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Expert Review of Vaccines

ISSN: 1476-0584 (Print) 1744-8395 (Online) Journal homepage: www.tandfonline.com/journals/ierv20

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To cite this article: Héloïse Lucaccioni , Francisco Pozo , Gloria Pérez-Gimeno , Ralf Dürrwald , Marina Uras , Lisa Domegan , Beatrix Oroszi , Adam Meijer , Camino Trobajo-Sanmartín , Dorina Ujvari , Ana Paula Rodrigues , Ivan Mlinarić , Mihaela Lazar , Eva Rivas Wagner , Annika Erdwiens , Vincent Enouf , Adele McKenna , Gergő Túri , Marit de Lange , Iván Martínez-Baz , Neus Latorre-Margalef , Raquel Guiomar , Sanja Kurečić Filipovic , Sorin Dinu , Olatz Mokoroa , Kristin Tolksdorf , Shirley Masse , Charlene Bennett , Katalin Kristóf , Mariette Hooiveld , Jesús Castilla , João Santos , Vesna Višekruna Vučina , Rodica Popescu , Sabrina Bacci , Marlena Kaczmarek & Esther Kissling (2026) Vaccine effectiveness against medically attended, laboratory-confirmed influenza in the I-MOVE primary care network in Europe, VEBIS project, 2024/25, Expert Review of Vaccines, 25:1, 2645378, DOI: 10.1080/14760584.2026.2645378

To link to this article: https://doi.org/10.1080/14760584.2026.2645378

EXPERT REVIEW OF VACCINES
2026, VOL. 25, NO. 1, 2645378
https://doi.org/10.1080/14760584.2026.2645378

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ORIGINAL RESEARCH

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Vaccine effectiveness against medically attended, laboratory-confirmed influenza in the I-MOVE primary care network in Europe, VEBIS project, 2024/25

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ABSTRACT

Background: We conducted a multicenter test-negative study to estimate vaccine effectiveness (VE) against medically attended, laboratory-confirmed influenza in primary care, Europe, 2024/25.

Research design and methods: Specimens were collected from patients with acute respiratory infection. All or a random sample of viruses were sequenced. VE was (1-odds ratio) × 100, adjusted for confounders.

Results: We included 7275 cases and 17,516 controls (weeks 40–2024–18–2025). The overall VE was 46% (95% CI: 40–52), lowest in adults ≥65 years at 28% (95% CI: 12–42). VE against influenza A(H1N1) pdm09 was 30% (95% CI: 19–40); ranging 16–34% by age and vaccination target group. Most (88%) circulating clades were 5a.2a, distinct from the vaccine clade. VE was 28% (95% CI: 7–45) against 5a.2a (C.1.9), and 6% (95% CI: −62–45) against the vaccine-matched clade 5a.2a.1 (D). VE against influenza A (H3N2) was 38% (95% CI: 26–49); ranging 20–66% by age and target group. Circulating viruses belonged to the vaccine clade 2a.3a.1, with 88% subclade (J.2). VE against influenza B was 76% (95% CI: 69–81); ranging 70–80% by age and target group; all viruses belonged to the vaccine clade V1A.3a.2, with diverse subclades.

Conclusions: Influenza vaccination protected approximately one in two vaccinated individuals against medically attended infection in primary care in Europe, 2024/25, varying by (sub)type and age.

ARTICLE HISTORY
Received 27 October 2025
Accepted 10 March 2026

KEYWORDS
Case control study; Europe; influenza; influenza vaccine; multicenter study; observational study; test-negative design; vaccine effectiveness

1. Introduction

In the European Union/European Economic Area (EU/EEA), seasonal influenza vaccination is recommended for older adults and individuals with chronic medical conditions. In addition, some countries have age-based recommendations for children [1].

The World Health Organization recommendation for the composition of the Northern Hemisphere 2024/25 trivalent influenza vaccines for egg-based vaccines was: A/Victoria/4897/2022 (H1N1)pdm09-like virus (clade 5a.2a.1), unchanged from 2023/24; A/Thailand/8/2022 (H3N2)-like virus (clade 2a.3a.1), updated from A/Darwin/9/2021 (clade 2a); and B/Austria/1359417/2021 (B/Victoria lineage)-like virus (clade V1A.3a.2), unchanged since 2022/23. For cell culture- or recombinant-based vaccines, the recommendation was A/Wisconsin/67/2022 (H1N1)pdm09-like virus, A/Massachusetts/

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/14760584.2026.2645378

18/2022 (H3N2)-like virus, and the same influenza B virus component as for egg-based vaccines [2].

The 2024/25 season in the EU/EEA was characterized by intense influenza activity with the co-circulation of influenza virus A(H1N1)pdm09 and A(H3N2) subtypes and influenza virus type B, with varying (sub)type dominance among different European countries [3]. There was a concomitant respiratory syncytial virus (RSV) epidemic and a low circulation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3].

The I-MOVE network (Influenza Monitoring Vaccine Effectiveness in Europe), operating under the VEBIS (Vaccine Effectiveness, Burden and Impact Studies) project, has been estimating influenza vaccine effectiveness (VE) in primary care in the EU/EEA since 2008/09 [4,5]. We present the 2024/25 VE estimates against medically attended, laboratory-confirmed influenza in primary care, by (sub)type and (sub)clade, in all ages, and, where sample size allowed, by age group (0–17, 18–64, ≥65 years) and in the vaccination target group (i.e. individuals for whom vaccination was recommended and fully reimbursed; see 2. Patients and methods). Additionally, we explored a potential birth cohort effect against influenza A(H1N1)pdm09, previously observed in 2023/24 [6]. Finally, to assess possible waning of vaccine-induced protection over time, we estimated the VE by (sub)type and time since vaccination (TSV).

2. Patients and methods

We conducted a multicenter test-negative case–control study in 11 study sites from 10 European countries (Croatia, Germany, France, Hungary, Ireland, the Netherlands, Spain national (12 regions), Spain Navarre region, Portugal, Romania, Sweden). Methods are based on a generic study protocol, adapted at each site [7].

Practitioners collected specimens and interviewed all or a systematic sample of patients attending primary care for acute respiratory infection (ARI) or influenza-like illness (ILI), depending on the study site (Supplementary material 1).

All specimens were tested by real-time reverse transcription-polymerase chain reaction (RT-PCR) for influenza virus and SARS-CoV-2 at all study sites, and for RSV at 8/11 study sites. Patients RT-PCR-positive for influenza virus were considered cases; those negative for any influenza virus were considered controls.

Study sites selected all or a random sample of influenza viruses for genetic sequencing. Most sites sequenced viruses with cycle threshold (Ct) values below a predefined threshold, which varied between study sites (e.g. from Ct <28 to Ct <39). Sequences were uploaded by each study site to GISAID and downloaded at the National Influenza Centre (Madrid, Spain) for centralized phylogenetic and amino acid substitution analysis using MEGA7 software.

Variables collected included symptoms, onset date, swab date, 2024/25 influenza vaccination status and date (if vaccinated), sex, age, and chronic conditions.

The vaccination target group was defined as individuals for whom seasonal influenza vaccination was recommended and fully reimbursed by the national health system in 2024/25 (age-based recommendations as in Supplementary material 1, and those with chronic conditions).

Influenza vaccination status was ascertained from medical records by practitioners, registry linkage, or self-report. Patients who received influenza vaccination at least 14 days before symptom onset were classified as vaccinated, those vaccinated 1–13 days before symptom onset were excluded, and all others were classified as unvaccinated.

We pooled individual patient data across all study sites, including patients swabbed within 7 days of symptom onset who met the EU-ARI case definition (i.e. Sudden onset of symptoms and at least one of four respiratory symptoms (cough, sore throat, shortness of breath, coryza) and a clinician's judgment that the illness is due to an infection) [8]. At each site, we included patients with symptom onset at least 14 days after the national (or regional) influenza vaccination campaign began (Supplementary material 1). We excluded controls presenting before/after the onset week of the first/last (sub)type- or (sub)clade-specific case under study. We excluded any study site with fewer than 10 influenza (sub)type-specific or five (sub)clade-specific cases or controls.

We conducted a complete case analysis, excluding patients with missing information on covariates (age, sex, presence of chronic condition), and described cases and controls by baseline characteristics.

We estimated the VE against each (sub)type and (sub)clade in all ages and, if sample size allowed, by age group (0–17, 18–64, ≥65 years) and in the vaccination target group. We used a one-stage model, with study site as fixed effects. We calculated the odds ratios (OR) of vaccination with their 95% confidence intervals (CI) using logistic regression adjusted for the following confounders: age, sex, presence of at least one commonly collected chronic condition (lung disease, heart disease, immunodeficiency, diabetes mellitus), and onset date. We estimated VE as (1-OR) × 100, expressed as a percentage. For continuous variables, we used age as narrow groups (using intervals empirically shown to reduce residual confounding in our study over the years: 0–1, 2, 3–4, 5–9, 10–19, 20–29, … , 60–69, ≥70 years), as a linear term or as a restricted cubic spline (three, four or five knots) and onset date as a restricted cubic spline (three, four or five knots). We used the Akaike information criterion (AIC) to select the best functional form of each continuous variable.

If the number of cases or controls was fewer than 10 times the number of model parameters, we used penalized logistic regression (Firth's method [9]) to assess small sample bias. If the VE differed by ≥10%, we assumed bias and did not present the results.

We used weighted logistic regression to estimate (sub)clade-specific VE, as not all study sites sequenced all viruses throughout the season. Weights were assigned to each case as the reciprocal of the sequencing fraction (proportion of viruses sequenced) within each period with different sampling fractions. The sequencing fraction was defined separately for each study site, (sub)type, and period. Controls were assigned a weight of 1. Robust standard errors were used for inference.

We defined influenza A(H1N1)pdm09 by birth cohort a priori, based on the first likely influenza A infection in Europe at 1 year of age [10–12]. To avoid sparse data, we

grouped major A(H1N1)pdm09 antigenic clusters and truncated the data at 91 years into the following groups: 0–6, 7–16, 17–26, 27–39, 40–48, 49–57, 58–68, 69–91 years (Supplementary material 2). We estimated the VE by year of age, modeling age as a restricted cubic spline (four, five, or six knots), including an interaction term between age in years and vaccination status. As in the main analysis, we selected the best-fitting model among fully adjusted models (adjusted for onset date, chronic condition, sex, study site), using the AIC.

We modeled TSV as a categorical variable (unvaccinated, 14–59 days (<2 months), 60–119 days (2–3 months), ≥120 days (4–7 months) since vaccination). We used Wald tests to conduct pairwise comparisons between TSV categories. We also modeled TSV as a continuous variable in days, exploring various functional forms (linear, restricted cubic spline with three, four, or five knots), and selected the best-fitting fully adjusted model using the AIC. Unvaccinated individuals were assigned a value of 0 days since vaccination.

We conducted sensitivity analyses to address the potential bias in VE estimates from correlated vaccination behavior [13]. To account for potentially correlated COVID-19 vaccination behavior, we excluded SARS-CoV-2-positive controls. In a similar way, we excluded RSV-positive controls among children under 2 years old from four study sites with a 2024/25 recommendation for monoclonal antibody use in infants.

All analyses were performed in R v.4.4.2/RStudio [14].

Ethical approval has been obtained from the appropriate local ethics committee or Institutional Review Board, and informed consent has been obtained as appropriate.

3. Results

3.1. Descriptive analyses

We included 17,516 controls and 7275 influenza cases between weeks 40–2024 and 18–2025. Among cases, there were 2304 (32%) influenza A(H1N1)pdm09 viruses, 1394 (19%) influenza A(H3N2), 633 (9%) influenza A viruses not subtyped, 2907 (40%) influenza B, and 84 (1%) influenza viruses with missing information on the type, noting there were 47 codetections (23 influenza A(H1N1)pdm09 and B viruses, 9 influenza A(H1N1)pdm09 and A(H3N2), 8 influenza A(H3N2) and B, and 7 influenza A (not subtyped) and B). For the analysis against influenza A(H3N2), we further excluded nine cases from one study site due to small sample size, leaving 1385 influenza A(H3N2) cases. Vaccination campaigns started from week 37–2024 and continued until week 9–2025 (Figure 1).

Characteristics of controls and cases included in each (sub) type-specific analysis are described in Table 1 and Supplementary material 3. The median age was 38 years among controls, 42 years among influenza A(H1N1)pdm09 cases, 33 years among influenza A(H3N2) cases, and 25 years among influenza B cases. Among controls, 16% were aged ≥65 years; this proportion varied between 2% and 12% by influenza (sub)type among cases.

Overall, 20% ($n = 3482$) of controls were vaccinated: 71% ($n = 2457$) received an inactivated egg-based influenza vaccine (49% standard dose non-adjuvanted; 14% adjuvanted, 8% high-dose vaccine), 7% ($n = 246$) a cell-passaged vaccine, 7% ($n = 238$) a live attenuated influenza vaccine, 5% ($n = 156$) another or unspecified inactivated vaccine (including aluminum phosphate-adjuvanted inactivated vaccine, unspecified egg- or cell-based vaccines), and 11% ($n = 385$) had missing information (Table 1).

The proportion of different vaccine types administered varied by age group (Figure 2 and Supplementary material 4).

3.2. Genetic characterization

Thirty-nine percent (903/2304) of influenza A (H1N1)pdm09, 31% of (434/1385) influenza A(H3N2) and 31% (915/2907) of influenza B Victoria viruses were sequenced (Table 2).

Of the 903 sequenced influenza A(H1N1)pdm09 viruses, 791 (88%) belonged to clade 5a.2a (C.1.9) and 112 (12%) to clade 5a.2a.1 (D). Clade 5a.2a (C.1.9) predominated early in the season but was gradually replaced by clade 5a.2a.1 (D) from week 11–2025 onward (Supplementary material 5). By the end of the season, clade 5a.2a (C.1.9) had split into four subclades (C.1.9.1, C.1.9.2, C.1.9.3, C.1.9.4), and clade 5a.2a.1 (D) into five (D.1, D.2, D.3+, D.4, D.5). In our study, the majority (78%, 620/791) of 5a.2a C.1.9 viruses belonged to subclade C.1.9.3, and the majority (86%, 96/112) of 5a.2a.1 (D) viruses belonged to subclade D.3+ (Supplementary material 6).

Of the 434 sequenced influenza A(H3N2) viruses, 350 (81%) belonged to subclade 2a.3a.1 (J.2), 63 (15%) to subclade 2a.3a.1 (J.2.2), 14 (3%) to subclade 2a.3a.1 (J.2.1), and 2% (7/431) to other subclades. Subclade 2a.3a.1 (J.2) predominated throughout the season (Supplementary material 5). Of the 434 A(H3N2) sequenced viruses, 66 (15%) harbored amino acid substitutions T135A and 26 (6%) T135K. Furthermore, 165 (38%) viruses carried an amino acid substitution at least at one of three so-called 'Koel' positions (S145N/G and/or N158K/S and/or K189R) [15]. A minority of viruses (6%; 25/434), all from one study site, carried the double substitution N158K +K189R. These substitutions were observed in 41% of viruses from subclade 2a.3a.1 (J.2), 33% of viruses from subclade 2a.3a.1 (J.2.2), and 14% of viruses from subclade 2a.3a.1 (J.1), with the double substitution N158K+K189R occurring exclusively in subclade 2a.3a.1 (J.2).

Of the 915 sequenced influenza B viruses, 534 (58%) belonged to subclade V1A.3a.2 (C.5.1), 211 (23%) to subclade V1A.3a.2 (C.5.6), 167 (18%) to subclade V1A.3a.2 (C.5.7), and <0.5% (3/534) to other subclades. The distribution of subclades remained relatively stable throughout the season, with subclade V1A.3a.2 (C.5.1) predominating in most weeks (Supplementary material 5).

3.3. Vaccine effectiveness estimates by influenza (sub) type and (sub)clade

The VE estimates for all ages, by age group (0–17, 18–64, and ≥65 years) and in the target group for influenza vaccination against any influenza and by (sub)type and (sub)clade, are shown in Table 3.

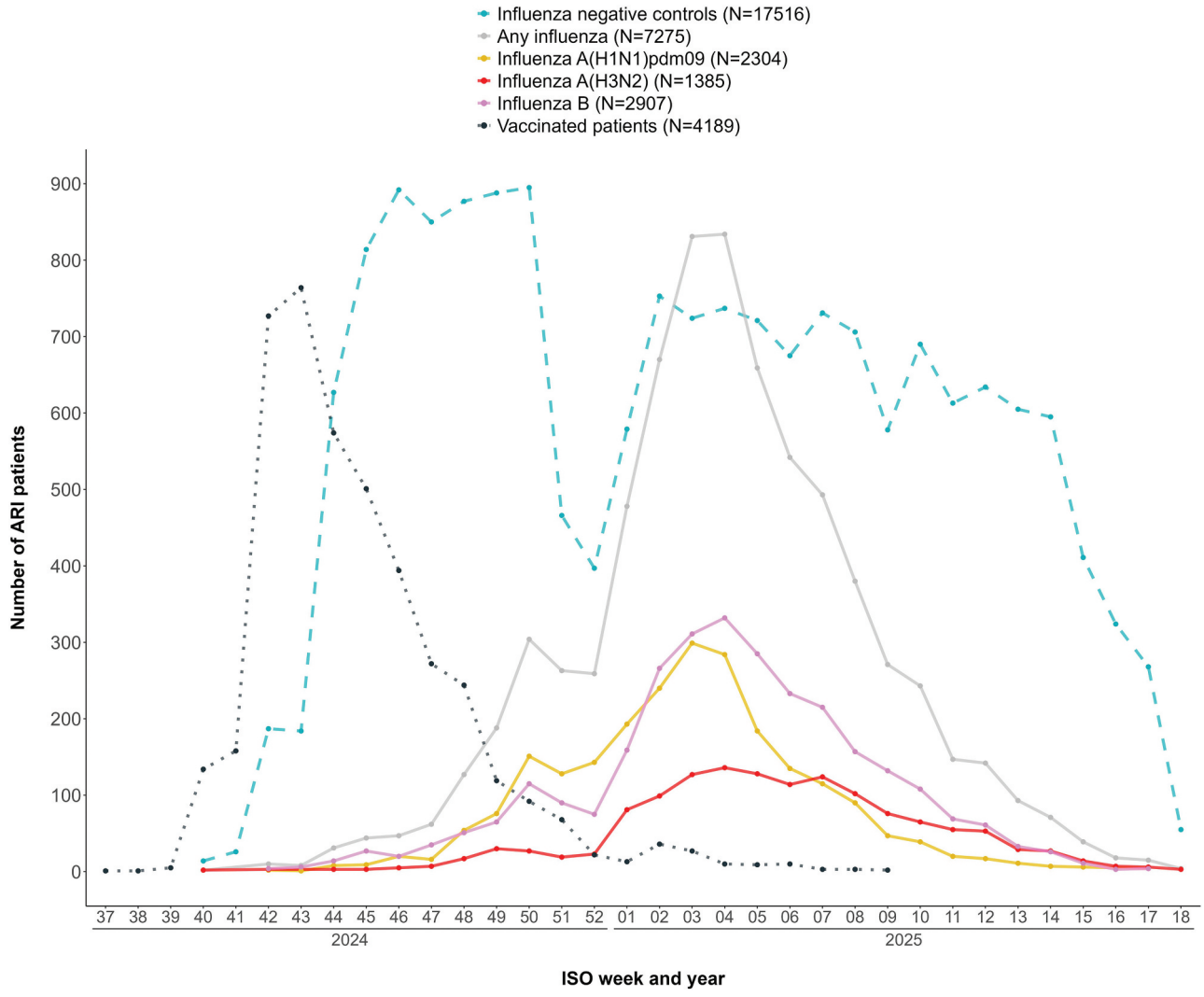

Figure 1. Number of influenza cases and test-negative controls by week of symptom onset, and number of vaccinated patients by week of vaccination, I-MOVE primary care multicenter study, Europe, 2024/25 influenza season.

3.3.1. Any influenza

The overall VE against any influenza was 46% (95% CI: 40–52), ranging from 28% (95% CI: 12–42) in older adults (≥65 years) to 61% (95% CI: 51–68) in children (0–17 years). The VE in the vaccination target group was 41% (95% CI: 33–48).

3.3.2. Influenza A(H1N1)pdm09

Against influenza A(H1N1)pdm09, the overall VE was 30% (95% CI: 19–40), ranging from 16% (95% CI: −12–36) in older adults (≥65 years) to 34% (95% CI: 19–48) in adults aged 18–64 years. The VE in the vaccination target group was 26% (95% CI: 12–38).

The overall VE against clade 5a.2a (C.1.9) was 28% (95% CI: 7–45), 19% (95% CI: −36–52) in children (0–17 years), 39% (95% CI: 12–58) in adults aged 18–64 years, and 29% (95% CI: 4–48) in the vaccination target group.

Against clade 5a.2a.1 (D), the overall VE was 6% (95% CI: −62–45), 47% (95% CI: −32–78) in adults aged 18–64 years.

VE estimates against the parental clade 5a.2a C.1.9 (excluding viruses from subclades C.1.9.1, C.1.9.2, C.1.9.3, and C.1.9.4), subclade 5a.2a (C.1.9.3), and subclade 5a.2a.1 (D.3+) are presented in Supplementary material 7.

No statistically significant differences in VE against influenza A(H1N1)pdm09 by birth cohort were observed (Supplementary material 8–9).

3.3.3. Influenza A(H3N2)

Against influenza A(H3N2), the overall VE was 38% (95% CI: 26–49), ranging from 20% (95% CI: −4–38) in adults (18–64 years) to 66% (95% CI: 46–79) in children (0–17 years). The VE was 32% (95% CI: 14–46) in the vaccination target group.

The overall VE against subclade 2a.3a.1 (J.2) was 37% (95% CI: 10–56), 48% (95% CI: −38–80) in children (0–17 years), 30% (95% CI: −16–58) in adults aged 18–64 years, and 30% (95% CI: −9–55) in the vaccination target group.

The overall VE against subclade 2a.3a.1 (J.2.2) was 32% (95% CI: −37–66).

It was not possible to estimate the VE for specific amino acid substitutions (e.g. T135A/K, S145N/G and/or N158K/S and/or K189R) because of the small sample size.

Table 1. Characteristics of influenza A(H1N1)pdm09, A(H3N2) and B cases, and controls included in the I-MOVE primary care multicenter study, Europe, 2024/25 influenza season.

Characteristics	Test-negative controls (*N* = 17516)[a] n (%)	All influenza cases (*N* = 7275) n (%)	Influenza A(H1N1)pdm09 cases (*N* = 2304) n (%)	Influenza A(H3N2) cases (*N* = 1385) n (%)	Influenza B cases (*N* = 2907) n (%)
Age					
Mean (SD)	37 (25)	33 (22)	39 (23)	35 (23)	26 (17)
Median (IQR)	38 (14–57)	33 (13–49)	42 (18–55)	33 (17–53)	25 (11–40)
Age group (years)					
0–4	2365 (14)	628 (9)	226 (10)	125 (9)	218 (8)
5–17	2596 (15)	1687 (23)	346 (15)	232 (17)	949 (33)
18–64	9775 (56)	4404 (61)	1463 (64)	877 (63)	1697 (58)
≥65	2780 (16)	556 (8)	269 (12)	151 (11)	43 (2)
Age by birth cohort (years)					
0–6	2850 (16)	953 (13)	306 (13)	186 (14)	379 (13)
7–16	1952 (11)	1263 (17)	252 (11)	155 (11)	728 (25)
17–26	1618 (9)	811 (11)	161 (7)	195 (14)	408 (14)
27–39	2678 (15)	1354 (19)	345 (15)	279 (20)	641 (22)
40–48	2039 (12)	1075 (15)	357 (16)	150 (11)	473 (16)
49–57	2055 (12)	827 (11)	396 (17)	156 (11)	189 (7)
58–68	2210 (13)	578 (8)	282 (12)	153 (11)	63 (2)
69–91	2050 (12)	405 (6)	203 (9)	108 (8)	25 (1)
Sex					
Female	9801 (56)	3953 (54)	1263 (55)	763 (55)	1539 (53)
Male	7715 (44)	3322 (46)	1041 (45)	622 (45)	1368 (47)
Seasonal influenza vaccination					
No	14,034 (80)	6568 (90)	1975 (86)	1198 (87)	2822 (97)
Yes	3482 (20)	707 (10)	329 (14)	187 (14)	85 (3)
Type of influenza vaccine (among vaccinated)[b]					
IIV4e-SD	1690 (49)	401 (57)	201 (61)	93 (50)	67 (79)
IIV4e-Adjuvanted	491 (14)	59 (8)	19 (6)	10 (5)	3 (4)
IIV4e-HD	276 (8)	36 (5)	22 (7)	8 (4)	2 (2)
IIV4cc-SD	246 (7)	17 (2)	4 (1)	5 (3)	1 (1)
LAIV (any valency)	238 (7)	44 (6)	17 (5)	9 (5)	4 (5)
Other or unspecified IIV[c]	156 (5)	24 (3)	6 (1.8)	8 (4)	3 (4)
Unknown	385 (11)	126 (18)	60 (18)	54 (29)	5 (6)
Chronic condition[d]					
Absence of chronic condition	12,841 (73)	5924 (81)	1774 (77)	1079 (78)	2545 (88)
Presence of at least one chronic condition	4675 (27)	1351 (19)	530 (23)	306 (22)	362 (13)

Abbreviations: I-MOVE, Influenza Monitoring Vaccine Effectiveness in Europe; SD, Standard deviation; IQR, Interquartile range.
[a]Controls for 'Any influenza' used here (number of controls differs slightly for influenza (sub)types analyses, due to the inclusion criteria).
[b]IIV4e-SD = Egg-based, inactivated, non-adjuvanted, standard dose; IIV4e-Adjuvanted = Egg-based, inactivated, adjuvanted with MF59; IIV4e-HD = Egg-based, inactivated, non-adjuvanted, high dose; LAIV = Live Attenuated Influenza Vaccine (any valency); IIV4cc-SD = Cell-passaged, inactivated, adjuvanted, normal dose.
[c]Aluminum phosphate-adjuvanted inactivated vaccine or unspecified egg-based or cell-based IIV.
[d]At least one of four commonly collected chronic condition (lung disease, heart disease, immunodeficiency, and diabetes mellitus).

3.3.4. Influenza B

The overall VE against influenza B was 76% (95% CI: 69–81), 80% (95% CI: 71–87) in children (0–17 years), 70% (95% CI: 59–78) in adults (18–64 years), and 73% (95% CI: 64–80) in the vaccination target group. It was not possible to estimate the VE in older adults (≥65 years) because of the small sample size.

The overall VE against subclade V1A.3a.2 (C.5.1) was 85% (95% CI: 69–93), 90% (95% CI: 46–98) in children (0–17 years), and 80% (95% CI: 51–92) in adults aged 18–64 years.

Against subclade V1A.3a.2 (C.5.6), the overall VE was 77% (95% CI: 42–91), 69% (95% CI: −1–90) in children (0–17 years), and 82% (95%: 31–96) in adults ages 18–64 years.

Against subclade V1A.3a.2 (C.5.7), the overall VE was 53% (95% CI: −21–82), and 65% (95% CI: 0–88) in adults aged 18–64 years.

3.4. Vaccine effectiveness estimates by time since vaccination

The VE estimates in all ages against each influenza (sub)type by categories of TSV are shown in Table 4. The VE by TSV modeled as a continuous variable (where a linear term was the best fit for all influenza (sub)types) is presented in Supplementary material 10.

The VE against influenza A(H1N1)pdm09 was 38% (95% CI: 22–51), 26% (95% CI: 12–39), and 20% (95% CI: −17–48) at 14–59 days (<2 months), 60–119 days (2–3 months), and 120–207 days (4–7 months) since vaccination, respectively. There were no statistically significant differences in pairwise comparisons among vaccinated individuals between categories of time since vaccination. In the continuous model, the VE declined by 0.3% per day since vaccination ($p = 0.131$).

The VE against influenza A(H3N2) was 62% (95% CI: 42–76), 36% (95% CI: 19–49), and 23% (95% CI: −6–45) at 14–59 days (<2 months), 60–119 days (2–3 months), and 120–196 days (4–7 months) since vaccination, respectively. Pairwise comparisons showed the VE at 60–119 days (2–3 months) since vaccination ($p = 0.031$) and 120–196 days (4–7 months) since vaccination ($p = 0.009$) were significantly lower than at 14–59 days (<2 months) since vaccination. Modeling TSV as a continuous variable, we observed a decline in VE of 0.4% per day ($p = 0.073$).

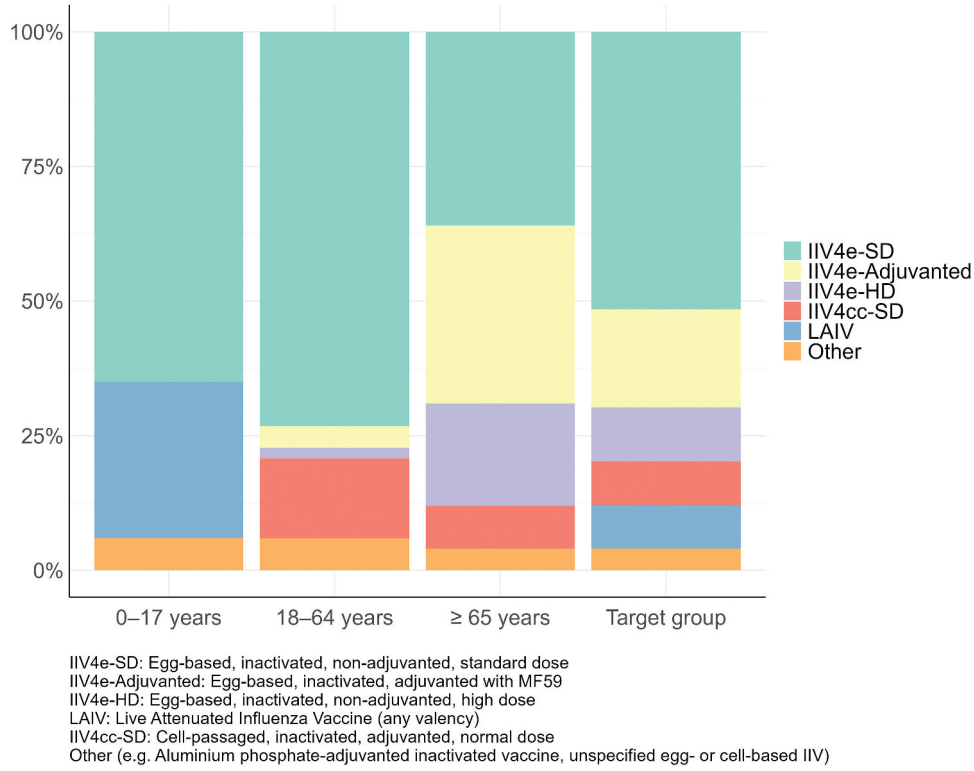

Figure 2. Percentage of vaccine types administered among vaccinated controls by age group and in the target group for influenza vaccination, I-MOVE primary care multicenter study, Europe, 2024/25 influenza season. IIV4e-SD = Egg-based, inactivated, non-adjuvanted, standard dose; IIV4e-Adjuvanted = Egg-based, inactivated, adjuvanted with MF59; IIV4e-HD = Egg-based, inactivated, non-adjuvanted, high dose; IIV4cc-SD = Cell-passaged, inactivated, adjuvanted, normal dose; LAIV = Live Attenuated Influenza Vaccine (any valency); Other (e.g. Aluminum phosphate-adjuvanted inactivated vaccine, unspecified egg- or cell-based IIV).

Table 2. Influenza viruses characterized by (sub)clade, I-MOVE primary care multicenter study, Europe, 2024/25 influenza season.

Reference influenza virus for indicated (sub)clade[a]	Clade	n	%
Total influenza A(H1N1)pdm09[b]		**n = 2304**	
Sequenced		**903**	**39%**
A/Lisboa/188/2023-like	5a.2a (C.1.9)	791	88%
A/Victoria/4897/2022-like[c]	5a.2a.1 (D)	112	12%
Total influenza A(H3N2)[b]		**n = 1385**	
Sequenced		**434**	**31%**
A/Thailand/8/2022-like[c]	2a.3a.1 (J)	0	0%
A/Croatia/10136RV/2023-like	2a.3a.1 (J.2)	350	81%
A/Lisboa/216/2023-like	2a.3a.1 (J.2.2)	63	15%
A/West Virginia/51/2024-like	2a.3a.1 (J.2.1)	14	3%
A/Finland/402/2023-like	2a.3a (G.1.3.1)	5	1%
A/Sydney/856/2023-like	2a.3a.1 (J.1)	2	0.5%
Total influenza B[b]		**n = 2907**	
Sequenced		**915**	**31%**
B/Austria/1359417/2021-like[c]	V1A.3a.2	0	0%
B/Catalonia/2279261NS/2023-like	V1A.3a.2 (C.5.1)	534	58%
B/Switzerland/329/2024-like	V1A.3a.2 (C.5.6)	211	23%
B/Guangxi-Beiliu/2298/2023-like	V1A.3a.2 (C.5.7)	167	18%
B/Stockholm/3/2022-like	V1A.3a.2 (C.5)	2	0.2%
B/Moldova/2030521/2023-like	V1A.3a.2 (C.3)	1	0.1%

[a]As defined by the World Health Organization Collaborating Center, London, for ECDC/WHO-Europe reporting.
[b]For one study site (France), only viruses from 1/4 laboratories are included in this count.
[c]Strain included in the 2024/25 northern hemisphere influenza vaccine.

The VE against influenza B was 76% (95% CI: 63–85), 76% (95% CI: 68–82), 73% (95% CI: 55–86) at 14–59 days (<2 months), 60–119 days (2–3 months), 120–198 days (4–7 months) since vaccination, respectively. Pairwise comparisons among vaccinated individuals between categories of time since vaccination showed no statistically significant differences. The continuous model indicated the VE increased by 0.2% per day since vaccination; this change was not statistically significant ($p = 0.494$).

Table 3. Pooled seasonal vaccine effectiveness against any influenza, influenza A(H1N1)pdm09, A(H3N2), and B, overall, by age group and in the vaccination target group, I-MOVE primary care multicenter study, Europe, 2024/25 influenza season.

Study population	N	Cases	Cases vaccinated	Controls	Controls vaccinated	VE[a] (95% CI)
Any influenza						
All ages	24 791	7 275	707	17 516	3 482	46 (40–52)
0–17 years	7 276	2 315	133	4 961	873	61 (51–68)
18–64 years	14 179	4 404	278	9 775	1 028	45 (36–52)
≥65 years	3 336	556	296	2 780	1 581	28 (12–42)
Target group	10 566	2 335	567	8 231	2 981	41 (33–48)
Influenza A(H1N1)pdm09						
All ages	19 109	2 304	329	16 805	3 400	30 (19–40)
0–17 years	5 432	572	52	4 860	867	32 (6–52)
18–64 years	10 734	1 463	126	9 271	992	34 (19–48)
≥65 years	2 943	269	151	2 674	1 541	16 (−12–36)
Target group	8 777	909	269	7 868	2 911	26 (12–38)
Influenza A(H1N1)pdm09 clade 5a.2a (C.1.9) Lisboa						
All ages	14 548	788	102	13 760	2 997	28 (7–45)
0–17 years	4 278	225	18	4 053	810	19 (−36–52)
18–64 years	7 928	489	38	7 439	832	39 (12–58)
Target group	6 854	265	78	6 589	2 578	29 (4–48)
Influenza A(H1N1)pdm09 clade 5a.2a.1 (D) Victoria						
All ages	10 198	110	21	10 088	2 553	6 (−62–45)
18–64 years	5 326	72	6	5 326	724	47 (−32–78)
Influenza A(H3N2)						
All ages	17 890	1 385	187	16 505	3 417	38 (26–49)
0–17 years	5 070	357	22	4 713	872	66 (46–79)
18–64 years	9 999	877	81	9 122	998	20 (−4–38)
≥65 years	2 821	151	84	2 670	1 547	30 (−2–52)
Target group	8 350	505	157	7 845	2 924	32 (14–46)
Influenza A(H3N2) subclade 2a.3a.1 (J.2)						
All ages	12 366	350	54	12 016	2 768	37 (10–56)
0–17 years	3 615	97	5	3 518	787	48 (−38–80)
18–64 years	6 654	207	20	6 447	732	30 (−16–58)
Target group	5 798	116	45	5 682	2 367	30 (−9– 5)
Influenza A(H3N2) subclade 2a.3a.1 (J.2.2)						
All ages	8 483	60	10	8 423	2 212	32 (−37–66)
Influenza B						
All ages	19 297	2 907	85	16 390	3 386	76 (69–81)
0–17 years	5 915	1 167	28	4 748	859	80 (71–87)
18–64 years	10 684	1 697	46	8 987	990	70 (59–78)
Target group	8 406	629	53	7 777	2 903	73 (64–80)
Influenza B subclade V1A.3a.2 (C.5.1)						
All ages	13 561	534	10	13 027	2 848	85 (69–93)
0–17 years	4 255	249	2	4 006	767	90 (46–98)
18–64 years	7 166	277	6	6 889	799	80 (51–92)
Influenza B subclade V1A.3a.2 (C.5.6)						
All ages	9 822	210	5	9 612	1 978	77 (42–91)
0–17 years	3 064	111	3	2 953	482	69 (−1–90)
18–64 years	5 210	97	2	5 113	582	82 (31–96)
Influenza B subclade V1A.3a.2 (C.5.7)						
All ages	8 852	162	6	8 690	1 808	53 (−21–82)
18–64 years	4 739	100	4	4 639	520	65 (0–88)

Abbreviations: I-MOVE, Influenza Monitoring Vaccine Effectiveness in Europe; CI, confidence interval; VE, vaccine effectiveness.
[a]Models adjusted by age, sex, presence of at least one of four commonly collected chronic conditions (lung disease, heart disease, immunodeficiency, and diabetes mellitus), date of symptom onset.

3.5. Sensitivity analyses

Excluding SARS-CoV-2 positive controls changed VE estimates by <1% absolute. Excluding RSV positive controls changed the VE by <2%.

4. Discussion

In this study, we found that approximately one in two vaccinated individuals were protected against medically attended, laboratory-confirmed influenza in primary care in Europe in 2024/25, although protection varied by (sub)type and age group.

There was evidence of low VE against influenza A(H1N1)pdm09, ranging from 16% to 34% across all age groups and in the vaccination target group, consistent with early-season findings [16]. These VE estimates were the lowest observed over the past four seasons in the I-MOVE primary care network in Europe, during which overall estimates ranged from 46% to 75% [6,17,18]. Higher 2024/25 interim VE estimates in primary care settings were reported from Canada [19] (50% in 1–64-year-olds; 57% in ≥65-year-olds), and the United States [20] (53% in children <18 years; 42% in adults ≥18 years). Interim estimates from the United Kingdom varied between 42% and 48% by age group [16].

As in 2023/24, clades 5a.2a (which would evolve next season to 5a.2a C.1.9) and 5a.2a.1 (evolving to 5a.2a.1 D) co-circulated in 2024/25 in Europe. The vaccine component belonged to clade 5a.2a.1, which remained unchanged from

Table 4. Pooled seasonal vaccine effectiveness against any influenza, influenza A(H1N1)pdm09, A(H3N2), and B, by time since vaccination, all ages, I-MOVE primary care multicenter study, Europe, 2024/25 influenza season.

Study population	Time since vaccination	N	Cases	Median TSV in days among cases (IQR)	Controls	Median TSV in days among controls (IQR)	VE[a] (95% CI)
Influenza A(H1N1)pdm09 (*N* = 19 109; Cases: 2304, Controls: 16,805)							
All ages	Unvaccinated	15 380	1 975	–	13 405	–	–
	14–59 days (<2 months)	1 311	102	44 (33–52)	1 209	35 (24–47)	38 (22–51)
	60–119 days (2–3 months)	1 441	197	83 (71–98)	1 244	89 (75–104)	26 (12–39)
	120–207 days (4–7 months)	977	30	134 (128–142)	947	147 (133–164)	20 (−17–48)
Influenza A(H3N2) (*N* = 17 890; Cases: 1385, Controls: 16,505)							
All ages	Unvaccinated	14 286	1 198	–	13 088	–	–
	14–59 days (<2 months)	1 237	22	40 (32–52)	1 215	35 (24–47)	62 (42–76)
	60–119 days (2–3 months)	1 366	116	88 (74–106)	1 250	89 (75–105)	36 (19–49)
	120–207 days (4–7 months)	1 001	49	137 (129–149)	952	147 (133–164)	23 (−6–45)
Influenza B (*N* = 19 297; Cases: 2907, Controls: 16,390)							
All ages	Unvaccinated	15 826	2 822	–	13 004	–	
	14–59 days (<2 months)	1 201	21	45 (22–53)	1 180	36 (25–47)	76 (63–85)
	60–119 days (2–3 months)	1 305	51	84 (74–94)	1 254	89 (75–104)	76 (68–82)
	120–207 days (4–7 months)	965	13	127 (124–135)	952	147 (133–163)	73 (55–86)

Abbreviations: I-MOVE, Influenza Monitoring Vaccine Effectiveness in Europe; CI, confidence interval; IQR, interquartile range; TSV, time since vaccination; VE, vaccine effectiveness.

[a]Models adjusted by age, sex, presence of at least one of four commonly collected chronic conditions (lung disease, heart disease, immunodeficiency, and diabetes mellitus), date of symptom onset.

the previous season [21]. Similar to observations from 2023/24 [6,22,23], we found a higher VE against 5a.2a (C.1.9) than against the vaccine-matched clade 5a.2a.1 D (28% versus 6% in all ages in 2024/25). It has been hypothesized that egg-adaptive mutations in the vaccine strain and/or immune imprinting effects may explain this difference [23].

Nonetheless, compared to 2023/24 [6], in 2024/25 we observed a VE against clade 5a.2a lower by 13% and up to 58% overall and in all age groups, except in younger adults aged 18–64 years. This could suggest genetic changes within clade 5a.2a (C.1.9) this season. The majority of the 2024/25 5a.2a (C.1.9) viruses in our study belonged to subclade C.1.9.3, characterized by amino acid substitution K169Q, and VE was lower against this subclade than against the parental clade C.1.9 (excluding viruses from subclades C.1.9.1–C.1.9.4) (20% versus 40% in all ages). Although we found evidence of a birth cohort effect in 2023/24 when we reported a lower VE among individuals born in 1976–1984 whose first encounter with previous seasonal influenza virus A(H1N1) infection was with A/USSR/90/77 or A/Chile/1/83 [6], we were unable to repeat this observation with our data in 2024/25. Further clade- and subclade-specific VE estimates, as well as birth cohort-specific VE estimates, from other studies around the world will help validate our findings.

We found a moderate overall VE (38%) against influenza A(H3N2). This estimate was higher than the 2024/25 interim VE (29%) [16], but broadly comparable to the 2023/24 end-of-season VE (35%) [6] and previous seasons [18,25]. The VE varied by age group, with a higher VE in children (66%), and a lower VE in adults, particularly younger adults (20% in 18–64-year-olds, 30% in those aged ≥65 years).

The circulating clades for influenza A(H3N2) were similar to the updated vaccine clade 2a.3a.1 [2]. Antigenic studies suggested reduced reactivity of ferret antibodies raised against the vaccine virus, including 2a.3a.1 (J.2), the predominant subclade in our study [24,25]. In our study, a moderate proportion (21%) of sequenced influenza A(H3N2) viruses, almost exclusively from subclade 2a.3a.1 (J.2), harbored amino acid substitutions T135A or T135K associated with the loss of a N-linked glycosylation site, which are linked to antigenic drift compared to the vaccine strain and may contribute to reduced VE (28,29). Furthermore, 38% of viruses harbored amino acid substitutions at one of three so-called 'Koel' positions [15] (S145N/G and/or N158K/S and/or K189R), which may significantly impact the antigenic properties of the virus. This proportion reached 41% among viruses from subclade 2a.3a.1 (J.2). Amino acid substitutions at these positions have previously been linked to a major antigenic drift [15]. In particular, viruses with the N158K+K189R combination showed highly reduced reactivity with ferret antisera directed at the vaccine strain [24].

Yet, the VE against subclade 2a.3a.1 (J.2) was not substantially lower than the VE against all influenza A(H3N2) viruses, and the all-ages VE estimates against subclade 2a.3a.1 (J.2) and against subclade 2a.3a.1 (J.2.2) were also comparable (37% and 32%, respectively). Our findings may partially reflect the combined effect of age- and (sub)clade- or amino acid substitution-specific VE, although it was not possible to fully disentangle their respective contributions due to low numbers.

The VE against influenza B was high (≥70%) for all age groups, and higher than the 2024/25 interim estimates [16]. All viruses belonged to the vaccine clade V1A.3a.2, although

there was some diversity in circulating subclades. In all age groups, the VE was higher for subclade V1A.3a.2 (C.5.1) and V1A.3a.2 (C.5.6) and lowest for subclade V1A.3a.2 (C.5.7) (overall VE 85%, 77%, 53%, respectively). Subclade V1A.3a.2 (C.5.7) represented 18% of the sequenced influenza B viruses and is characterized by amino acid substitution E128G located in the 120-loop of the hemagglutinin, a major target for neutralizing antibodies, which could explain the lower VE observed for these subclades.

For all influenza (sub)types, there was some decline in VE over time; however, statistically significant differences were observed for influenza A(H3N2) only, consistent with observations from previous seasons [17]. Larger sample sizes and clade-specific VE estimates by time since vaccination are needed to better understand the potential decline in VE in relation to intraseasonal waning immunity and changes in the circulating clades driven by antigenic drift.

Limitations include the small sample size for sequencing and for some sub-analyses (e.g. (sub)clade-specific VE), which resulted in wide confidence limits of some estimates. In particular, we were unable to estimate the VE estimates against influenza B in older adults (≥65 years) due to the small number of cases in this age group. Similarly, the sample size did not allow to conduct VE analyses against specific amino acid substitutions in influenza A(H3N2) viruses. As in any observational study, there is a potential risk for unmeasured confounding.

5. Conclusions

The 2024/25 end-of-season estimates from the European I-MOVE primary care multicenter network showed that influenza vaccination protected approximately one in two vaccinated individuals against medically attended, laboratory-confirmed influenza. The VE against influenza A(H1N1)pdm09 was low (VE ranging between 16% and 34% by age group), and moderate against influenza A(H3N2) (VE ranging between 20% and 66% by age group). Protection was highest against influenza B (VE ≥70% across all age groups), consistent with observations from previous seasons.

Funding

This manuscript was funded by the European Centre for Disease Prevention and Control under the framework contract [ECDC/2021/019]. The funder of the study had a role in the study design, data interpretation, and the writing of the report, but no role in data collection or data analysis. The corresponding author had full access to all the data in the study, and final responsibility for the decision to submit for publication was by consensus. For the Netherlands, this work has received additional funding from the Dutch Ministry of Health, Welfare and Sport. This funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Declaration of interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Ethics statement

The planning, conduct and reporting of the studies was in line with the Declaration of Helsinki. Some countries/studies did not require official ethical approval or patient consent as they are part of routine care/surveillance: Ireland; Spain, national. Other study sites received local ethical approval from a national or regional review board: Germany: EA2/126/11; France: 471393; Hungary: IV/1885-5/2021/EKU Authorization Decision (29 September 2021) and BM/25007-2/2024 Decision authorizing the request for modification (4 October 2024). Written informed consent was recorded by the GP; The Netherlands: RIVM has obtained a formal statement by a medical ethical review committee that the Dutch Medical Research Involving Human Subjects Act (WMO) does not apply to the VE primary care studies; Navarra, Spain: Approved by the Ethical Committee for Clinical Research of Navarre (PI2024/150); Sweden: Approved ethical permit for Sweden: 2006/1040-31/2 revised Drn2024-06069-02; Portugal: Ethical clearance nº90/2022, updated at 15 November 2023; Croatia: Ethical Committee approval of the Ethics Committee of the Croatian Institute of Public Health, class: 030-02/23-01/1, issued on 19 April 2023; Romania: CE387/2024.

Data availability statement

Data is available from the corresponding author on request. The 2252 sequences generated in connection with this analysis have been submitted to GISAID.

AI-based tools and technologies

No generative AI tools were used in the preparation of this manuscript.

Acknowledgments

I-MOVE primary care group in Croatia: Bernard Kaić, Maja Ilić, Ivana Ferenčak, Dragan Jurić, Katica Čusek Adamić, Mirjana Lana Kosanović Ličina, Ivana Mihin Huskić, Diana Nonković, Morana Tomljenović. For Germany: We want to thank Carolin Hackmann and Ute Preuss from the Department of Infectious Disease Epidemiology, Respiratory Infections Unit, Robert Koch Institute as well as Barbara Biere, Djin-Ye Oh, Janine Reiche and Marianne Wedde from the National Reference Centre for Influenza, Robert Koch Institute. In addition, we want to thank the laboratory team at the National Reference Centre for Influenza and the colleagues at the sequencing core facility of the Genome Competence Center, Robert Koch Institute that contributed to the study. We sincerely appreciate the scientific support of Thomas Krannich, Marie Lataretu, Sofia Paraskevopoulou, and Dimitri Ternovoj from the Genome Competence Center, Robert Koch Institute for their assistance with genome assembly. The Hungarian study team works as part of the National Laboratory for Health Security Hungary (RRF-2.3.1-21-2022-00006) supported by the National Research, Development and Innovation Office (NKFIH). The Netherlands Lynn Aarts, Danytza Berry, Sanne Bos, Jasper van den Brink, Sharon van den Brink, Dirk Eggink, Rianne van Gageldonk-Lafeber, Gabriel Goderski, Maxime Hartwig, Marit de Lange, Tara Sprong, Anne Teirlinck, Eline in 't Velt, molecular pool and virus isolation and characterization technicians, National Institute for Public Health and the Environment (RIVM), Bilthoven; Nivel Primary Care Database – Sentinel Practices team, Nienke Veldhuijzen, Safira Wortel, Ruben van der Burgh, Ruud van den

Broek, Cathrien Kager, Marloes Riethof, Marloes Hellwich, Bart Knottnerus, participating general practices and their patients, Nivel, Utrecht. For Sweden: We are grateful to the GP network in Sweden for providing samples. At the Public Health Agency of Sweden, we thank colleagues at the influenza team: Elin Arvesen, Nora Nid, Tove Samuelsson-Hagey, Viktor Persson, Dorina Ujvari, Emmi Andersson, Lena Dillner, AnnaSara Carnahan and sequencing platform. For Portugal: Ausenda Machado, Licínia Gomes, Daniela Dias, Camila Henriques, Nuno Verdasca, and Portuguese GP and Health Units Sentinel Network. For Romania: Olivia Carmen Timnea, Adrian Jidovu, Catalina Pascu, Oana Vitencu, Nicoleta Tudor, Alina Ivanciuc, Ene Mirela, Iulia Bistriceanu, Mihaela Oprea, Maria Elena MihaiParts of this work were previously presented as a poster at ESCAIDE 2025, and is acknowledged here.

Author contributions

CRediT: **Héloïse Lucaccioni:** Data curation, Formal analysis, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing; **Francisco Pozo:** Data curation, Formal analysis, Investigation, Validation, Writing – review & editing; **Gloria Pérez-Gimeno:** Investigation, Validation, Writing – review & editing; **Ralf Dürrwald:** Investigation, Validation, Writing – review & editing; **Marina Uras:** Investigation, Validation, Writing – review & editing; **Lisa Domegan:** Investigation, Validation, Writing – review & editing; **Beatrix Oroszi:** Investigation, Validation, Writing – review & editing; **Adam Meijer:** Formal analysis, Validation, Writing – review & editing; **Camino Trobajo-Sanmartín:** Investigation, Validation, Writing – review & editing; **Dorina Ujvari:** Investigation, Validation, Writing – review & editing; **Ana Paula Rodrigues:** Investigation, Validation, Writing – review & editing; **Ivan Mlinarić:** Investigation, Validation, Writing – review & editing; **Mihaela Lazar:** Investigation, Validation, Writing – review & editing; **Eva Rivas Wagner:** Investigation, Validation, Writing – review & editing; **Annika Erdwiens:** Investigation, Validation, Writing – review & editing; **Vincent Enouf:** Investigation, Validation, Writing – review & editing; **Adele McKenna:** Investigation, Validation, Writing – review & editing; **Gergő Túri:** Investigation, Resources, Validation, Writing – review & editing; **Marit de Lange:** Investigation, Validation, Writing – review & editing; **Iván Martínez-Baz:** Investigation, Validation, Writing – review & editing; **Neus Latorre-Margalef:** Investigation, Validation, Writing – review & editing; **Raquel Guiomar:** Investigation, Validation, Writing – review & editing; **Sanja Kurečić Filipovic:** Investigation, Validation, Writing – review & editing; **Sorin Dinu:** Investigation, Validation, Writing – review & editing; **Olatz Mokoroa:** Investigation, Validation, Writing – review & editing; **Kristin Tolksdorf:** Investigation, Validation, Writing – review & editing; **Shirley Masse:** Investigation, Validation, Writing – review & editing; **Charlene Bennett:** Investigation, Validation, Writing – review & editing; **Katalin Kristóf:** Investigation, Validation, Writing – review & editing; **Mariette Hooiveld:** Investigation, Validation, Writing – review & editing; **Jesús Castilla:** Investigation, Validation, Writing – review & editing; **João Santos:** Investigation, Validation, Writing – review & editing; **Vesna Višekruna Vučina:** Investigation, Validation, Writing – review & editing; **Rodica Popescu:** Investigation, Validation, Writing – review & editing; **Sabrina Bacci:** Conceptualization, Project administration, Validation, Writing – review & editing; **Marlena Kaczmarek:** Conceptualization, Project administration, Validation, Writing – review & editing; **Esther Kissling:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. European Centre for Disease Prevention and Control (ECDC). Survey report on national seasonal influenza vaccination recommendations and coverage rates in EU/EEA countries [Internet]. 2024 [cited 2024 Dec 31]. Available from: https://www.ecdc.europa.eu/en/publications-data/survey-report-national-seasonal-influenza-vaccination-recommendations

• **This reference provides an overview of national seasonal influenza vaccination recommendations and coverage in Europe in 2024.**

2. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2024–2025 northern hemisphere influenza season [Internet]. 2024 Feb [cited 2025 Jan 31]. Available from: https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-2025-northern-hemisphere-influenza-season
3. European Centre for Disease Prevention and Control. European respiratory virus surveillance summary (ERVISS), 2024, week 04 [Internet]. 2024 [cited 2025 Jan 31]. Available from: https://erviss.org/
4. Kissling E, Valenciano M, Falcao J, et al. 'I-MOVE' towards monitoring seasonal and pandemic influenza vaccine effectiveness: lessons learnt from a pilot multi-centric case-control study in Europe, 2008–9. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2009;14(44):19388.
5. Maurel M, Howard J, Kissling E, et al. Interim 2023/24 influenza a vaccine effectiveness: VEBIS European primary care and hospital multicentre studies, September 2023 to January 2024. Eurosurveillance. 2024;29(8):2400089. doi: 10.2807/1560-7917.ES.2024.29.8.2400089
6. Kissling E, Maurel M, Pozo F, et al. Influenza vaccine effectiveness in Europe and the birth cohort effect against influenza A(H1N1) pdm09: VEBIS primary care multicentre study, 2023/24. Eurosurveillance. 2025;30(23):2500011. doi: 10.2807/1560-7917.ES.2025.30.23.2500011

•• **This reference presents vaccine effectiveness estimates in Europe in the 2023/24 influenza season, including a birth cohort effect against influenza A(H1N1)pdm09.**

7. European Centre for Disease Prevention and Control (ECDC). Core protocol for ECDC studies of vaccine effectiveness against symptomatic laboratory-confirmed influenza or SARS-CoV-2 infection at primary care level, 2024 [Internet]. Stockholm: ECDC; 2024. p. 67 p. Available from: https://www.ecdc.europa.eu/en/publications-data/core-protocol-ecdc-studies-vaccine-effectiveness-against-symptomatic-laboratory

•• **This reference details the core protocol for the VEBIS (Vaccine Effectiveness, Burden and Impact Studies) study.**

8. European Centre for Disease Prevention and Control (ECDC). EU case definitions [Internet]. 2024 [cited 2024 Dec 31]. Available from: https://www.ecdc.europa.eu/en/all-topics/eu-case-definitions
9. Firth D. Bias reduction of maximum likelihood estimates. Biometrika. 1993;80(1):27–38. doi: 10.1093/biomet/80.1.27
10. Liu M, Zhao X, Hua S, et al. Antigenic patterns and evolution of the human influenza A (H1N1) virus. Sci Rep. 2015;5(1):14171. doi: 10.1038/srep14171
11. Liu M, Liu J, Song W, et al. Development of PREDAC-H1pdm to model the antigenic evolution of influenza A/(H1N1) pdm09 viruses. Virol Sin. 2023;38(4):541–548. doi: 10.1016/j.virs.2023.05.008
12. Cheng P, Zhai K, Han W, et al. Characterizing the antigenic evolution of pandemic influenza a (H1N1) pdm09 from 2009 to 2023. J Med Virol. 2024;96(5):e29657. doi: 10.1002/jmv.29657
13. Doll MK, Pettigrew SM, Ma J, et al. Effects of confounding bias in coronavirus disease 2019 (COVID-19) and influenza vaccine effectiveness test-negative designs due to correlated influenza and COVID-19 vaccination behaviors. Clin Infect Dis. 2022 Aug 24;75(1):e564–e571.
14. RStudio Team. Rstudio: integrated development environment for R. 2016.
15. Koel BF, Burke DF, Bestebroer TM, et al. Substitutions near the receptor binding site determine major antigenic change during influenza virus evolution. Science. 2013;342(6161):976–979. doi: 10.1126/science.1244730
16. Rose AM, Lucaccioni H, Marsh K, et al. Interim 2024/25 influenza vaccine effectiveness: eight European studies, September 2024 to January 2025. Eurosurveillance. 2025;30(7):2500102. doi: 10.2807/1560-7917.ES.2025.30.7.2500102

17. Maurel M, Pozo F, Pérez-Gimeno G, et al. Influenza vaccine effectiveness in Europe: results from the 2022–2023 VEBIS (vaccine effectiveness, burden and impact studies) primary care multicentre study. Influenza Other Respir Viruses. 2024;18(1):e13243. doi: 10.1111/irv.13243
18. Kissling E, Pozo F, Martínez-Baz I, et al. Influenza vaccine effectiveness against influenza A subtypes in Europe: Results from the 2021–2022 I-MOVE primary care multicentre study. Influenza Other Respir Viruses. 2023;17(1):e13069.
19. Separovic L, Zhan Y, Kaweski SE, et al. Interim estimates of vaccine effectiveness against influenza A(H1N1)pdm09 and A(H3N2) during a delayed influenza season, Canada, 2024/25. Eurosurveillance. 2025;30(4):2500059. doi: 10.2807/1560-7917.ES.2025.30.4.2500059
20. Frutos AM, Cleary S, Reeves EL, et al. Interim estimates of 2024–2025 seasonal influenza vaccine effectiveness — four vaccine effectiveness networks, United States, October 2024–February 2025. Morb Mortal Wkly Rep. 2025;74(6):83–90. doi: 10.15585/mmwr.mm7406a2
21. World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC). Influenza virus characterization: summary report, Europe, May 2024. [Internet]. Copenhagen and Stockholm: WHO Regional Office for Europe and European Centre for Disease Prevention and Control; 2024. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/TD-6189-E_Euro-report_May24_final.pdf
22. Chung JR, Price AM, Zimmerman RK, et al. Influenza vaccine effectiveness against medically attended outpatients illness, United States, 2023–2024 season. Clin Infect Dis. 2025;81(4):e184–e191. doi: 10.1093/cid/ciae658
23. Skowronski DM, Zhan Y, Kaweski SE, et al. 2023/24 mid-season influenza and Omicron XBB.1.5 vaccine effectiveness estimates from the Canadian sentinel practitioner surveillance network (SPSN). Eurosurveillance. 2024;29(7):2400076. doi: 10.2807/1560-7917.ES.2024.29.7.2400076
24. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2025–2026 northern hemisphere influenza season [Internet]. 2025 Feb [cited 2025 Jun 13]. Available from: https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2025-2026-nh-influenza-season
25. World Health Organization (WHO), European Centre for Disease Prevention and Control. Influenza virus characterization: summary report, Europe, September 2024 [Internet]. Copenhagen and Stockholm: WHO Regional Office for Europe and European Centre for Disease Prevention and Control; 2024. Available from: https://www.ecdc.europa.eu/en/publications-data/influenza-virus-characterization-summary-europe-september-2024
•• **This reference presents the influenza virus characterization in Europe in September 2024.**