results show lower effectiveness for Janssen compared to other vaccines for all outcomes, similar to Navarre **(10)**. VE against infection was similar in both studies (of 54% and 56%, respectively), but our estimate of VE against hospitalization was higher, of 86%, compared to 74%. In the United States, protection of full mRNA vaccination against hospitalization was 91-93%, but only 68% for Janssen **(7)**.

In summary, our results suggest that, compared to the Pfizer vaccine, Moderna vaccine has higher effectiveness, while Janssen has lower, in the prevention of SARS-CoV-2 infections and symptomatic COVID-19; Astra Zeneca vaccine also shows a decreased effectiveness, although less consistently. However, VE against COVID-19 hospitalization and mortality remains high in a Delta-dominant period

Figure 1
Vaccine effectiveness of laboratory confirmed SARS-CoV-2 infection, symptomatic infection, hospitalization, and mortality in people completely vaccinated with Pfizer, Moderna, Astra Zeneca (in homologous or heterologous scheme with mRNA vaccines) or Janssen vaccines. Spain, August, 2021.



for all vaccine-brands, with a slightly lower protection with the Janssen vaccine. These results endorse the current vaccination strategy and, together with other upcoming evidences, will contribute to inform vaccination policies in Spain.

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Complete vaccination was defined differently depending on the vaccine-brand, and including the period of induction of the immune response, according to product specifications:

- For Pfizer vaccine: Two vaccine-doses separated by at least 19 days and 7 days after the second dose, or only one dose in a person with previous documented SARS-CoV-2 infection, 7 days after that single dose.
- For Moderna vaccine: Two vaccine-doses separated by at least 25 days and 14 days after the second dose, or only one dose in a person with previous documented SARS-CoV-2 infection, 14 days after that single dose.
- For Astra Zeneca vaccine: Two vaccine-doses separated by at least 21 days and 14 days after the second dose, or only one dose in a person with previous documented SARS-CoV-2 infection, 14 days after that single dose.
- For Astra Zeneca/mRNA combination: A first dose of Astra Zeneca vaccine followed a minimum of 21 days later by a dose of mRNA vaccine, after 7 or 14 days of the second dose, depending on whether it was Pfizer (the vast majority) or Moderna.
- For Janssen vaccine: One vaccine-dose, after 14 days of this single dose.

Individuals were first selected from cases notified to the National epidemiological surveillance network (RENAVE), applying the following criteria:

- A SARS-CoV-2 infection between August 1 and August 31 (with date of infection being the date of onset of symptoms or, if asymptomatic, the date of diagnosis minus three days).
- Born 1962-1971.
- Not known to have been exposed at socio-sanitary centers.
- Were either not vaccinated or had achieved complete vaccination (including the induction period) during weeks 23 to 26, both included.
- Not known to be imported cases.
- Excluding cases from one region with a high proportion of COVID-19 vaccine information missing at the time of analysis.

The proportion of cases vaccinated (PCV) with a given vaccine-brand was calculated as the number completely vaccinated with that brand during weeks 23 to 26, divided by the number that had been vaccinated with that brand during weeks 23 to 26 or were not vaccinated.

The PCV was compared to the corresponding vaccination coverage (or, equivalently, the proportion of population vaccinated, PPV), which represented the expected PCV under the null hypothesis of no effect of the vaccine. COVID-19 vaccination data were extracted from the National vaccination registry (REGVACU) applying the following criteria:

- People born 1962-1971.
- Not residents of care-homes or, institutions or prisons and did not have a high degree of dependency.
- Achieved complete vaccination during weeks 23 to 26, both included.

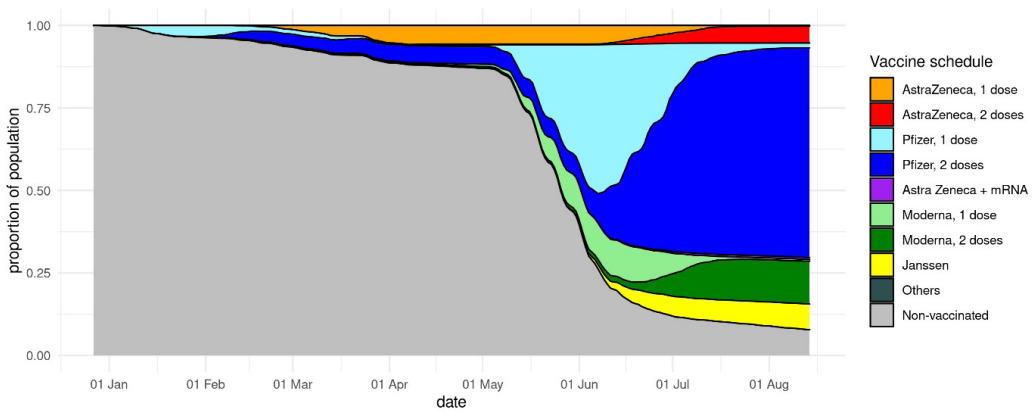
Appendix I (continuación)
Methodological appendix.

REGVACU records all vaccine doses administered throughout the country on real-time. The number of persons who fulfilled the selection criteria, completely vaccinated with each vaccine-brand was calculated for each region (17 autonomous communities and 2 autonomous cities) and each sex (Male or Female). Finally, the number of unvaccinated on August 15 was computed by subtracting those who had received at least one vaccine dose by August 15 but did not meet the criteria to be included in the study, to the administrative denominator, by region and sex. Equivalently to the PCV, the PPV for a given vaccine brand was calculated as the number completely vaccinated with that brand on weeks 23 to 26, divided by the number who either had been vaccinated with that brand on weeks 23 to 26 o were not vaccinated as of August 15. Cases from RENAVE in the study were assigned the PPV for their same sex and region.

Vaccine effectiveness is estimated following the method proposed by Farrington (Farrington CP. Estimation of vaccine effectiveness using the screening method. Int J Epidemiol 1993;22:742-6). In this approach, a generalized linear model with logit link is fit with vaccination status of the cases (PCV) as independent variable and the logit of the PPV as offset. The odds ratio (OR) estimated by the model and 1 – OR is the vaccine effectiveness, according to the following formula:

$$VE = 1 - \left(\frac{PCV}{(1 - PCV)} \times \frac{(1 - PPV)}{PPV} \right)$$

Appendix II
Evolution of vaccination coverage in cohorts born from 1962 to 1971 (50-59 years) in Spain, by vaccine schedule (excluding residents in care homes and other institutions).



Appendix III

Description of the number of days from the administration of the last dose of COVID-19 vaccine to the onset of symptoms in fully vaccinated cases notified to epidemiological surveillance, by vaccine brand.

Vaccine brand	Number of fully vaccinated	Days from last dose to onset			
		Min value	*Max value*	*Mean*	*SD*
Pfizer	10,810	35	91	60.27	11.49
Moderna	955	42	93	62.81	10.49
AstraZeneca	1,897	44	98	70.59	10.93
Janssen	1,056	42	94	66.73	11.02
AZ/mRNA	59	39	88	61.49	12.28

Appendix IV

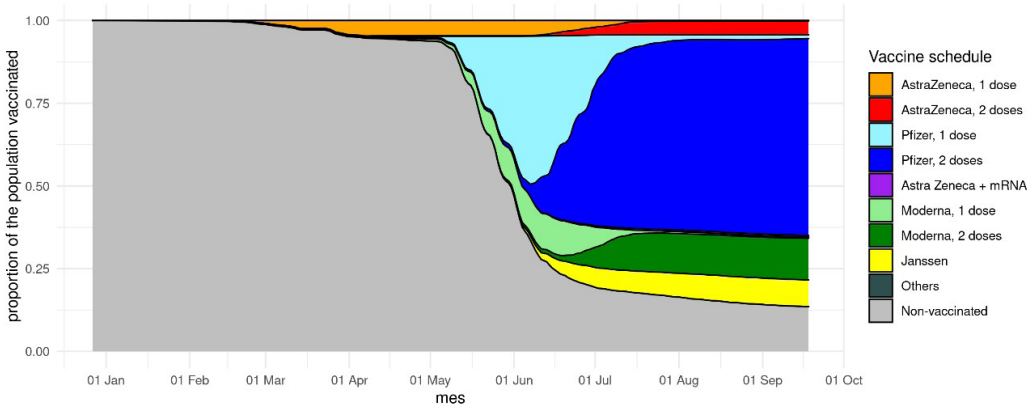
Estimation of Vaccine Effectiveness based on cases notified to epidemiological surveillance using the screening method. Detailed results.

Variable	Vaccine	N vaccinated	N total	%	Vaccine Effectiveness	(95% Confidence Interval)
SARS-CoV-2 laboratory confirmed infection	Janssen	1,897	9,550	19.86	64%	(62%-66%)
	AstraZeneca	1,056	8,709	12.13	68%	(66%-70%)
	Moderna	955	8,608	11.09	87%	(86%-88%)
	Pfizer	10,810	18,463	58.55	77%	(76%-78%)
	AZ/mRNA	59	7,712	0.77	90%	(88%-93%)
COVID-19 symptomatic infection	Janssen	1,345	6,053	22.22	56%	(53%-59%)
	AstraZeneca	665	5,373	12.38	68%	(65%-70%)
	Moderna	484	5,192	9.32	89%	(88%-90%)
	Pfizer	6,426	11,134	57.72	78%	(77%-78%)
	AZ/mRNA	36	4,744	0.76	86%	(80%-90%)
COVID-19 hospitalization	Janssen	92	1,053	8.74	86%	(83%-89%)
	AstraZeneca	14	975	1.44	97%	(95%-98%)
	Moderna	18	979	1.84	98%	(97%-99%)
	Pfizer	167	1,128	14.80	97%	(97%-98%)
	AZ/mRNA	1	962	0.10	98%	(88%-100%)
COVID-19 mortality	Janssen	3	42	7.14	89%	(64%-97%)
	AstraZeneca	0	39	0	-	
	Moderna	2	41	4.88	94%	(76%-99%)
	Pfizer	8	47	17.02	97%	(93%-99%)
	AZ/mRNA	0	39	0	-	

Appendix V

Sensitivity analysis eliminating Healthcare Workers from the registry-based study.

Evolution of the vaccination coverage in cohorts born 1962 to 1971 (50-59 years of age) in Spain, by vaccine schedule (excluding residents in care homes and other institutions), for the sensitivity analysis not including healthcare workers. Proportion of population according to vaccine schedule by month. Y axis is proportion of population in each category and Y axis calendar time.



Nota: Proportion of the population according to the vaccination schedule per month. The Y axis is the proportion of population in each category and the X axis is the calendar time.

Appendix VI

Sensitivity analysis eliminating Healthcare Workers from the registry-based study.

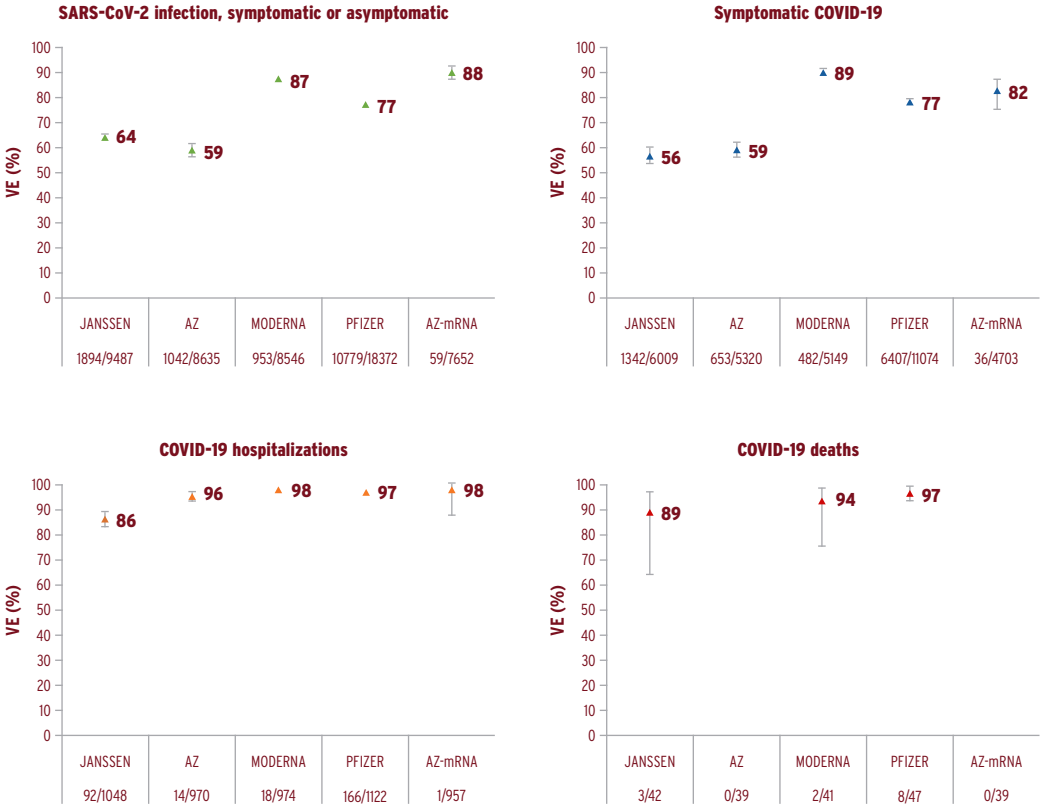
Estimation of Vaccine Effectiveness based on cases notified to epidemiological surveillance using the screening method, for the sensitivity analysis not including healthcare workers. Detailed results.

Variable	Vaccine	N vaccinated	N total	%	Vaccine Effectiveness	(95% Confidence Interval)
SARS-CoV-2 laboratory confirmed infection	Janssen	1,894	9,487	19.96	64%	(62%-66%)
	AstraZeneca	1,042	8,635	12.07	59%	(56%-61%)
	Moderna	953	8,546	11.15	87%	(86%-87%)
	Pfizer	10,779	18,372	58.67	77%	(76%-77%)
	AZ/mRNA	59	7,652	0.77	88%	(85%-91%)
COVID-19 symptomatic infection	Janssen	1,342	6,009	22.33	56%	(53%-59%)
	AstraZeneca	653	5,320	12.27	59%	(55%-62%)
	Moderna	482	5,149	9.36	89%	(88%-90%)
	Pfizer	6,407	11,074	57.86	77%	(76%-78%)
	AZ/mRNA	36	4,703	0.77	82%	(75%-87%)
COVID-19 hospitalization	Janssen	92	1,048	8.78	86%	(83%-89%)
	AstraZeneca	14	970	1.44	96%	(93%-98%)
	Moderna	18	974	1.85	98%	(97%-99%)
	Pfizer	166	1,122	14.80	97%	(97%-98%)
	AZ/mRNA	1	957	0.10	98%	(84%-100%)
COVID-19 mortality	Janssen	3	42	7.14	89%	(64%-97%)
	AstraZeneca	0	39	0		-
	Moderna	2	41	4.88	94%	(75%-99%)
	Pfizer	8	47	17.02	97%	(93%-99%)
	AZ/mRNA	0	39	0		-

Appendix VII

Sensitivity analysis eliminating Healthcare Workers from the registry-based study.

Vaccine effectiveness of laboratory confirmed SARS-CoV-2 infection, symptomatic infection, hospitalization, and mortality in people completely vaccinated with Pfizer, Moderna, Astra Zeneca (in homologous or heterologous scheme with mRNA vaccines) or Janssen vaccines. Spain, August, 2021, for the sensitivity analysis not including healthcare workers.



Appendix VIII

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