

Estimates of COVID-19 Vaccine Effectiveness against SARS-CoV-2 infection following a nationwide vaccination campaign: a population-based cohort study

Austria, calendar week 05 -35, 2021

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Introduction

We estimated the real-world effectiveness of the COVID19 vaccines against infection of SARS-CoV-2 and COVID19 in Austria after launching of the vaccination campaign in the end of December 2020.

The Austrian ministry of health (MoH) is leading the nationwide vaccination campaign, which subsequently introduced the mRNA-vaccines, BNT162b2-, mRNA-1273-vaccine, and AZD1222- and Ad26.COV2-S (J&J)-vaccine. From January 2021, the campaign initially targeted individuals above 80 years old, high-risk patients, staff and residents of nursing homes, health-care workers (HCW) at high risk of infection, and handicapped persons and their nursing staff, providing mainly mRNA-vaccines. From March 2021 onwards, the availability of the vaccines (including mRNA-vaccines and AZD1222-vaccine) was extended to the age group 65-79 years, HCWs at moderate/low risk of infection, and staff in schools, nurseries and child-care facilities. Since May 2021, the third phase has covered the remaining vaccine-eligible population aged 12-64 years. Administration of the Ad26.COV2-S (J&J)-vaccine started with the third phase of the vaccine campaign.

This is the first study on COVID19 vaccine effectiveness (VE) at population-level in Austria. We present nationwide estimates of the effectiveness of the two mRNA-vaccines (BNT162b2- and mRNA-1273-vaccine, combined), AZD1222- and Ad26.COV2-S (J&J)-vaccine against SARS-CoV-2 infection and symptomatic infection. In addition, we estimated VE against the Alpha-variant and Delta-variant, by defining two study periods during which each variant accounted for more than 90% of typed isolates.

Methods

Study design, data-sources and study cohort

We applied a population-based retrospective cohort study using nationwide surveillance data on SARS-CoV-2 cases, which are mandatorily registered into the national infectious disease recording system. The study period started in calendar week 05 (February 1, 2021), corresponding to the time, when first infections among vaccinated individuals were possible. End of the study period was calendar week 35 (September 05, 2021), using data status as of September 20, 2021. We linked the national surveillance data on SARS-CoV-2-cases with vaccinee data from the national COVID19 vaccine register using a personal identifier consisting of age, sex, date of vaccination and district of residence. The vaccination data included information on the administered vaccine (BNT162b2-, mRNA-1273-, AZD1222- or Ad26.COV2-S (J&J)-vaccine) and date of administration for each dose. Case data included date of laboratory confirmation of SARS-CoV-2 infection, gender, date of birth, clinical presentation and district of residence.

The study cohort consisted of the Austrian residents (i.e. the census population), aged 12 years and older. We defined individuals of the study cohort as fully vaccinated if more than 28 or 14 days had passed since last dose according to the dose regimen and individuals as unvaccinated, if they had not received any COVID-19 vaccine doses. A case was an individual with a laboratory confirmed SARS-CoV2 infection. A study case was classified as fully vaccinated if the date of laboratory confirmation of infection occurred at least 14 days after the second dose of a 2-doses regimen (BNT162b2-, mRNA-1273-, AZD1222-vaccine) or at least 28 days after the single dose of the 1-dose vaccine regimen (J&J-vaccine). A study case was a case, which had not received any dose of BNT162b2-, mRNA-1273-, AZD1222-, Ad26.COV2-S (J&J)-vaccine prior to the date of laboratory confirmation of infection. We excluded an individual as a case from the analyses, if the case (1) had a laboratory confirmation of SARS-CoV-2 infection prior to calendar week 05, (2) had received only the first dose of a 2-dosis vaccine-regimen, (3) received 2 doses but fewer than 14 days had passed since second dose or (4) received the single dose of the 1-dose vaccine regimen with fewer than 28 days since vaccination. The linkage of surveillance case data and vaccinee data allowed to identify the group of fully vaccinated cases (group 1), fully vaccinated non-cases (group 2) and of unvaccinated cases (group 3). The unvaccinated non-case group (group 4) was

determined by subtracting the study subjects of the groups 1, 2 and 3 from the Austrian vaccine-eligible population estimate, stratified by age, gender and province of residence (nine Austrian provinces). Person-days for the fully vaccinated group was the number of individuals' days at risk of infection, starting with the date of being fully vaccinated (as defined above) and lasting either until (1) date of laboratory confirmation of infection or (2) until the end of the study period. The pd for the unvaccinated group was the number of individuals' days at infection risk, starting with calendar week 05 (February 01, 2021) and lasting until (1) administration of the first vaccine dose, (2) the day of laboratory confirmation of infection or (3) the end of the study period. Individuals' person-days not included were days from first dose-administration of a 2-dosis vaccine-regimen until 14th day after second dose-administration or until 28th day after the single dose administration of the 1-dose vaccine regimen.

Variant-specific study cohort

For the variant-specific VE analyses, we divided the study period according to the occurrence of the two dominant variants, the Alpha-variant and Delta-variant (figure 1). Calendar week 16 to 22 (April 19 – June 06), during which the Alpha-variant accounted on average for 92% of the PCR- or sequence-based typed isolates per calendar week defined study period I (named as Alpha-period). Study period II, from calendar week 27 to 35 (July 05 – September 05), during which the Delta-variant was predominantly circulating with a weekly average proportion of 92%, was named as Delta-period. During the Alpha-period, the person-days of the fully vaccinated group was the number of individuals' days at risk beginning with the date of fully vaccination after April 18, until (1) date of laboratory confirmation of infection or (2) the end of study period I (cw 22). The person-days of the unvaccinated group was the number of individuals' days at risk from April 19 onwards until (1) first vaccine dose administration or (2) the date of laboratory confirmation of infection or (3) until the end of study period I. Inclusion and exclusion criteria for cases and individuals were as given above. During the Alpha-period, the mRNA-vaccinees accounted on average for 89.6% (IQR 73.9%-99.5%), with 99.9% in cw 16 and 66.7% in cw 22, of the fully vaccinated individuals. Due to too small counts, the pd of AZD1222- and J&J-vaccine recipients were excluded from the pd for the Alpha-period analyses. For the Delta-study period, the individuals' pd of the fully vaccinated and unvaccinated group were calculated according to the timespan of study period II.

Outcome measures and analyses

We calculated incidence rates per 100 000 person-days for the fully vaccinated and unvaccinated group of individuals, and the VE estimates against the three outcomes, the infection regardless of clinical presentation, the symptomatic infection and asymptomatic infection, according to the formulation of relative risk reduction, equal to vaccine effectiveness, VE = $(1 - IRR) \times 100$ using negative binomial regression models. Including the covariates age (18-29, 30-39, 40-49, 50-59, 60-75, 75+ years), sex, province of residence and calendar week, we calculated adjusted VE estimates against the three outcomes, as given above, for the total study period, the Alpha-period and the Delta-period. We calculated unadjusted and adjusted VE estimates stratified by the age-groups, 18-39, 40-59 and \geq 60 years and three vaccine groups (mRNA-vaccines, AZD1222-vaccine, J&J-vaccine) each, and by both variables combined. VE estimates with 95% confidence intervals (CIs) that did not overlap were considered statistically different.

Results

Study cases and study cohort of the entire study period, calendar week 05-35

From February 01, 2021 to September 05, 2021, 252 044 cases of laboratory confirmed SARS-CoV-2 infection were registered, and 237 702 cases were included in the analyses. Table 1 describes the study cases by age, sex, province of residence, clinical presentation and vaccination status. Table 2 describes the vaccine-eligible population by age, sex and province of residence, and the individuals' person-days of the fully vaccinated and unvaccinated group by sex, age, province of residence, and shows the fully vaccinated individuals' person-days by vaccine and age group, 12-17, 18-39, 40-59 and \geq 60 years old. Among the fully vaccinated individuals, the mRNAvaccinees' person-days accounted for the largest portion in all age groups, with 75.97% in the 18-39 years old, 80.61% in the 40-59 and with 88.50% the \geq 60 years old, compared to the other the other vaccinees. The 18-39 years old had the highest portion of J&J-vaccinees' person-days, with 6.31% compared to 2.98% among the 40-59 and 0.65% among the \geq 60 years old. Table 1. Study cases (N= 237 702) described by age, sex, province of residence, clinical presentation (asymptomatic, symptomatic including robust symptoms and other) and vaccination status (fully vaccinated by vaccine type and unvaccinated), Austria, February 01, 2021- September 05, 2021

Feature	Categories	n	%
Age group	12-17	22 807	9.59%
	18-39	99 997	42.07%
	40-59	79 206	33.32%
	≥ 60	35 692	15.02%
Sex	male	121 000	50.90%
	female	116 702	49.10%
Province	В	6 815	2.87%
	С	13 994	5.89%
	LA	44 076	18.54%
	UA	38 811	16.33%
	S	17 056	7.18%
	St	29 618	12.46%
	Ту	18 235	7.67%
	Vo	8 840	3.72%
	Vie	60 257	25.35%
Clinical presentation	robust*	137 236	57.73%
	other	22 105	9.30%
	asymptomatic	66 942	28.16%
	unknown	11 419	4.80%
Vaccination status	AZD1222-vaccine	1 951	0.82%
	J&J-vaccine	1 128	0.47%
	mRNA-vaccine	7 508	3.16%
	unvaccinated	227 115	95.55%

* robust symptoms defined as shortness of breath, difficulty breathing sore throat, congestion or runny nose, diarrhea, new loss of taste or smell; others included fatigue, muscle or body aches, headache, nausea or vomiting

B: Burgenland, C: Carinthia, LA: Lower Austria, UA: Upper Austria, S: Salzburg, St: Styria, Ty: Tyrol, Vo: Vorarlberg, Vie: Vienna

Table 2. Vaccine eligible individuals (n) and individuals' person-days of the fully vaccinated group (**pd**_{vac}) described by sex, province of residence, age group, and vaccine type, stratified by age group (**pd**_{vac}%) and individuals' person-days of the unvaccinated group by sex, age group and province of residence (**pd**_{unvac}, **pd**_{unvac}%), Austria, calendar week 05 – calendar week 35, 2021 (total study-period)

Characteristics	Category I	Category II	Vaccine eligible individuals	Fully vaccinated	Fully vaccinated	Unvaccinated	Unvaccinated
			n	\mathbf{pd}_{vac}	pd _{vac} %	pd _{unvac}	pd _{unvac} %
Sex	male	-	3 866 415	157 069 175	45.95%	486 768 679	50.12%
	female	-	4 035 002	184 735 646	54.05%	484 399 970	49.88%
Age group (agr)	12-17	-	512 639	3 048 986	0.89%	93 350 524	9.61%
	18-39	-	2 506 531	65 419 053	19.14%	360 956 458	37.17%
	40-59	-	2 578 730	105 593 330	30.89%	316 197 257	32.56%
	≥ 60	-	2 303 517	167 743 452	49.08%	200 664 410	20.66%
Age group (agr)	12-17	all	512 639	3 048 986	-	93 350 524	-
Agr/Vaccine	12-17	mRNA	-	3 048 986	100.00%	-	-
	18-39	all	2 506 531	65 419 053	-	360 956 458	-
	18-39	mRNA	-	49 698 956	75.97%	-	-
	18-39	AZD1222	-	11 591 620	17.72%	-	-
	18-39	J&J	-	412 877	6.31%	-	-
	40-59	all	2 578 730	105 593 330	-	316 197 257	-
	40-59	mRNA	-	85 119 483	80.61%	-	-
	40-59	AZD1222	-	17 331 636	16.41%	-	-
	40-59	J&J	-	3 142 211	2.98%	-	-
	≥ 60	all	2 303 517	167 743 452	-	200 664 410	-
	≥ 60	mRNA	-	148 456 169	88.50%	-	-
	≥ 60	AZD1222	-	18 195 311	10.85%	-	-
	≥ 60	J&J	-	1 091 972	0.65%	-	-
Province	В	-	265 337	12 907 730	3.78%	30 871 330	3.18%
	С	-	503 359	21 822 187	6.38%	62 661 717	6.45%
	LA	-	1 496 659	69 200 614	20.24%	178 967 353	18.43%
	UA	-	1 313 490	54 719 787	16.01%	163 492 165	16.83%
	S	-	494 692	20 662 314	6.04%	60 726 339	6.25%
	St	-	1 113 007	44 763 707	13.10%	140 017 204	14.42%
	Ту	-	671 314	31 380 274	9.18%	78 165 525	8.05%
	Vo	-	348 160	16 318 470	4.77%	40 918 305	4.21%
	Vie	-	1 695 399	70 053 453	20.49%	215 348 711	22.17%



Figure 1. Proportion of B.1.1.7 variant (Alpha-variant) and B.1617.2 variant (Delta-variant) of all typed isolates by calendar week, defining study period I (i.e. Alpha-period) and study period II (i.e. Delta-period), cw 05, 2021 – cw 35, 2021

Beginning in cw 16, the Alpha-variant accounted for 88.8% of all typed isolates, with a weekly average proportion of 92.17% until cw 22. Since cw 25, the Delta-variant has been predominantly circulating, with a weekly average proportion of 92.1% of all typed isolates between cw 27 and cw 35 (figure 1).



Figure 2. Age group-specific cumulative proportion fully vaccinated of the vaccineeligible population (proportion population fully vaccinated, PPV) by cw, study period I (cw 16-22), study period II (cw 27-35)

The cumulative proportion fully vaccinated of the vaccine-eligible population (PPV) by calendar week was calculated by the number of individuals having received all doses according to the vaccine-schedule and passed 14 days (2-doses regimen) or 28 days (1-dose-regimen) divided by the population estimate for the vaccine-eligible individuals for each calendar week. Figure 2 illustrates the cumulative age groupspecific PPVs over time. From cw 16 to 22 (Alpha-period), the 12-17 age group-PPV increased from 0.26% to 0.31%, the 18-59 age group-PPV from 4.22% to 8.57% and the \geq 60 age group-PPV from 17.78% to 35.41%. From cw 27 to 35 (Deltaperiod), the 12-17 age group-PPV increased from 1.27% to 26.50%, the 18-59 age group-PPV from 26.95% to 59.18% and the \geq 60 age group-PPV from 64.78% to 81.24%. In calendar week 37, the 12-17 age group-PPV reached 30.02%, the 18-59 age group-PPV 60.66% and the \geq 60 age group-PPV 81.88%. Figure 3 illustrates the cumulative PPV with mRNA-vaccines, AZD1222- and with the J&J-vaccine (i.e. mRNA-PPV, AZD1222-PPV, J&J-PPV) by calendar week. From the beginning of the Alpha-period in cw 16, the mRNA-PPV increased from 7.91% to 14.30%, the AZD1222-PPV from 0.0% to 1.48% and the J&J-PPV from 0.0% to 0.08% in cw 22. Beginning in calendar week 27, the mRNA-PPV increased from 29.44% to 51.39% in cw 35, the AZD1222-PPV from 5.91% to 9.49% and the J&J-PPV from 0.97% to 2.61% in cw 35. In calendar week 37, the mRNA-vaccine-PPV achieved 52.43%, the AZD1222-PPV 9.53% and the J&J-PPV 2.90%.



Figure 3. Vaccine-specific cumulative proportion fully vaccinated of the vaccineeligible population (proportion population fully vaccinated, PPV) by cw; study period I (cw 16 -22), study period II (cw 27-35).

Study cases and study cohort of the Alpha-period, calendar week 16 to 22

During the Alpha-period, of the 40 729 cases of laboratory confirmed SARS-CoV-2 infection registered during ca 16 to 22, 36 805 cases were included in the analyses. Table 3 describes the included case-persons by age, sex, province of residence, clinical presentation and vaccination status. Table 4 characterizes the vaccine eligible population and the individuals' pd of the fully vaccinated and unvaccinated group by sex, age and province of residence. The VE analyses were restricted to the mRNA-vaccines.

Table 3. Study cases (N=36 805) described by age, sex, province of residence, clinical presentation (asymptomatic, symptomatic including robust symptoms and other, unknown) and vaccination status, (the fully vaccinated include mRNA-vaccine recipients only), Austria, Alpha-period

Characteristics	Categories	n	%
Age group	18-39	17 717	48.16%
	40-59	14 115	38.37%
	≥ 60	4 953	13.46%
Sex	male	18 821	51.16%
	female	17 964	48.84%
Province	В	651	1.77%
	С	2 268	6.17%
	LA	5 202	14.14%
	UA	6 555	17.82%
	S	2 209	6.01%
	St	5 669	15.41%
	Ту	3 640	9.90%
	Vo	2 732	7.43%
	Vie	7 859	21.36%
Clinical presentation	robust*	22 351	60.76%
	other	4 198	11.41%
	asymptomatic	9 597	26.09%
	unknown	639	1.74%
Vaccination status	mRNA-vaccine	724	1.97%
	unvaccinated	36 061	98.03%

* Robust symptoms were defined as shortness of breath, difficulty breathing sore throat, congestion or runny nose, diarrhea, new loss of taste or smell; others included fatigue, muscle or body aches, headache, nausea or vomiting

Table 4. Vaccine eligible individuals (n) and individuals' person-days of the fully vaccinated group (**pd**_{vac}) (including mRNA-vaccine recipients only), and of the unvaccinated group (**pd**_{unvac}) described by sex, age group and province of residence (**pd**_{vac}%, **pd**_{unvac}%), Austria, April 19 – June 06, 2021 (Alpha-period).

Characteristics	Categories	Vaccine eligible individuals	Fully vaccinated	Fully vaccinated	Unvaccinated	Unvaccinated
		n	\mathbf{pd}_{vac}	pd _{vac} %	pd _{unvac}	pd _{unvac} %
Sex	male	3 866 415	15 816 709	41.69%	93 020 999	49.98%
	female	4 035 002	22 119 647	58.31%	93 109 764	50.02%
Age group	18-39	2 506 531	4 156 852	10.96%	84 821 200	45.57%
	40-59	2 578 730	7 779 352	20.50%	71 414 649	38.37%
	≥ 60	2 303 517	26 000 152	68.54%	29 894 914	16.06%
Province	В	265 337	1 184 888	3.12%	5 848 111	3.14%
	С	503 359	2 209 923	5.83%	11 803 104	6.34%
	LA	1 496 659	8 321 799	21.94%	35 372 051	19.00%
	UA	1 313 490	5 917 708	15.60%	31 103 908	16.71%
	S	494 692	2 249 689	5.93%	11 418 085	6.13%
	St	1 113 007	4 226 394	11.14%	27 695 121	14.88%
	Ту	671 314	4 802 633	12.66%	14 377 254	7.72%
	Vo	348 160	1 614 855	4.26%	7 541 631	4.05%
	Vie	1 695 399	7 408 467	19.53%	40 971 498	22.01%

Study cases and study cohort of the Delta-period, calendar week 27 to 35

A total of 38 137 out of 42 128 reported cases of laboratory confirmed SARS-CoV-2 infection were included in the analyses during the Delta-study period. Table 5 shows the study cases by age, sex, province of residence, clinical presentation and vaccination status. Table 6 displays the frequency distribution of the vaccine eligible individuals and the individuals' person-days of the fully vaccinated and unvaccinated group by sex, age group and province of residence and, in addition for the fully vaccinated group, by administered vaccine type for each age group.

Characteristics	Categories	n	%
Age group	12-17	4 432	11.62%
	18-39	20 800	54.54%
	40-59	9 759	25.59%
	≥ 60	3 146	8.25%
Sex	male	19 217	50.39%
	female	18 920	49.61%
Province	В	735	1.93%
	С	1 741	4.57%
	LA	5 341	14.00%
	UA	7 431	19.49%
	S	3 286	8.62%
	St	3 952	10.36%
	Ту	3 051	8.00%
	Vo	1 832	4.80%
	Vie	10 768	28.24%
Clinical presentation	robust	24 599	64.50%
	other	2 821	7.40%
	asymptomatic	9 938	26.06%
	unknown	779	2.04%
Vaccination status	AZD1222-vaccine	1 902	4.99%
	J&J-vaccine	1 122	2.94%
	mRNA-vaccine	5 534	14.51%
	Unvaccinated	29 579	77.56%

Table 5. Study cases (N=38 137) described by age, sex, province of residence, clinical presentation (asymptomatic, symptomatic including robust symptoms and other) and vaccination status, fully vaccinated (by vaccine type) and unvaccinated, Austria, July 05 to September 05 (Delta-period)

* Robust symptoms as defined above

Table 6. Vaccine eligible population (n) and individuals' person-days of the fully vaccinated group (**pd**_{vac}) described by sex, province of residence, age group, and by vaccine type, stratified by age group (**pd**_{vac}%), and individuals' person-days of the unvaccinated group (**pd**_{unvac}) by sex, province of residence and age group (**pd**_{unvac}%), Austria, July 05 - September 05 (Delta-period)

			Vaccine eligible				
Characteristics	Category I	Category II	individual s	Fully vaccinated	Fully vaccinated	Unvaccinated	Unvaccinated
			n	pd _{vac}	pd _{vac} %	pd _{unvac}	pd _{unvac} %
Sex	male		3 866 415	114 901 912	47.70%	73 036 718	49.54%
	female		4 035 002	125 982 043	52.30%	74 403 974	50.46%
Agr	12-17		512 639	2 924 834	1.21%	20 752 473	14.08%
	18-39		2 506 531	51 850 899	21.53%	61 706 812	41.86%
	40-59		2 578 730	80 628 010	33.47%	44 884 171	30.44%
	≥ 60		2 303 517	105 480 212	43.79%	20 084 266	13.62%
Agr	12-17	all	512 639	2 924 834	-	20 752 473	-
Agr_Vaccine	12-17	mRNA	-	2 924 834	100.00%	-	-
	18-39	all	2 506 531	51 850 899	-	61 706 812	-
	18-39	mRNA	-	38 918 477	75.06%	-	-
	18-39	AZD1222	-	9 056 414	17.47%	-	-
	18-39	J&J	-	3 876 008	7.48%	-	-
	40-59	all	2 578 730	80 628 010	-	44 884 171	-
	40-59	mRNA	-	63 914 722	79.27%	-	-
	40-59	AZD1222	-	13 859 737	17.19%	-	-
	40-59	J&J	-	2 853 551	3.54%	-	-
	≥ 60	all	2 303 517	105 480 212	-	20 084 266	-
	≥ 60	mRNA	-	88 008 769	83.44%	-	-
	≥ 60	AZD1222	-	16 511 289	15.65%	-	-
	≥ 60	J&J	-	960 154	0.91%	-	-
Province	В		265 337	9 435 758	3.92%	3 887 230	2.64%
	С		503 359	15 332 558	6.37%	10 509 950	7.13%
	LA		1 496 659	48 595 903	20.17%	24 513 154	16.63%
	UA		1 313 490	38 605 231	16.03%	26 844 806	18.21%
	S		494 692	14 808 375	6.15%	9 823 201	6.66%
	St		1 113 007	32 636 852	13.55%	21 001 356	14.24%
	Ту		671 314	20 561 479	8.54%	12 183 763	8.26%
	Vo		348 160	11 581 874	4.81%	6 202 678	4.21%
	Vie		1 695 399	49 325 925	20.48%	32 474 554	22.03%

Among the fully vaccinated individuals, the mRNA-vaccinees' person-days accounted for the largest fraction across age groups, with 75.06% among 18-39 years old, 79.27% among 40-59 and with 83.44% among the \geq 60 years old, compared to the other vaccines. The fraction of the J&J vaccinees' pd was highest among the 18-39 years old, with 7.48%, compared to 3.54% among 40-59 and 0.91% among \geq 60 years old.

Incidence rates by vaccination status and vaccine effectiveness, for the total study period

The adjusted VE estimate against infection, regardless of clinical presentation, was lowest among the 18-39 years old, with 74.62% (95%CI: 73.09%-76.07%), compared to 92.50% (95%CI: 90.45% - 94.19%) in the 12-17 years old, 80.31% (95%CI: 79.22% - 81.35%) in the 40.59 years old and 80.80% (95%CI: 79.65% - 81.90%) in the \geq 60 years old (table 7).

Table 8a and Table 8b display incidence rates of infection (all) and symptomatic infection for the unvaccinated and fully vaccinated individuals per 100 000 pd, stratified by age groups and the three vaccines, mRNA-vaccine group, AZD1222- and J&J-vaccine. It shows the resulting strata-specific VE estimates, unadjusted and adjusted. We found lowest adjusted estimates of VE against infection (all) and symptomatic infection for the J&J-vaccine in the 18-39 and 40-59 years old. The analyses retrieved highest adjusted VE estimates for the mRNA-vaccines against outcomes infection, all, and symptomatic infection in all age groups.

Table 7. Incidence rates (IR)/100 000 pd of infection, total (**asymptomatic and symptomatic**) for unvaccinated and fully vaccinated individuals; VE estimates against infection total, unadjusted and adjusted for age, sex, province and cw for each age-group (18-39, 40-49, \geq 60 years), across all vaccines (mRNA-vaccines, AZD1222- and J&J-vaccine), total study period (cw 05-cw 35)

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-17	All	22 727	24.35	80	2.62	90.02%	86.63% - 92.62%	92.50%	90.45% - 94.19%
18-39	All	95 620	26.49	4 377	6.69	72.83%	70.58% - 74.91%	74.62%	73.09% - 76.07%
40-59	All	75 743	23.95	3 463	3.28	82.03%	80.39% - 83.55%	80.31%	79.22% - 81.35%
≥ 60	All	33 025	16.46	2 667	1.59	85.59%	84.12% - 86.93%	80.80%	79.65% - 81.90%

Table 8a. Incidence rates (IR)/100 000 pd of infection (**asymptomatic and symptomatic**) for unvaccinated and fully vaccinated individuals; VE against infection, unadjusted and adjusted for age, sex, province, and calendar weeks, stratified by age groups and vaccines (AZD1222-, J&J-, mRNA-vaccine); total study period

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-17	mRNAv	22 727	24.35	80	2.62	90.02%	86.63% - 92.62%	92.50%	90.45% - 94.19%
18-39	AZD1222v	95 620	26.49	1 026	8.85	69.00%	65.24% - 72.35%	61.56%	58.07% - 64.79%
	J&Jv	95 620	26.49	783	18.97	38.15%	29.53% - 45.71%	40.26%	33.85% - 46.11%
	mRNAv	95 620	26.49	2 568	5.17	82.82%	81.13% - 84.35%	82.41%	81.23% - 83.51%
40-59	AZD1222v	75 743	23.95	648	3.74	83.15%	80.83% - 85.19%	73.37%	70.66% - 75.86%
	J&Jv	75 743	23.95	308	9.8	57.21%	49.82% - 63.56%	44.02%	36.28% - 50.97%
	mRNAv	75 743	23.95	2 507	2.95	85.36%	83.80% - 86.76%	83.34%	82.33% - 84.30%
≥ 60	AZD1222v	33 025	16.46	277	1.52	89.74%	87.91% - 91.31%	81.33%	78.58% - 83.79%
	J&Jv	33 025	16.46	37	3.39	76.80%	67.58% - 83.88%	62.96%	49.15% - 73.88%
	mRNAv	33 025	16.46	2 353	1.59	84.48%	82.72% - 86.05%	81.04%	79.87% - 82.15%

Table 8b. Incidence rates (IR)/100 000 pd of **symptomatic infection** for unvaccinated and fully vaccinated individuals; VE against symptomatic infection, unadjusted and adjusted, stratified by age groups and vaccines (AZD1222-, J&J-, mRNA-vaccine); total study period

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-1	l7 mRNAv	13 001	13.93	33	1.08	92.36%	88.75% - 94.96%	95.22%	93.27% - 96.72%
18-3	39 AZD1222v	65 969	18.28	776	6.7	65.95%	61.61% - 69.80%	61.24%	57.43% - 64.75%
	J&Jv	65 969	18.28	600	14.54	31.13%	21.02% - 39.97%	37.96%	30.80% - 44.47%
	mRNAv	65 969	18.28	1712	3.44	84.39%	82.77% - 85.85%	84.59%	83.43% - 85.67%
40-5	59 AZD1222v	52 244	16.52	511	2.95	80.73%	77.97% - 83.16%	71.56%	68.47% - 74.40%
	J&Jv	52 244	16.52	234	7.45	52.59%	43.77% - 60.13%	41.58%	32.72% - 49.50%
	mRNAv	52 244	16.52	1 590	1.87	88.17%	86.86% - 89.34%	85.95%	84.98% - 86.86%
≥ 6	50 AZD1222v	21 239	10.58	195	1.07	88.52%	86.23% - 90.47%	80.47%	77.12% - 83.42%
	J&Jv	21 239	10.58	23	2.11	76.91%	65.32% - 85.39%	64.71%	47.77% - 77.40%
	mRNAv	21 239	10.58	1 214	0.82	90.09%	88.92% - 91.13%	85.82%	84.73% - 86.83%



Figure 4. Age-group specific adjusted VE estimates of the AZD1222-vaccine, J&J-vaccine and the mRNA-vaccines against symptomatic infection; total study period

Alpha-study period: Incidence rates by vaccination status and vaccine effectiveness

During the Alpha-period the adjusted VE of the mRNA-vaccines against infection (symptomatic and asymptomatic) was 86.10% (95%CI: 84.91%-87.21%), across all age groups (\geq 18 years). Table 9 shows the age group-specific IR per 100.000 pd of symptomatic infection for unvaccinated and fully vaccinated individuals in the Alpha-period and the corresponding age group-specific VE estimates of the mRNA-vaccine group, unadjusted and adjusted. The adjusted VE estimate against symptomatic infection was 92.05% (95%CI: 90.63% - 93.30%) in the \geq 60 years old, slightly higher compared to the 40-59 years old and 18-39 years old, with an adjusted VE of 88.49% (95%CI: 86.06% - 90.61%) and of 89.42% (95%CI: 86.34% - 92.00%).

Table 9. Age group-specific IR per 100 000 pd of **symptomatic infection** for unvaccinated and fully vaccinated individuals (including mRNA-vaccine recipients only); VE estimates against symptomatic infection, unadjusted and adjusted for age, sex, province and cw; Alpha-study period (cw 16-cw 22)

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
18-39	mRNAv	12 825	13.98	55	1.32	90.35%	87.13% - 92.89%	89.42%	86.34% - 92.00%
40-59	mRNAv	10 290	13.42	101	1.3	89.92%	87.28% - 92.07%	88.49%	86.06% - 90.61%
≥ 60	mRNAv	3 114	9.62	164	0.63	93.28%	91.64% - 94.62%	92.05%	90.63% - 93.30%



Figure 5. Age group-specific adjusted VE estimates of the mRNA-vaccines against symptomatic infection; Alpha-study period (cw 16cw 22)

Delta-study period: Incidence rates by vaccination status and vaccine effectiveness

For all vaccines combined, the estimated VE (adjusted) against infection (including asymptomatic and symptomatic) in the Delta-period was lowest (adjVE: 71.17%; 95%CI: 68.89%-73.29%) in the 18-39 years old, compared with 12-17, 40-59 and \geq 60 years old individuals (Table 10a). Similar findings were seen for the study outcome symptomatic infection, illustrated in table 10b.

Stratifying by age group and vaccine yielded lowest adjusted VE estimates against infection, all (data not shown) and symptomatic infection for the J&J-vaccine, in all three age groups (18-39 years, **40.43%** [95%CI: 33.79%-46.49%]; 40-59 years old, **40.98%** [95%CI: 32.47%-48.66%]; \geq 60 years old, **63.20%** (95%CI: 45.68%-76.39%), compared to age group-specific VE estimates for mRNA-vaccines and AZD1222-vaccine. Among the 12-17-. 18-39 and the 40-59 years old, the mRNA vaccines showed highest VE estimates (12-17 years old: 95.36%; 18-39 years old: 83.64%; 40-59 years old: 84.76%, adjusted). In the \geq 60 years old, the adjusted mRNA-VE and AZD1222-VE estimates were comparably high, with 81.87% (95%CI: 79.90% - 83.65%) and 80.11% (95%CI: 76.70% - 83.10%), respectively (Table 11).

Table 10a. Age group-specific IR per 100 000 pd of **symptomatic and asymptomatic infection** for unvaccinated and fully vaccinated individuals; VE estimates against symptomatic infection, unadjusted and adjusted for age, sex, province and cw; Delta-study period (cw 27-cw 35)

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-17	All	4 353	20.96	79	2.70	88.53%	84.15% - 91.76%	92.52%	90.57% - 94.15%
18-39	All	16 789	27.21	4 011	7.74	66.14%	61.93% - 69.93%	71.17%	68.89% - 73.29%
40-59	All	6 925	15.43	2 834	3.51	72.87%	68.80% - 76.46%	79.83%	78.65% - 80.96%
≥ 60	All	1 512	7.53	1 634	1.55	80.43%	77.05% - 83.33%	81.15%	79.48% - 82.68%

Table 10b. Age group-specific IR per 100 000 pd of **symptomatic infection** for unvaccinated and fully vaccinated individuals; VE estimates against symptomatic infection, unadjusted and adjusted for age, sex, province and cw; Delta-study period (cw 27-cw 35)

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-17	All	2 845	13.70	32	1.09	92.44%	88.54% - 95.14%	95.36%	93.45% - 96.83%
18-39	All	12 435	20.15	2 903	5.60	66.61%	62.34% - 70.43%	72.15%	69.81% - 74.33%
40-59	All	5 088	11.34	2 037	2.53	73.16%	69.02% - 76.78%	79.98%	78.59% - 81.30%
≥ 60	All	1 016	5.06	1 064	1.01	80.11%	76.41% - 83.24%	81.21%	79.26% - 82.96%

Table 11. Incidence rates (IR)/100 000 pd of **symptomatic infection** for unvaccinated and fully vaccinated individuals; VE against symptomatic infection, unadjusted and adjusted, stratified by the age groups and vaccines (AZD1222-, J&J-, mRNA-vaccine); Delta-study period

Agr	Vaccine	Unvaccinated cases	Unvaccinated IR	Vaccinated cases	Vaccinated IR	Unadjusted VE	Unadjusted 95%CI	Adjusted VE	Adjusted 95%CI
12-17	mRNAv	2845	13.7	32	1.09	92.44%	88.54% - 95.14%	95.36%	93.45% - 96.83%
18-39	AZD1222v	12435	20.15	755	8.34	60.72%	54.45% - 66.13%	61.32%	57.59% - 64.75%
	J&Jv	12435	20.15	598	15.43	33.89%	22.63% - 43.55%	40.43%	33.79% - 46.49%
	mRNAv	12435	20.15	1550	3.98	82.92%	80.50% - 85.04%	83.64%	82.33% - 84.86%
40-59	AZD1222v	5088	11.34	496	3.58	69.95%	64.41% - 74.65%	71.44%	68.50% - 74.17%
	J&Jv	5088	11.34	234	8.2	34.55%	20.12% - 46.49%	40.98%	32.47% - 48.66%
	mRNAv	5088	11.34	1307	2.04	84.40%	81.71% - 86.71%	84.76%	83.65% - 85.80%
≥ 60	AZD1222v	1016	5.06	192	1.16	78.68%	73.13% - 83.13%	80.11%	76.70% - 83.10%
	J&Jv	1016	5.06	23	2.4	55.93%	31.91% - 72.73%	63.20%	45.68% - 76.39%
	mRNAv	1016	5.06	849	0.96	81.77%	78.04% - 84.87%	81.87%	79.90% - 83.65%



Figure 6. Age group-specific adjusted VE estimates of the AZD1222-vaccine, J&J-vaccine and the mRNA-vaccines against symptomatic infection; Delta-stud period

Discussion

Several factors should be taken into consideration, which may have affected the calculated VE estimates. A differential probability of case detection between vaccinated and unvaccinated individuals results from vaccination-specific test strategy. Unvaccinated individuals are obliged to be tested on several occasions (e.g. entry tests). Therefore, infected unvaccinated individuals are more likely to be detected as a case compared to vaccinated individuals, which results in overestimation of the VE for all three vaccine-groups. Vaccinee-cases may be more likely to report symptoms, which will result in an underestimation of the VE, similarly affecting all three vaccine-types. Underestimation of the VE of all three vaccines cannot be ruled out due to possibly undetected and unreported cases. The extent of missing cases is thought to be low in Austria, compared to other countries, because of high test-frequency (screening testing. contact person testing) in Austria. Vaccinees are less likely to adhere to non-pharmaceutical interventions (more risky behaviour) and are, therefore, more likely to be exposed to the virus than nonvaccinees. This might be even more pronounced in recipients of the 1-dose regimen J&J-vaccine, compared to the mRNA- and AZD1222-vaccinees. This difference in healthy vaccinee behaviour between the vaccinees may partly explain the low VE estimates found for the J&J vaccine s. Adjustment by time using regression models minimised the effect of changing risk of exposure to the virus over time on the VE estimates. However, extending the study period may still have an effect on the VE estimates due to continuing increase of the risk of exposure beyond calendar week 35. We want to emphasize, it is unlikely that waning immunity can explain the low VE estimated for the J&J vaccine, as the J&J vaccine has been administered only since beginning of May.

Conclusions

Overall, we found high VE estimates in all age groups for the mRNA-vaccines against infection (all) ranging from 81% to 93%, and symptomatic infection ranging from 85% to 95%, between February 02 and September 05. 2021. The effectiveness of the mRNA-vaccines in preventing symptomatic infection was lower for the Delta-variant as compared with the Alpha-variant (18-39 yrs. old: 89%; 40-59 yrs. old: 88%; \geq 60 yrs. old: 92%) among all age groups. Nevertheless, the VE against Delta-variant was still high (18-39 yrs. old: 84%; 40-59 yrs. old: 85%; \geq 60 yrs. old: 82%). During the Delta-period, we found effectiveness estimates against symptomatic infection for AZ1222-vaccine between 61% and 80%. Considerably lower was the effectiveness against Delta-variant infection, observed for the J&J-vaccine, in all three age groups. (18-39 yrs. old: 40%; 40-59 yrs. old: 41%; \geq 60 yrs. old: 63%). Our findings support the recently updated recommendation of the National Immunization Technical Advisory Group for a second dose with mRNA-vaccine among all J&J vaccine recipients.



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