

# Supplement

**Supplement Table S1.** Baseline characteristics of SARS-CoV-2 cases and test-negative controls included in at least one booster CVE analysis, VEBIS primary care study, Hungary, September 2022 -March 2023.

Characteristics	18+ included in at least first booster analyses (Full primary series + at least 1 booster VS. Unvaccinated)					
	SARS-CoV-2 cases (n = 247)		Test-negative controls (n = 1,073)		p-value	
	n	%	n	%		
Age (median [IQR])		53 [41–68]		51 [37–66]		0.015
	Missing	0	0.00	0	0.00	
Age group (years)						
	18-59	137	55.47	693	64.59	
	60+	110	44.53	380	35.41	0.007
Sex						
	Female	146	59.11	650	60.58	
	Male	101	40.89	423	39.42	0.671
	Missing	0	0.00	0	0.00	
BMI <sup>a</sup>						
	max. 29	172	69.64	736	68.59	
	30+	75	30.36	337	31.41	0.750
	Missing	0	0.00	0	0.00	
Symptoms						
	Cough	210	85.02	864	80.52	0.102
	Short breath	31	12.55	148	13.81	0.604
	Sore throat	212	85.83	845	78.75	0.012
	Coryza	209	84.62	930	86.67	0.397
	Fever	167	67.61	603	56.20	0.001
	Malaise	222	89.88	860	80.15	0.000
	Myalgia	166	67.21	534	49.77	0.000
	Headache	171	69.23	600	55.97	0.000
	Anosmia	17	6.88	28	2.61	0.001
	Ageusia	14	5.67	24	2.24	0.004
Chronic condition <sup>ba</sup>						
	Presence of chronic condition	69	27.94	278	25.91	0.480
	No chronic condition	174	70.45	784	73.07	
	Missing	4	1.62	11	1.03	
Chronic condition <sup>bb</sup>						
	Presence of chronic condition	113	45.75	497	46.32	0.842

No chronic condition		134	54.25	573	53.40	
Missing		0	0.00	3	0.28	
Severity <sup>c</sup>						
0		231	93.52	979	91.24	
1+		16	6.48	94	8.76	0.242
Missing		0	0.00	0	0.00	
GP consultation <sup>d</sup>						
0-1		27	10.93	145	13.51	
2+		220	89.07	928	86.49	0.277
Missing		0	0.00	0	0.00	
0-4		102	41.30	505	47.06	
5+		145	58.70	568	52.94	0.101
Missing		0	0.00	0	0.00	
Smoking <sup>e</sup>						
Never or former		191	77.33	798	74.37	
Current		32	12.96	225	20.97	0.011
Missing		24	9.72	50	4.66	
Swab delay <sup>f</sup>						
max. 2 days		119	48.18	630	58.71	
3+ days		128	51.82	443	41.29	0.003
Missing		0	0.00	0	0.00	
Previous SARS-CoV-2 test <sup>g</sup>						
Previous test		98	39.68	215	20.04	0.000
No previous test		149	60.32	858	79.96	
Missing		0	0.00	0	0.00	
Self-reported prior SARS-CoV-2 infection <sup>h</sup>						
Prior		45	18.22	225	20.97	0.334
No prior		202	81.78	848	79.03	
Missing		0	0.00	0	0.00	
Self-reported prior SARS-CoV-2 infection <sup>h</sup>						
Prior (60-365 days)		13	6.05	109	11.39	0.020
No prior		202	93.95	848	88.61	
Self-reported prior SARS-CoV-2 infection <sup>h</sup>						
Prior (366+ days)		32	13.68	116	12.03	0.494
No prior		202	86.32	848	87.97	
COVID-19 vaccination status						
Unvaccinated						
All		57	23.08	234	21.81	
18-59 years (age)		40	29.20	205	29.58	
60+ years (age)		17	15.45	29	7.63	

**Full primary series plus at least one booster dose**

<b>All</b>	190	76.92	839	78.19	0.664
<b>18-59 years (age)</b>	97	70.80	488	70.42	0.928
<b>60+ years (age)</b>	93	84.55	351	92.37	0.013
<b>14-180 days (time since last vaccination)</b>	7	2.83	45	4.19	0.296
<b>181-365 days (time since last vaccination)</b>	66	26.72	252	23.49	0.720
<b>366+ days (time since last vaccination)</b>	117	47.37	542	50.51	0.501
<b>Homologous series <sup>i</sup></b>	76	30.77	420	39.14	0.123
<b>Heterologous series <sup>i</sup></b>	114	46.15	419	39.05	0.542

<sup>a</sup> BMI calculated as weight/(height\*height).

<sup>ba</sup> The presence of chronic condition is defined as reporting at least one of the following conditions: diabetes, heart disease, lung disease, immunodeficiency.

<sup>bb</sup> The presence of chronic condition is defined as reporting at least one of the following conditions: diabetes, heart disease, hypertension, lung disease, immunodeficiency, cancer, renal disease.

<sup>c</sup> Severity: number of hospitalizations in the previous 12 months for chronic disease.

<sup>d</sup> Number of GP consultations in the previous 12 months.

<sup>e</sup> Former: stopped smoking at least 1 year before inclusion in the study. Current smoker: any smoking can be included: cigarettes, cigars, vaping, etc.

<sup>f</sup> Swab delay: number of days between date of swab and date of onset.

<sup>g</sup> Previous SARS-CoV-2 test: Has the patient had a previous SARS-CoV-2 test (e.g. PCR, antigen, both, unknown) related to his/her current symptoms?

<sup>h</sup> Previous SARS-CoV-2 infection: Has the patient had a positive SARS-CoV-2 test prior to this illness episode? (At all, 60-365, 366+ days before current onset)

<sup>i</sup> Homologous series: primary series and at least one dose booster dose are all mRNA vaccines. Heterologous series: primary series and at least one dose booster are not all mRNA vaccines.

**Supplement Table S2.** COVID-19 vaccine effectiveness estimates for at least first booster vaccination among 18+ adults, VEBIS primary care study, Hungary, September 2022 -March 2023.

Population	Time since last booster vaccination (days)	Adjusted CVE (95% CI)*	N	Vaccinated cases	Unvaccinated cases	Vaccinated controls	Unvaccinated controls
Adults aged 18 years and above	14+	20.4 (-13.9; 44.4)	1,320	190	57	839	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 infection)	14+	20.4 (-14.0; 44.4)	1,320	190	57	839	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 test)	14+	20.3 (-14.9; 44.7)	1,320	190	57	839	234
Adults aged 18 years and above reporting no previous SARS-CoV-2 test	14+	29.5 (-9.4; 54.6)	1,007	112	37	671	187
Adults aged 18 years and above reporting previous SARS-CoV-2 test	14+	10.5 (-114.6; 43.1)	313	78	20	168	47
Adults aged 18-59 years	14+	2.3 (-50.0; 36.3)	830	97	40	488	205
Adults aged 18-59 years (plus adjustment for previous SARS-CoV-2 infection)	14+	1.4 (-51.5; 35.8)	830	97	40	488	205
Adults aged 18-59 years and above (plus adjustment for previous SARS-CoV-2 test)	14+	0.7 (-53.8; 35.9)	830	97	40	488	205
Adults aged 60 years and above	14+	56.8 (11.9; 78.8)	490	93	17	351	29
Adults aged 60 years and above (plus adjustment for previous SARS-CoV-2 infection)	14+	57.7 (13.3; 79.4)	490	93	17	351	29
Adults aged 60 years and above (plus adjustment for previous SARS-CoV-2 test)	14+	58.3 (14.2; 79.7)	490	93	17	351	29

Adults aged 18 years and above	14-180	63.8 (-14.0; 88.5)	343	7	57	45	234
Adults aged 18 years and above	181-365	57.4 (30.5; 73.9)	609	66	57	252	234
Adults aged 18 years and above	14-365	55.4 (28.9; 72.1)	661	73	57	297	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 infection)	14-365	54.6 (27.4; 71.6)	661	73	57	297	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 test)	14-365	55.9 (29.0; 72.6)	661	73	57	297	234
Adults aged 18 years and above reporting no previous SARS-CoV-2 test	14-365	57.6 (24.2; 76.3)	488	38	37	226	187
Adults aged 18 years and above reporting previous SARS-CoV-2 test	14-365	51.5 (-16.5; 79.8)	173	35	20	71	47
Adults aged 18 years and above	366+	-18.9 (-83.2; 22.8)	950	117	57	542	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 infection)	366+	-19.1 (-83.5; 22.7)	950	117	57	542	234
Adults aged 18 years and above (plus adjustment for previous SARS-CoV-2 test)	366+	-20.0 (-86.0; 22.5)	950	117	57	542	234
Adults aged 18-59 years	14-365	52.9 (15.2; 73.9)	461	38	40	178	205
Adults aged 60 years and above	14-365	72.3 (32.0; 88.7)	200	35	17	119	29
Adults aged 18-59 years	366+	-85.7 (-225.5; -5.9)	614	59	40	310	205
Adults aged 60 years and above	366+	39.8 (-31.0; 72.3)	336	58	17	232	29

---

\* adjusted for symptom onset week, age, sex, and presence of at least one chronic condition including diabetes, immunodeficiency, lung disease, and heart disease

CVE: COVID-19 vaccine effectiveness

CI: confidence interval

**Supplement Table S3.** Protection conferred by prior infection and/or vaccine effectiveness COVID-19 vaccine effectiveness for at least first booster vaccination among 18+ adults (reference group: no prior infection and no vaccination), VEBIS primary care study, Hungary, September 2022 -March 2023.

Population	Time since last booster vaccination (days)	Adjusted CVE (95% CI)*	N	Vaccinated cases	Unvaccinated cases	Vaccinated controls	Unvaccinated controls
Adults aged 18 years and above unvaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	-246.1 (-929.3; -16.4)	244	8	40	20	176
Adults aged 18 years and above unvaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	-210.8 (-787; -8.9)	263	9	40	38	176
Adults aged 18 years and above vaccinated, never infected VS. unvaccinated, never infected	14+	12.0 (-34.4; 42.4)	1,050	162	40	672	176
Adults aged 18 years and above vaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	84.8 (50.1; 95.4)	310	5	40	89	176
Adults aged 18 years and above vaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	-45.3 (-191.6; 27.6)	317	23	40	78	176
Adults aged 18-59 years unvaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	-367 (-1395.1; -45.9)	203	8	25	17	153
Adults aged 18-59 years unvaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	-212.4 (-882.2; 0.6)	220	7	25	35	153
Adults aged 18-59 years vaccinated, never infected VS. unvaccinated, never infected	14+	-18.6 (-99.0; 29.3)	620	75	25	367	153

Adults aged 18-59 years vaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	63.0 (-28.0; 89.3)	244	4	25	62	153
Adults aged 18-59 years vaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	-108.1 (-382.9; 10.3)	255	18	25	59	153
Adults aged 60 years and above unvaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	49.5 (-1307.0; 98.2)	41	0	15	3	23
Adults aged 60 years and above unvaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	-54.8 (-2388.4; 90.4)	43	2	15	3	23
Adults aged 60 years and above vaccinated, never infected VS. unvaccinated, never infected	14+	55.1 (1.2; 79.6)	430	87	15	305	23
Adults aged 60 years and above vaccinated, previously infected (60-365 days) VS. unvaccinated, never infected	14+	87.6 (26.4; 97.9)	66	1	15	27	23
Adults aged 60 years and above vaccinated, previously infected (366+ days) VS. unvaccinated, never infected	14+	39.0 (-138.4; 84.4)	62	5	15	19	23

\* adjusted for symptom onset week, age, sex, and presence of at least one chronic condition including diabetes, immunodeficiency, lung disease, and heart disease

CVE: COVID-19 vaccine effectiveness (When comparing unvaccinated patients, the measure of effect is the protection conferred by infection rather than vaccine effectiveness.)

CI: confidence interval



**Supplement Table S4.** Baseline characteristics of those had previous SARS-CoV-2 test and those without previous SARS-CoV-2 test, VEBIS primary care study, Hungary, September 2022 -March 2023.

Characteristics	Previous SARS-CoV-2 test VS. No previous SARS-CoV-2 test					p-value
	Previous SARS-CoV-2 test (n = 432)		No previous SARS-CoV-2 test (n = 1,531)			
	n	%	n	%		
Age (median [IQR])	49 [35–64.5]		48 [34–63]		0.155	
Missing	0	0.00	0	0.00		
Age group (years)						
18-59	288	66.67	1064	69.50		
60+	144	33.33	467	30.50	0.262	
Sex						
Female	268	62.04	904	59.05		
Male	164	37.96	627	40.95	0.263	
Missing	0	0.00	0	0.00		
BMI <sup>a</sup>						
max. 29	300	69.44	1,060	69.24		
30+	132	30.56	471	30.76	0.934	
Missing	0	0.00	0	0.00		
Chronic condition <sup>ba</sup>						
Presence of chronic condition	128	29.63	328	21.42	0.000	
No chronic condition	301	69.68	1,185	77.40		
Missing	3	0.69	18	1.18		
Chronic condition <sup>bb</sup>						
Presence of chronic condition	201	46.53	591	38.60	0.003	
No chronic condition	231	53.47	936	61.14		
Missing	0	0.00	4	0.26		
Severity <sup>c</sup>						
0	399	92.36	1,419	92.68		
1+	33	7.64	112	7.32	0.820	
GP consultation <sup>d</sup>						
0-1	48	11.11	235	15.35	0.027	
2+	384	88.89	1,296	84.65		
Missing	0	0.00	0	0.00		
0-4	178	41.20	759	49.58	0.002	
5+	254	58.80	772	50.42		
Missing	0	0.00	0	0.00		

Smoking <sup>e</sup>						
Never or former	313	72.45	1,126	73.55		
Current	82	18.98	340	22.21	0.305	
Missing	37	8.56	65	4.25		
Swab delay <sup>f</sup>						
max. 2 days	243	56.25	873	57.02	0.775	
3+ days	189	43.75	658	42.98		
Missing	0	0.00	0	0.00		
Case status						
SARS-CoV-2 case	132	30.56	223	14.57	0.000	
Test-negative control	300	69.44	1,308	85.43		
Missing	0	0.00	0	0.00		
Self-reported prior SARS-CoV-2 infection <sup>g</sup>						
Prior	134	31.02	296	19.33	0.000	
No prior	298	68.98	1,235	80.67		
Missing	0	0.00	0	0.00		
Self-reported prior SARS-CoV-2 infection <sup>g</sup>						
Prior (60-365 days)	70	19.02	126	9.26	0.000	
No prior	298	80.98	1,235	90.74		
Self-reported prior SARS-CoV-2 infection <sup>g</sup>						
Prior (366+ days)	64	17.68	170	12.10	0.005	
No prior	298	82.32	1,235	87.90		
COVID-19 vaccination status						
Unvaccinated						
All	67	15.51	224	14.63		
18-59 years (age)	56	19.44	189	17.76		
60+ years (age)	11	7.64	35	7.49		
Full primary series plus at least one booster dose						
All	246	56.94	783	51.14	0.755	
18-59 years (age)	137	47.57	448	42.11	0.861	
60+ years (age)	109	75.69	335	71.73	0.924	
14-180 days (time since last vaccination)	18	4.17	34	2.22	0.075	
181-365 days (time since last vaccination)	88	20.37	230	15.02	0.188	
366+ days (time since last vaccination)	140	32.41	519	33.90	0.540	
Homologous series <sup>h</sup>	130	30.09	366	23.91	0.319	
Heterologous series <sup>h</sup>	116	26.85	417	27.24	0.677	

<sup>a</sup> BMI calculated as weight/(height\*height).

<sup>a</sup> BMI calculated as weight/(height\*height).

---

<sup>ba</sup> The presence of chronic condition is defined as reporting at least one of the following conditions: diabetes, heart disease, lung disease, immunodeficiency.

---

<sup>bb</sup> The presence of chronic condition is defined as reporting at least one of the following conditions: diabetes, heart disease, hypertension, lung disease, immunodeficiency, cancer, renal disease.

---

<sup>c</sup> Severity: number of hospitalizations in the previous 12 months for chronic disease.

---

<sup>d</sup> Number of GP consultations in the previous 12 months.

---

<sup>e</sup> Former: stopped smoking at least 1 year before inclusion in the study. Current smoker: any smoking can be included: cigarettes, cigars, vaping, etc.

---

<sup>f</sup> Swab delay: number of days between date of swab and date of onset.

---

<sup>g</sup> Previous SARS-CoV-2 infection: Has the patient had a positive SARS-CoV-2 test prior to this illness episode? (At all, 60-365, 366+ days before current onset)

---

<sup>h</sup> Homologous series: primary series and at least one dose booster dose are all mRNA vaccines. Heterologous series: primary series and at least one dose booster are not all mRNA vaccines.

---