

1 [Supplementary material](#)

- 2 **Supplementary table 1:** Table of patients meeting the EU ARI and the EU ILI case definitions by
3 age group among study sites using the EU ARI case definition to recruit patients (n=31 645), study
4 on effect of case definition on influenza vaccine effectiveness, VEBIS primary care multicentre
5 case-control study, EU/EEA, 2022–23

	Meets ARI case definition	Age group			Total	
		No	Yes	Missing ^b		
All	No	0-4	542	0	542	
		15-64	1219	0	1219	
		65+	270	0	270	
	Yes	0-4	766	7160	136	8062
		15-64	1161	13926	232	15319
		65+	636	3141	102	3879
	Missing ^a	0-4	9	0	621	630
		15-64	10	0	1245	1255
		65+	4	0	448	452
	Total	0-4	1317	7160	757	9234
		15-64	2390	13926	1477	17793
		65+	910	3141	550	4601
Influenza cases	No	0-4	151	0	151	
		15-64	269	0	269	
		65+	19	0	19	
	Yes	0-4	44	2508	9	2561
		15-64	93	3673	16	3782
		65+	23	337	6	366
	Missing ^a	0-4	0	0	205	205
		15-64	0	0	246	246
		65+	0	0	28	28
	Total	0-4	195	2508	214	2917
		15-64	362	3673	262	4297
		65+	42	337	34	413
Controls	No	0-4	391	0	391	
		15-64	950	0	950	
		65+	251	0	251	
	Yes	0-4	722	4652	127	5501
		15-64	1068	10253	216	11537
		65+	613	2804	96	3513
	Missing ^a	0-4	9	0	416	425
		15-64	10	0	999	1009
		65+	4	0	420	424
	Total	0-4	1122	4652	543	6317
		15-64	2028	10253	1215	13496
		65+	868	2804	516	4188

6 ^aThe ARI case definition was coded as “missing” among patients with missing information for “sudden onset” or where at least
7 one of the four respiratory symptoms was coded as missing and none was coded as “yes”.

8 ^bThe ILI case definition was coded as “missing” among patients with missing information for “sudden onset” or where at least one
9 of the four systemic symptoms was coded as missing and none was coded as “yes” or where at least one of the three respiratory
10 symptoms (cough, sore throat, shortness of breath) was coded as missing and none was coded “yes”.

12 **Supplementary table 2:** Descriptive analysis of pooled data by case-control status among **EU ARI patients**
13 (N=27 277) in study sites collecting information on symptoms and recruiting patients meeting the EU ARI
14 case definition, study on effect of case definition on influenza vaccine effectiveness, VEBIS primary care
15 multicentre case-control study, EU/EEA, 2022–23

Variable	Test-negative controls (N=20562)	All influenza cases (N=6715)	Influenza A cases (N=4363)	Influenza A(H3N2) cases (N=2796)	Influenza A(H1N1)pdm09 cases (N=1129)	Influenza B cases (N=2347)
Age						
Mean (SD)	37.3 (25.6)	27.8 (20.8)	30.4 (22.4)	27.2 (21.8)	37.8 (22)	23.1 (16.5)
Median (IQR)	39 (13–58)	24 (9–43)	28 (10–48)	20 (9–44)	41 (17–54)	18 (8–36)
Missing, n (%)	11 (0.1)	6 (0.1)	5 (0.1)	4 (0.1)	1 (0.1)	1 (0)
Age in groups, n (%)						
0-4	3153 (15)	704 (10)	493 (11)	336 (12)	116 (10)	212 (9)
5-14	2348 (11)	1857 (28)	1063 (24)	808 (29)	146 (13)	795 (34)
15-64	11537 (56)	3782 (56)	2468 (57)	1463 (52)	757 (67)	1308 (56)
65 +	3513 (17)	366 (5)	334 (8)	185 (7)	109 (10)	31 (1)
Missing	11 (0)	6 (0)	5 (0)	4 (0)	1 (0)	1 (0)
Sex, n (%)						
Female	11856 (58)	3403 (51)	2249 (52)	1435 (52)	591 (52)	1150 (49)
Male	8675 (42)	3295 (49)	2102 (48)	1350 (48)	537 (48)	1192 (51)
Missing	31 (0)	17 (0)	12 (0)	11 (0)	1 (0)	5 (0)
Seasonal influenza vaccination, n (%)						
No	16469 (80)	6254 (93)	3969 (91)	2569 (92)	1002 (89)	2281 (97)
Yes	4093 (20)	461 (7)	394 (9)	227 (8)	127 (11)	66 (3)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Delay between onset of symptoms and swabbing in days						
Mean (SD)	2.8 (1.8)	2.6 (1.6)	2.5 (1.6)	2.5 (1.6)	2.5 (1.5)	2.8 (1.6)
Median (IQR)	3 (1-4)	2 (1-4)	2 (1-3)	2 (1-3)	2 (1-3)	3 (2-4)
Missing, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Any chronic condition, n (%)						
No presence of chronic disease	12901 (70)	5061 (84)	3210 (81)	2167 (83)	802 (77)	1847 (89)
Presence of chronic disease	5441 (30)	977 (16)	755 (19)	448 (17)	241 (23)	221 (11)
Missing	2220 (11)	677 (10)	398 (9)	181 (6)	86 (8)	279 (12)
Target group for influenza vaccination, n (%)						
No	10795 (58)	4520 (75)	2806 (71)	1917 (74)	664 (64)	1709 (83)
Yes	7800 (42)	1521 (25)	1168 (29)	691 (26)	378 (36)	353 (17)
Missing	1967 (10)	674 (10)	389 (9)	188 (7)	87 (8)	285 (12)
SARS-CoV-2 result, n (%)						
Negative	18040 (88)	6593 (98)	4282 (98)	2755 (99)	1106 (98)	2307 (99)
Positive	2505 (12)	102 (2)	73 (2)	38 (1)	22 (2)	28 (1)
Missing	17 (0)	20 (0)	8 (0)	3 (0)	1 (0)	12 (1)
Study site, n (%)						
Croatia	158 (1)	54 (1)	48 (1)	8 (0)	14 (1)	2 (0)
Germany	2506 (12)	1146 (17)	905 (21)	842 (30)	65 (6)	243 (10)
Hungary	1094 (5)	147 (2)	125 (3)	36 (1)	87 (8)	22 (1)
Ireland	299 (1)	151 (2)	109 (2)	53 (2)	56 (5)	45 (2)
Portugal	475 (2)	289 (4)	260 (6)	224 (8)	36 (3)	29 (1)
Romania	83 (0)	32 (0)	29 (1)	11 (0)	18 (2)	3 (0)
Spain	15429 (75)	4642 (69)	2751 (63)	1581 (57)	758 (67)	1885 (80)
The Netherlands	518 (3)	254 (4)	136 (3)	41 (1)	95 (8)	118 (5)

17 **Supplementary table 3:** Descriptive analysis of pooled data by case-control status among **EU ILI patients**
18 (N=24 243) among study sites collecting information on symptoms and recruiting patients meeting the EU
19 ARI case definition, study on effect of case definition on influenza vaccine effectiveness, VEBIS primary
20 care multicentre case-control study, EU/EEA, 2022–23

Variable	Test-negative controls (N=17719)	All influenza cases (N=6524)	Influenza A cases (N=4245)	Influenza A(H3N2) cases (N=2737)	Influenza A(H1N1)pdm09 cases (N=1106)	Influenza B cases (N=2275)
Age						
Mean (SD)	37 (25.1)	27.6 (20.7)	30 (22.2)	27 (21.6)	37.7 (21.9)	23 (16.5)
Median (IQR)	38 (13–57)	24 (9–43)	27 (10–47)	20 (9–44)	41 (17–54)	18 (8–36)
Missing, n(%)	10 (0.1)	6 (0.1)	5 (0.1)	4 (0.1)	1 (0.1)	1 (0)
Age in groups, n(%)						
0-4	2655 (15)	691 (11)	485 (11)	330 (12)	114 (10)	207 (9)
5-14	1997 (11)	1817 (28)	1044 (25)	799 (29)	143 (13)	774 (34)
15-64	10253 (58)	3673 (56)	2404 (57)	1432 (52)	745 (67)	1264 (56)
65 +	2804 (16)	337 (5)	307 (7)	172 (6)	103 (9)	29 (1)
Missing	10 (0)	6 (0)	5 (0)	4 (0)	1 (0)	1 (0)
Sex, n(%)						
Female	10319 (58)	3309 (51)	2187 (52)	1402 (51)	580 (52)	1119 (49)
Male	7372 (42)	3198 (49)	2046 (48)	1324 (49)	525 (48)	1151 (51)
Missing	28 (0)	17 (0)	12 (0)	11 (0)	1 (0)	5 (0)
Seasonal influenza vaccination, n(%)						
No	14364 (81)	6093 (93)	3876 (91)	2522 (92)	985 (89)	2214 (97)
Yes	3355 (19)	431 (7)	369 (9)	215 (8)	121 (11)	61 (3)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Delay between onset of symptoms and swabbing in days						
Mean (SD)	2.8 (1.7)	2.6 (1.6)	2.5 (1.6)	2.5 (1.6)	2.5 (1.5)	2.9 (1.6)
Median (IQR)	3 (1–4)	2 (1–4)	2 (1–3)	2 (1–3)	2 (1–3)	3 (2–4)
Missing, n(%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Any chronic condition, n(%)						
No presence of chronic disease	11352 (71)	4943 (84)	3145 (81)	2131 (83)	787 (77)	1795 (89)
Presence of chronic disease	4627 (29)	939 (16)	722 (19)	431 (17)	234 (23)	216 (11)
Missing	1740 (10)	642 (10)	378 (9)	175 (6)	85 (8)	264 (12)
Target group for influenza vaccination, n(%)						
No	9551 (59)	4424 (75)	2756 (71)	1891 (74)	652 (64)	1664 (83)
Yes	6576 (41)	1458 (25)	1116 (29)	664 (26)	369 (36)	342 (17)
Missing	1592 (9)	642 (10)	373 (9)	182 (7)	85 (8)	269 (12)
SARS-CoV-2 result, n(%)						
Negative	15389 (87)	6411 (99)	4171 (98)	2698 (99)	1084 (98)	2237 (99)
Positive	2318 (13)	94 (1)	67 (2)	36 (1)	22 (2)	26 (1)
Missing	12 (0)	19 (0)	7 (0)	3 (0)	0 (0)	12 (1)
Study site, n(%)						
Croatia	158 (1)	54 (1)	48 (1)	8 (0)	14 (1)	2 (0)
Germany	2220 (13)	1127 (17)	892 (21)	830 (30)	64 (6)	237 (10)
Hungary	1027 (6)	144 (2)	124 (3)	36 (1)	86 (8)	20 (1)
Ireland	238 (1)	143 (2)	105 (2)	51 (2)	55 (5)	41 (2)
Portugal	426 (2)	286 (4)	257 (6)	221 (8)	36 (3)	29 (1)
Romania	83 (0)	32 (0)	29 (1)	11 (0)	18 (2)	3 (0)
Spain	13123 (74)	4495 (69)	2661 (63)	1542 (56)	742 (67)	1829 (80)
The Netherlands	444 (3)	243 (4)	129 (3)	38 (1)	91 (8)	114 (5)

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22 **Supplementary table 4:** Overall influenza and influenza A, A(H3N2), A(H1N1)pdm09 and B vaccine

23 effectiveness among study sites collecting information on symptoms and recruiting patients meeting the

- 24 EU ARI case definition, study on effect of case definition on influenza vaccine effectiveness, VEBIS primary
 25 care multicentre case-control study, EU/EEA, 2022–23

Influenza type	Study population	Case definition	N	Cases	Cases vaccinated	Controls	Controls vaccinated	Adjusted VE (95% CI)
Any influenza	All ages	EU ARI	24 319	6 017	417	18 302	3 578	53 (47–59)
		EU ILI	21 804	5 861	391	15 943	2 974	54 (47–59)
	0–14 years	EU ARI	6 893	2 216	62	4 677	372	68 (58–76)
		EU ILI	6 163	2 174	60	3 989	323	68 (57–76)
	15–64 years	EU ARI	13 910	3 471	174	10 439	1 177	53 (44–61)
		EU ILI	12 770	3 383	166	9 387	1 029	53 (44–61)
	≥65 years	EU ARI	3 516	330	181	3 186	2 029	35 (16–49)
		EU ILI	2 871	304	165	2 567	1 622	33 (12–48)
	Target group	EU ARI	8 832	1 456	318	7 376	2 862	43 (33–51)
		EU ILI	7 666	1 398	296	6 268	2 347	44 (34–52)
Influenza A	All ages	EU ARI	22 193	3 949	357	18 244	3 571	40 (32–48)
		EU ILI	19 740	3 851	334	15 889	2 967	41 (32–49)
	0–14 years	EU ARI	6 039	1 370	46	4 669	372	52 (33–66)
		EU ILI	5 328	1 346	45	3 982	323	51 (31–66)
	15–64 years	EU ARI	12 675	2 279	146	10 396	1 172	42 (30–52)
		EU ILI	11 576	2 229	139	9 347	1 024	42 (29–53)
	≥65 years	EU ARI	3 479	300	165	3 179	2 027	32 (12–48)
		EU ILI	2 836	276	150	2 560	1 620	31 (8–48)
	Target group	EU ARI	8 462	1 115	284	7 347	2 858	33 (21–44)
		EU ILI	7 308	1 068	264	6 240	2 343	34 (21–44)
Influenza A(H3N2)	All ages	EU ARI	18 687	2 593	211	16 094	3 213	32 (19–43)
		EU ILI	16 513	2 540	199	13 973	2 666	32 (18–44)
	0–14 years	EU ARI	4 999	1 039	31	3 960	321	48 (20–67)
		EU ILI	4 386	1 025	30	3 361	278	46 (17–66)
	15–64 years	EU ARI	10 640	1 385	89	9 255	1 038	30 (10–45)
		EU ILI	9 658	1 359	85	8 299	903	29 (9–46)
	≥65 years	EU ARI	3 048	169	91	2 879	1 854	26 (–5–48)
		EU ILI	2 469	156	84	2 313	1 485	27 (–5–49)
	Target group	EU ARI	7 252	663	161	6 589	2 585	24 (5–39)
		EU ILI	6 219	636	151	5 583	2 120	23 (3–39)
Influenza A(H1N1)pd m09	All ages	EU ARI	19 076	1 041	118	18 035	3 569	54 (42–63)
		EU ILI	16 733	1 019	112	15 714	2 965	54 (42–63)
	0–14 years	EU ARI	4 790	228	11	4 562	372	66 (38–83)
		EU ILI	4 121	224	11	3 897	323	65 (37–83)
	15–64 years	EU ARI	11 019	713	48	10 306	1 172	59 (44–70)
		EU ILI	9 968	701	47	9 267	1 024	59 (43–70)
	≥65 years	EU ARI	3 267	100	59	3 167	2 025	39 (4–61)
		EU ILI	2 644	94	54	2 550	1 618	39 (3–61)
	Target group	EU ARI	7 672	367	99	7 305	2 856	43 (25–57)
		EU ILI	6 563	358	93	6 205	2 341	44 (25–58)
Influenza B	All ages	EU ARI	19 165	2 058	59	17 107	3 468	76 (69–82)
		EU ILI	16 843	2 001	56	14 842	2 874	77 (69–83)
	0–14 years	EU ARI	5 391	848	16	4 543	369	84 (74–91)
		EU ILI	4 708	830	15	3 878	320	85 (75–92)
		EU ARI	10 754	1 181	28	9 573	1 137	75 (63–83)

Influenza type	Study population	Case definition	N	Cases	Cases vaccinated	Controls	Controls vaccinated	Adjusted VE (95% CI)
	15–64 years	EU ILI	9 714	1 144	27	8 570	991	75 (63–84)
	Target group	EU ARI	7 189	339	33	6 850	2 772	70 (55–80)
		EU ILI	6 113	328	31	5 785	2 267	72 (58–82)

26 **Supplementary table 5:** Overall influenza and influenza A, A(H3N2), A(H1N1)pdm09 and B vaccine
27 effectiveness excluding SARS-CoV-2 controls among study sites collecting information on symptoms and
28 recruiting patients meeting the EU ARI case definition, study on effect of case definition on influenza
29 vaccine effectiveness, VEBIS primary care multicentre case-control study, EU/EEA, 2022–23

Influenza type	Study population	Case definition	N	Cases	Cases vaccinated	Controls	Controls vaccinated	Adjusted VE (95% CI)	
Any influenza	All ages	EU ARI	22 028	6 017	417	16 011	3 154	55 (49–60)	
		EU ILI	19 674	5 861	391	13 813	2 586	55 (49–61)	
	0–14 years	EU ARI	6 709	2 216	62	4 493	365	69 (59–77)	
		EU ILI	6 004	2 174	60	3 830	318	69 (58–77)	
	15–64 years	EU ARI	12 290	3 471	174	8 819	1 018	54 (45–62)	
		EU ILI	11 230	3 383	166	7 847	879	54 (45–62)	
	≥65 years	EU ARI	3 029	330	181	2 699	1 771	38 (20–52)	
		EU ILI	2 440	304	165	2 136	1 389	39 (20–53)	
	Target group	EU ARI	7 766	1 456	318	6 310	2 505	44 (35–53)	
		EU ILI	6 687	1 398	296	5 289	2 022	45 (35–54)	
	Influenza A	All ages	EU ARI	19 912	3 949	357	15 963	3 149	43 (35–50)
			EU ILI	17 619	3 851	334	13 768	2 581	43 (34–51)
0–14 years		EU ARI	5 856	1 370	46	4 486	365	53 (35–67)	
		EU ILI	5 170	1 346	45	3 824	318	52 (33–67)	
15–64 years		EU ARI	11 062	2 279	146	8 783	1 015	44 (32–54)	
		EU ILI	10 042	2 229	139	7 813	876	44 (31–54)	
≥65 years		EU ARI	2 994	300	165	2 694	1 769	35 (15–50)	
		EU ILI	2 407	276	150	2 131	1 387	34 (12–50)	
Target group		EU ARI	7 401	1 115	284	6 286	2 502	35 (23–45)	
		EU ILI	6 334	1 068	264	5 266	2 019	35 (23–46)	
Influenza A(H3N2)		All ages	EU ARI	16 783	2 593	211	14 190	2 873	37 (24–47)
			EU ILI	14 742	2 540	199	12 202	2 353	36 (23–47)
	0–14 years	EU ARI	4 847	1 039	31	3 808	317	49 (23–68)	
		EU ILI	4 254	1 025	30	3 229	275	48 (20–68)	
	15–64 years	EU ARI	9 279	1 385	89	7 894	911	34 (15–49)	
		EU ILI	8 367	1 359	85	7 008	784	34 (14–49)	
	≥65 years	EU ARI	2 657	169	91	2 488	1 645	31 (2–51)	
		EU ILI	2 121	156	84	1 965	1 294	32 (1–53)	
	Target group	EU ARI	6 377	663	161	5 714	2 295	28 (9–42)	
		EU ILI	5 415	636	151	4 779	1 854	27 (8–42)	
	Influenza A(H1N1)pdm09	All ages	EU ARI	16 817	1 041	118	15 776	3 148	54 (42–64)
			EU ILI	14 634	1 019	112	13 615	2 580	54 (42–64)
0–14 years		EU ARI	4 609	228	11	4 381	365	67 (40–83)	
		EU ILI	3 965	224	11	3 741	318	66 (39–83)	

Influenza type	Study population	Case definition	N	Cases	Cases vaccinated	Controls	Controls vaccinated	Adjusted VE (95% CI)
Influenza B	15–64 years	EU ARI	9 423	713	48	8 710	1 015	58 (43–70)
		EU ILI	8 451	701	47	7 750	876	58 (42–70)
	≥65 years	EU ARI	2 785	100	59	2 685	1 768	42 (8–63)
		EU ILI	2 218	94	54	2 124	1 386	42 (763)
	Target group	EU ARI	6 620	367	99	6 253	2 501	45 (27–58)
		EU ILI	5 598	358	93	5 240	2 018	45 (26–59)
	All ages	EU ARI	17 118	2 058	59	15 060	3 078	77 (69–83)
		EU ILI	14 953	2 001	56	12 952	2 520	77 (69–83)
	0–14 years	EU ARI	5 210	848	16	4 362	362	85 (75–91)
		EU ILI	4 552	830	15	3 722	315	85 (75–92)
15–64 years	EU ARI	9 319	1 181	28	8 138	988	74 (62–83)	
	EU ILI	8 358	1 144	27	7 214	851	74 (62–83)	
Target group	EU ARI	6 254	339	33	5 915	2 444	70 (55–80)	
	EU ILI	5 262	328	31	4 934	1 971	71 (57–81)	

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