Interim 2024/25 influenza vaccine effectiveness: eight European studies, September 2024 to January 2025

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The 2024/25 influenza season in Europe is currently characterised by co-circulation of influenza A(H1N1)pdm09, A(H3N2) and B/Victoria viruses, with influenza A(H1N1)pdm09 predominating. Interim vaccine effectiveness (VE) estimates from eight European studies (17 countries) indicate an all-age influenza A VE of 32–53% in primary care and 33–56% in hospital settings, with some signals of lower VE by subtype and higher VE against influenza B (≥ 58% across settings). Where feasible, influenza vaccination should be encouraged and other prevention measures strengthened.

For the northern hemisphere, the World Health Organization (WHO) recommended the following 2024/25 influenza virus strains for egg-based vaccines: an A/Victoria/4897/2022 (H1N1)pdm09-like, an A/Thailand/8/2022 (H3N2)-like and a B/Austria/1359417/2021 (B/Victoria lineage)-like virus for trivalent vaccines. For cell culture- or recombinant-based vaccines, the WHO recommended inclusion of an A/Wisconsin/67/2022 (H1N1)pdm09-like and an A/Massachusetts/18/2022 (H3N2)-like virus, with the same influenza B virus component as for egg-based vaccines. For both egg- and non-egg-based vaccines, the WHO recommended inclusion of an additional B/Phuket/3073/2013 (B/Yamagata lineage)-like virus for quadrivalent vaccines [1].
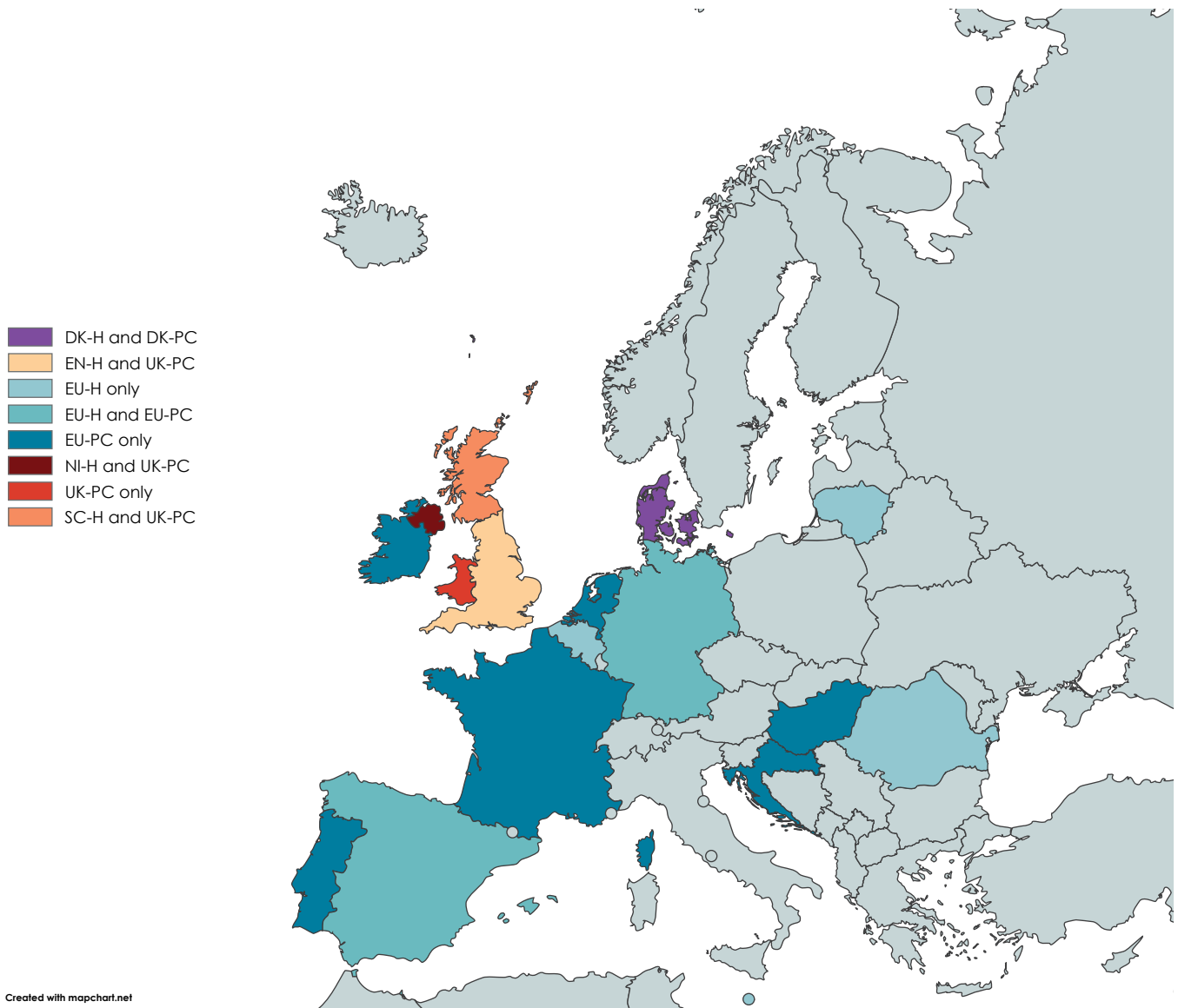
European primary care and hospital-based studies to measure influenza vaccine effectiveness in 2024/25

We report interim results from five single- and three multi-country studies (17 countries), including both primary care and hospital settings, to help guide influenza prevention and control measures for the rest of the 2024/25 season and to inform preparation for the 2025/26 season.

The primary care (PC) studies were conducted in Denmark (DK-PC), the United Kingdom (UK) (UK-PC: four countries), and through the European Union (EU) Vaccine Effectiveness, Burden and Impact Studies (VEBIS) multi-country primary care network (EU-PC: eight of 10 countries contributing to the interim analysis). The hospital setting (H) studies were conducted in Denmark (DK-H), England (EN-H), Northern Ireland (NI-H), Scotland (SC-H), and through the EU VEBIS multi-country hospital network (EU-H: six of 10 countries contributing to the interim analysis) (Figure 1).

Study design and vaccine effectiveness analyses

The EU VEBIS project has been estimating influenza vaccine effectiveness (VE) through multicentre primary care and hospital studies since the 2022/23 influenza season. Before this, many VEBIS study sites (primary care and hospital) participated in the Influenza – Monitoring Vaccine Effectiveness in Europe (I-MOVE)

FIGURE 1

European countries contributing results[a] for interim influenza vaccine effectiveness, influenza season 2024/25 (n = 17)

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DK-H/DK-PC: Denmark hospital and primary care studies; EN-H: England hospital study; EU-H/EU-PC: European Union hospital-/primary care-based multi-country VEBIS studies; NI-H: Northern Ireland hospital study; SC-H: Scotland hospital study; UK-PC: United Kingdom primary care multi-country study; VEBIS: Vaccine Effectiveness, Burden and Impact Studies.

[a] Countries contributing to EU-H but not included in the analysis (as too few cases remained after applying exclusions and restrictions): Croatia, Hungary, Ireland, Portugal. Countries contributing to EU-PC but not included in the analysis: Romania, Sweden.

network, measuring annual influenza VE from 2008/09 to 2021/22 [2,3]. The UK and Denmark were I-MOVE partners until 2021/22 and have estimated influenza VE in single-country studies since 2006 and 2009, respectively. We have jointly published interim season influenza VE results since 2017/18 [4]. All studies use the test-negative design [5], with methods previously described [6–9]. There are some differences in recruitment practice or collection of data by study; we summarise methods by study in Table 1.

Briefly, three of the multicentre studies (EU-H, EU-PC and UK-PC) used prospective patient recruitment,

while five studies used electronic database linkage (DK-H, DK-PC, EN-H, NI-H, SC-H). Patients presenting with influenza-like illness (ILI) or acute respiratory infection (ARI) symptoms in the primary care studies had nasopharyngeal or combined oro-nasopharyngeal specimens (or saliva specimens, in France) collected. In EU-H, patients admitted with severe ARI (SARI) symptoms were swabbed. In EN-H, NI-H and SC-H, all patients entering hospital via an emergency department who were tested for influenza were assumed to have had at least one ARI symptom. In each study, either all or a systematic selection of patients were

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swabbed, or the physician's discretion was used to select patients for swabbing.

For influenza virus detection, samples were tested by reverse transcription (RT)-PCR for type A and type B viruses, followed by type A subtyping or B lineage determination. We defined cases as patients whose tests were positive for any influenza virus (sub)type; controls were those testing RT-PCR-negative for all influenza viruses. Most studies recruited all children and adults, while some applied age restrictions (Table 1).

We defined vaccinated patients as those having had the 2024/25 influenza vaccine at least 14 days before symptom onset. Those vaccinated < 14 days before symptom onset, or with unknown vaccination date, were excluded.

Most study countries (six from EU-PC, three from EU-H, and Denmark) selected all or a random sample of influenza virus-positive specimens for haemagglutinin genome segment and/or whole genome sequencing. Sequencing was followed by phylogenetic analysis to determine clade distribution, with results provided for both studies in Denmark together (DK-PC and DK-H).

Statistical analysis
In each study, we calculated VE as 1 minus the adjusted ratio of the odds of vaccination in cases and controls, expressed as a percentage: $VE = (1 - OR_a) \times 100$. We used logistic regression to adjust for measured potential confounding variables (Table 1).

We estimated study-specific VE against any influenza, influenza A overall, and against influenza A(H1N1) pdm09, A(H3N2) and B. We performed sensitivity analyses using Firth's method of penalised logistic regression (PLR) to assess small sample bias [10] for analyses with fewer than 10 cases or controls per parameter. We considered > 10% difference between the original and the PLR estimates as indicating small sample bias and do not show these estimates.

Virus characteristics
In this season, influenza A virus subtypes and influenza B co-circulated in Europe [11]. Influenza A(H1N1) pdm09 was the main subtype among all studies, ranging between 57% and 93% of influenza A subtypes (Figure 2). The proportion of influenza B cases varied considerably, from 2% in SC-H to 37% in EU-PC. Within the EU-PC and EU-H multicentre studies, the proportion of influenza B varied by country (data not shown).

Among genetically characterised influenza A(H1N1) pdm09 viruses, the majority (> 80%) belonged to the C.1.9 subclade of 5a.2a (Table 2). Most characterised influenza A(H3N2) viruses belonged to the J.2 subclade of 2a.3a.1. There was some genetic variation of influenza B viruses across studies, but all belonged to clade V1A.3a.2.

Vaccine effectiveness overall and against influenza A
In the primary care setting, VE for any influenza among all ages ranged from 40% to 53%, with lowest age-stratified VE among adults ≥ 65 years (null in EU-PC, 38% in UK-PC). In the hospital setting, the all-age any influenza VE was 34–52%. We append the detailed results for VE against influenza A in Supplementary Figure S1.

Vaccine effectiveness against influenza A(H1N1)pdm09
The VE against influenza A(H1N1)pdm09 ranged between 30% and 72% among all ages in primary care settings. Age-specific results were similar among 18–64-year-olds in EU-PC and UK-PC at 46–48%, but higher in DK-PC at 77% (Figure 3). Age-specific VE was lower among children and adults ≥ 65 years in UK-PC (42% for both age groups) and even lower in EU-PC (12% and −22%), although confidence limits were wide.

In the hospital setting across studies, VE against influenza A(H1N1)pdm09 ranged between 46% and 53% among all ages. The VE was lower in adults ≥ 65 years (38–45%) than among children aged 2–17 years (52–61%) (Figure 3).

Most sequenced samples of influenza A(H1N1)pdm09 belonged to the 5a.2a clade which, although genetically different to the vaccine strain, was protective for about one-third of those vaccinated among all ages (Figure 3).

Vaccine effectiveness against influenza A(H3N2)
The VE against influenza A(H3N2) ranged between 29% and 47% among all ages in primary care settings (Figure 3), while VE in adults ranged between −13% and 34%, with higher VE among children (83% in UK-PC).

In the hospital setting, VE against influenza A(H3N2) ranged between 31% and 49% among all ages. The VE in adults ranged from 7% to 47% and in SC-H (the only study with a VE estimate in children for this setting), VE among those aged 2–17 years was negative, noting that numbers were low. In particular, in SC-H, the proportion of influenza A cases subtyped (677/5,304; 13%) was very small (and only 50/677 (7%) of those subtyped were influenza A(H3N2)). There is a potential for some bias towards subtyping of more severe cases in this study as in some health boards in Scotland, patients admitted to intensive care or high-dependency wards are more likely to have their samples subtyped.

Vaccine effectiveness against influenza B
The VE against influenza B was high across all studies, with all-age estimates ranging between 58% and

TABLE 1A

Summary of methods for the eight European interim influenza vaccine effectiveness studies, influenza season 2024/25 (n = 17 countries)

Study characteristics	Study							
	DK-PC	EU-PC	UK-PC	DK-H	EN-H	EU-H	NI-H	SC-H
Period	30 Sep 2024– 31 Jan 2025	4 Oct 2024– 14 Jan 2025	30 Sep 2024– 10 Jan 2025	30 Sep 2024– 31 Jan 2025	30 Sep 2024– 5 Jan 2025	15 Oct 2024– 17 Jan 2025	29 Sep 2024– 20 Jan 2025	1 Oct 2024– 21 Jan 2025
Setting	Non-hospitalised patients[a]	Primary care	Primary care	Hospital	Hospital	Hospital	Hospital	Hospital
Location	DK	HR, FR, DE, HU, IE, NL, PT, ES	EN, NI, SC, WA	DK	EN	74 hospitals in BE, DE, ES, LT, MT, RO	NI	SC
Design	TND	TND	TND	TND	TND	TND	TND	TND
Data source(s)	Data linkage of Danish Microbiology Database, the Danish Vaccination Register and the Danish National Discharge Register	Sentinel physicians and laboratories; in some sites data linkage to electronic health records	Sentinel physicians and laboratories; in some sites data linkage to vaccine registries	Data linkage of Danish Microbiology Database, the Danish Vaccination Register and the Danish National Discharge Register	Data linkage of laboratory surveillance, the Immunisations Information System, and the Secondary Uses Service	Hospital charts, vaccine registers, interviews with patients, laboratory records	Linkage of vaccination status from the Northern Ireland Vaccine Management System, influenza tests from the regional laboratory surveillance system, and administrative admissions data from Health and Social Care information systems	National patient-level dataset based on GP records, Electronic Communication of Surveillance in Scotland ECOSS (all virology testing national database), Rapid Preliminary Inpatient Data RAPID (Scottish hospital admissions data), National Records of Scotland NRS (death certification), National Clinical Data Store NCDS (vaccination events in Scotland)
Age groups of study population	All ages	≥6 months	≥ 2 years	All ages	≥ 2 years	All ages	Adults ≥18 years	≥ 2 years
Case definition for patient recruitment	Sudden onset of symptoms with fever, myalgia and respiratory symptoms[b]	EU ARI[c] or EU ILI[c]	ARI	Sudden onset of symptoms with fever, myalgia and respiratory symptoms among hospitalised patients	ARI-coded hospital visit with a swab taken 14 days before to 2 days after admission	SARI (hospitalised person with fever cough, or shortness of breath) at admission or within 48 h after admission); some countries recruit those with fever or cough; some include those only with fever and cough	Patients with a positive influenza test performed either up to 7 days before admission or up to 1 day after admission. Limited to emergency care[d]	Patients with a positive influenza test 14 days before admission or within 48 h of admission. Limited to emergency care[d]

aQIV: adjuvanted QIV; ARI: acute respiratory infection; BE: Belgium; DE: Germany; DK: Denmark; DK-H: DK hospital study; DK-PC: DK primary care study; EN: England; EN-H: EN hospital study; ES: Spain; EU: European Union; EU-H: EU hospital multicentre VEBIS study; EU-PC: EU primary care multicentre VEBIS study; FR: France; GP: general practitioner; HR: Croatia; HU: Hungary; IE: Ireland; ILI: influenza-like illness; LAIV: live attenuated influenza vaccine; LT: Lithuania; LRI: lower respiratory infection; MT: Malta; NI: Northern Ireland; NL: Netherlands; PT: Portugal; QIV: quadrivalent inactivated influenza vaccine; QIVc: cell-based QIV; QIVe: egg-grown QIV; QIV-HD: QIV – high-dose; RCS: restricted cubic spline; RO: Romania; SARI: severe acute respiratory infection; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SC: Scotland; SC-H: SC hospital study; SIMD: Scottish Index of Multiple Deprivation; SE: Sweden; TIV: trivalent inactivated influenza vaccine; TND: test-negative design; UK: United Kingdom; UK-PC: UK primary care multicentre study; VE: vaccine effectiveness; VEBIS: VE, Burden and Impact Studies; WA: Wales.

[a] Patients are seen by the GP, but also in emergency care.

[b] This is the case definition for patient recruitment by sentinel GPs within DK-PC who follow the EU-ILI case definition (sudden onset of symptoms, AND at least one of: fever > 38° C, feverishness, malaise, headache, myalgia, AND at least one of: cough, sore throat, shortness of breath).

[c] The EU-ARI definition is sudden onset of symptoms AND at least one of: fever or feverishness, malaise, headache, myalgia AND at least one of: cough, sore throat, shortness of breath. The EU-ILI definition is sudden onset of symptoms AND at least one of cough, sore throat, shortness of breath or coryza, AND a clinician's judgement that the illness is due to an infection. The EU-ARI case definition. Most EU-PC sites recruit according to the EU-ARI case definition, although there are some site-specific differences in ARI (and/or ILI) definitions for recruitment.

[d] All patients entering hospital via an emergency department who were tested for influenza were assumed to have had an ARI symptom.

[e] Vaccines were prepared from egg-grown vaccine viruses, non-adjuvanted and administered intramuscularly unless otherwise specified.

[f] Where indicated, vaccine coverage among controls was used as representative of the source population from which the cases arose.

TABLE 1B

Summary of methods for the eight European interim influenza vaccine effectiveness studies, influenza season 2024/25 (n = 17 countries)

Study characteristics	Study							
	DK-PC	EU-PC	UK-PC	DK-H	EN-H	EU-H	NI-H	SC-H
Selection of patients	At practitioner's/clinician's judgement	Systematic	At practitioner's/clinician's judgement	At practitioner's/clinician's judgement	Exhaustive	Exhaustive (DE, LT, MT, RO, some hospitals in ES). Systematic (BE, ES; some hospitals in BE: exhaustive on either 1 or 2 days per week, depending on workload)	Exhaustive (all patients who fit the case definition and are captured via the linkage of the named datasets)	Exhaustive (all patients who fit the case definition above and are captured via the linkage of the named datasets)
Vaccine types used nationally or in the study[e,f]	In the population: 50% QIV, 45% aQIV (offered to individuals ≥ 70 years), 5% QIV-HD (offered to individuals ≥ 65 years)	In the study among controls: 48% QIV, 13% aQIV, 10% QIV-HD, 8% QIVc, 8% LAIV (trivalent and quadrivalent), 2% TIV, and 12% unknown	In the study among controls: ages 2–17 years 90% LAIV, 5% QIVc, 5% unknown; ages 18–64 years 67% QIVc, 2% aQIV, 1% QIV, 0.2% QIV-HD, 29% unknown; ages ≥ 65 years 72% aQIV, 2% QIV-HD, 1% QIVc, 0.1% QIV, 25% unknown	In the population: 50% QIV, 45% aQIV (offered to individuals ≥ 70 years), 5% QIV-HD (offered to individuals ≥ 65 years)	In the study among controls: ages 2–17 years 80% LAIV, 13% QIVc, 6% unknown; ages 18–64 years 84% QIVc, 6% aQIV, 4% QIV, 1% QIV-HD, 6% unknown; ages ≥ 65 years 88% aQIV, 4% QIV-HD, 3% QIVc, 5% unknown	In the study among controls: 45% QIV, 21% aQIV, 15% QIV-HD, 5% QIVc, 4% LAIV (trivalent and quadrivalent), 12% unknown	In the study among controls: 26.5% QIVc, 73.5% aQIV	23% QIVc; 77% aQIV
Variables of adjustment	Age group, sex, presence of chronic conditions, calendar time as month (Oct–Jan) or if possible, week	Age (modelled as RCS, age group or linear term depending on analysis), sex, presence of chronic conditions, onset date (RCS) and study site	Age group, sex, country, clinical risk status, calendar time as week (spline)	Age group, sex, presence of chronic conditions, calendar time as month (Oct–Jan) or if possible, week	Age group, region, clinical risk status, calendar time as week (spline)	Age (modelled as RCS, age group or linear term depending on analysis), sex, presence of chronic conditions, time (onset date as RCS or month of swab as categorical term) and study site	Age group, sex, month of the test, and Health and Social Care Trust	Age (spline), sex, number of clinical risk groups (0,1,2,3,4, ≥ 5), time (days, spline), setting (community or hospital) and deprivation quintile (SIMD)

aQIV: adjuvanted QIV; ARI: acute respiratory infection; BE: Belgium; DE: Germany; DK: Denmark; DK-H: DK hospital study; DK-PC: DK primary care study; EN: England; EN-H: EN hospital study; ES: Spain; EU: European Union; EU-H: EU hospital multicentre VEBIS study; EU-PC: EU primary care multicentre VEBIS study; FR: France; GP: general practitioner; HR: Croatia; HU: Hungary; IE: Ireland; ILI: influenza-like illness; LAIV: live attenuated influenza vaccine; LT: Lithuania; LRI: lower respiratory infection; MT: Malta; NI: Northern Ireland; NL: Netherlands; PT: Portugal; QIV: quadrivalent inactivated influenza vaccine; QIVc: cell-based QIV; QIVc: egg-grown QIV; QIV-HD: QIV – high-dose; RCS: restricted cubic spline; RO: Romania; SARI: severe acute respiratory infection; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SC: Scotland; SC-H: SC hospital study; SIMD: Scottish Index of Multiple Deprivation; SE: Sweden; TIV: trivalent inactivated influenza vaccine; TND: test-negative design; UK: United Kingdom; UK-PC: UK primary care multicentre study; VE: vaccine effectiveness; VEBIS: VE, Burden and Impact Studies; WA: Wales.

[a] Patients are seen by the GP, but also in emergency care.

[b] This is the case definition for patient recruitment by sentinel GPs within DK-PC who follow the EU-ILI case definition (sudden onset of symptoms, AND at least one of: fever > 38° C, feverishness, malaise, headache, myalgia, AND at least one of: cough, sore throat, shortness of breath).

[c] The EU-ILI definition is sudden onset of symptoms AND at least one of cough, sore throat, shortness of breath or coryza, AND a clinician's judgement that the illness is due to an infection. The EU-ILI definition is sudden onset of symptoms AND at least one of: fever or feverishness, malaise, headache, myalgia AND at least one of: cough, sore throat, shortness of breath. Most EU-PC sites recruit according to the EU-ARI case definition, although there are some site-specific differences in ARI (and/or ILI) definitions for recruitment.

[d] All patients entering hospital via an emergency department who were tested for influenza were assumed to have had an ARI symptom.

[e] Vaccines were prepared from egg-grown vaccine viruses, non-adjuvanted and administered intramuscularly unless otherwise specified.

[f] Where indicated, vaccine coverage among controls was used as representative of the source population from which the cases arose.

FIGURE 2

Proportion of influenza virus infections, eight European studies, interim influenza season 2024/25 (n = 27,170)[a]

A. Infections by influenza type

Legend: A (subtyped) ■ | A unsubtyped ■ | B ■ | Influenza-positive, no (sub)type ■

B. Infections by influenza A subtype

Legend: A(H1N1)pdm09 ■ | A(H3N2) ■

DK-H: Denmark hospital study; DK-PC: Denmark primary care study; EN-H: England hospital study; EU: European Union; EU-H: EU hospital multicentre VEBIS study; EU-PC: EU primary care multicentre VEBIS study; PC: primary care; NI-H: Northern Ireland hospital study; SC-H: Scottish hospital study; UK-PC: United Kingdom multicentre primary care study; VEBIS: Vaccine Effectiveness, Burden and Impact Studies.

[a] Includes 15 influenza A and B co-infections in DK-PC, 13 in EN-H, seven in EU-PC, six in UK-PC; six influenza A(H1N1)pdm09 and A(H3N2) co-infections in UK-PC, one in DK-PC and one in DK-H; and one influenza A(H1N1)pdm09 and B co-infection in DK-PC.

Characterised viruses	Clade	Subclade	DK-H/DK-PC[b]		EU-H		EU-PC		UK-PC	
			n	%	n	%	n	%	n	%
Influenza A(H1N1)pdm09			n = 564[c]		n = 212[c]		n = 712[c]		n = 2,444[c]	
A/Lisboa/188/2023	5a.2a	C.1.9	76	83	13	NC	160	90	195	91
A/Michigan/62/2023	5a.2a	C.1.8	0	0	0	0	0	0	0	0
A/Victoria/4897/2022[d]	5a.2a.1	D	16	17	0	0	17	10	20	9
Total (n=497)[e]			92	100	13	NC	177	100	215	100
Influenza A(H3N2)			n = 389[c]		n = 66[c]		n = 187[c]		n = 292[c]	
A/Thailand/8/2022[d]	2a.3a.1	J	0	0	0	0	0	0	0	0
A/Sydney/856/2023	2a.3a.1	J.1	0	0	0	0	0	0	0	0
A/Croatia/10136RV/2023	2a.3a.1	J.2	20	31	4	NC	34	NC	31	NC
A/West Virginia/51/2024	2a.3a.1	J.2.1	41	63	1	NC	1	NC	2	NC
A/Lisboa/216/2023	2a.3a.1	J.2.2	4	6	0	0	3	NC	2	NC
A/France/IDF-IPP29542/2023	2a.3a.1	J.4	0	0	0	0	0	0	0	0
A/Finland/402/2023	2a.3a	G.1.3.1	0	0	0	0	1	NC	1	NC
Total (n=145)[e]			65	100	5	NC	39	NC	36	NC
Influenza B/Victoria			n = 721[c]		n = 84[c]		n = 639[c]		n = 184[c]	
B/Netherlands/10335/2023	V1A.3a.2	C.2	0	0	0	0	0	0	0	0
B/Moldova/2030521/2023	V1A.3a.2	C.3	0	0	0	0	0	0	1	NC
B/Stockholm/3/2022	V1A.3a.2	C.5	1	NC	0	0	0	0	1	NC
B/Catalonia/2279261NS/2023	V1A.3a.2	C.5.1	7	NC	2	NC	61	50	13	NC
B/Switzerland/329/2024	V1A.3a.2	C.5.6	9	NC	1	NC	29	24	9	NC
B/Guangxi-Beiliu/2298/2023	V1A.3a.2	C.5.7	11	NC	1	NC	33	27	8	NC
Total (n=187)[e]			28	NC	4	NC	123	100	32	NC

DK-H: Denmark hospital study; DK-PC: Denmark primary care study; EU-H: European Union hospital multicentre VEBIS study; EU-PC: European Union primary care multicentre VEBIS study; NC: not calculated (percentages not shown where denominators ‹60); UK-PC: United Kingdom multicentre primary care study; VEBIS: Vaccine Effectiveness, Burden and Impact Studies.

[a] Genetic characterisation results not available from the England, Northern Ireland and Scotland hospital studies.

[b] DK-H and DK-PC samples are combined.

[c] n: total numbers of viruses (sub)typed.

[d] Strain included in the 2024/25 northern hemisphere influenza vaccine.

[e] Total: total number of (sub)typed viruses sequenced.

74% in primary care and 73–88% in hospital settings (Figure 3). Age-specific estimates were all ≥ 50%, except one (42%, among those ≥ 65 years in EN-H).

Discussion

The influenza epidemic is ongoing in Europe [11,12]. Results from eight European influenza studies in the early phase of the winter 2024/25 influenza season indicated that influenza vaccination prevented from one-third to more than three-quarters of influenza infections medically attended in the primary care or hospital settings among the vaccinated, although protection varied by age group and study. Canadian interim 2024/25 VE in the primary care setting was in between our European study estimates at 50–57% [13].

This season, C.1.9, harbouring the K169Q amino acid substitution, is the main circulating A(H1N1)pdm09 5a.2a subclade. The influenza A(H1N1)pdm09 clade 5a.2a also dominated in Europe last season [14], and the vaccine, unchanged since 2023/24, provided protection during the 2023/24 interim A(H1N1)pdm09 VE season similar to or higher than we present for interim

2024/25 season VE [6,15]. The 2023/24 clade-specific VE point estimate for primary care settings was higher than in the current season (52% vs 28–33% among all ages) [15], indicating that virological change within the 5a.2a clade may be causing immune escape. Some VE estimates by age group were low, although antigenic studies with ferret sera indicate that circulating 5a.2a viruses are generally well recognised by sera raised against the clade 5a.2a.1 vaccine virus [14]. Repeat vaccination may play a role in lower VE, as previously hypothesised in some studies [16]; however, small sample size affecting the point estimates may be more likely.

In general, VE against influenza A(H3N2) in the primary care setting was lower than the 54% observed in Canada in this 2024/25 season [13], but due to low circulation of influenza A(H3N2) in Europe to date, all VE estimates had wide confidence intervals. The VE estimates later in the season with more cases will help confirm the VE against circulating A(H3N2) viruses which, although clade-matched to the clade 2a.3a.1 vaccine virus, harbour some genetic variation. Antigenic studies indicate

FIGURE 3

Interim vaccine effectiveness overall, against influenza A subtypes and influenza B, by age and target group for vaccination and by study, eight European studies, influenza season 2024/25

A. All laboratory-confirmed influenza

Study	Population[a]	Cases n	vacc	%	Controls n	vacc	%	VE (95% CI)[b]
Primary care								
DK–PC[c]	All ages	4,160	571	14	32,347	6,877	21	53 (47–58)
	0–17 years	1,195	7	1	8,583	71	1	53 (–5–79)
	18–64 years	2,487	260	11	16,991	2,435	1	52 (44–58)
	65 years and above	478	304	64	6,773	4,371	65	55 (44–64)
EU–PC	All ages	1,756	168	10	7,463	1,111	15	40 (26–52)
	0–17 years[d]	462	21	5	2,234	251	11	60 (33–77)
	18–64 years	1,152	72	6	4,071	314	8	42 (21–58)
	65 years and above	142	75	53	1,158	546	47	0 (–54–34)
	Target group[e]	593	133	22	3,379	966	29	31 (11–47)
UK–PC	All ages	3,201	665	21	12,965	3,314	26	44 (37–51)
	2–17 years	594	183	31	2,656	843	32	46 (33–57)
	18–64 years	2,217	229	10	7,701	1,072	14	47 (36–56)
	65 years and above	390	253	65	2,608	1,399	54	38 (18–53)
Hospital								
DK–H[c]	All ages	1,287	443	34	23,621	9,115	39	52 (45–58)
	18–64 years	507	91	18	6189	1,128	18	44 (28–57)
	65 years and above	649	350	54	14,984	7,950	53	55 (47–62)
EN–H	All ages	8,655	2,461	28	20,703	6,423	31	51 (48–55)
	2–17 years	1,563	302	19	3,067	745	24	56 (47–64)
	18–64 years	3,766	552	15	6,850	1,187	17	53 (46–59)
	65 years and above	3,326	1,607	48	10,786	4,491	42	48 (42–53)
EU–H	All ages	651	189	29	4,577	1,684	37	52 (40–62)
	0–17 years	88	3	3	1,270	203	16	90 (69–98)
	18–64 years	179	18	10	788	135	17	52 (16–74)
	65 years and above	384	168	44	2,519	13,46	53	49 (34–61)
	Target group[e]	572	186	33	4,044	16,36	40	53 (42–63)
NI–H	All adults	1,340	440	33	182	68	37	60 (39–74)
	18–64 years	561	80	14	80	18	23	72 (50–87)
	65 years and above	779	360	46	102	50	49	52 (20–72)
SC–H	All ages	5,416	1,473	27	26,056	7,556	29	34 (28–39)
	2–17 years	638	60	9	2,060	130	6	58 (19–76)
	18–64 years	2,005	182	9	8,214	721	9	28 (13–40)
	65 years and above	2,618	1,116	43	14,991	5,914	39	29 (23–36)

VE (%) scale: −20 0 20 40 60 80 100

B. Influenza A(H1N1)pdm09

Study	Population[a]	Cases n	vacc	%	Controls n	vacc	%	VE (95% CI)[b]
Primary care								
DK–PC	All ages	446	41	9	32,347	6,877	21	72 (60–81)
	18–64 years	298	17	6	16,991	2,435	14	77 (61–86)
EU–PC[f]	All ages	712	100	14	6,635	1,043	16	30 (7–47)
	0–17 years[d]	154	9	6	2,145	248	12	12 (–83–61)
	18–64 years	463	38	8	3,442	284	8	46 (19–65)
	65 years and above	95	53	56	1,048	511	49	–22 (–105–27)
	Target group[e]	303	82	27	2,981	910	31	23 (–7–45)
UK–PC	All ages	2,444	547	22	12,965	3,314	26	44 (36–51)
	2–17 years	454	154	34	2,656	843	32	42 (26–54)
	18–64 years	1,664	181	11	7,701	1,072	14	48 (36–58)
	65 years and above	326	212	65	2,608	1,399	54	42 (21–57)
Hospital								
EN–H	All ages	880	234	27	20,703	6,423	31	53 (44–61)
	2–17 years	193	36	19	3,067	745	24	61 (41–74)
	18–64 years	397	56	14	6,850	1,187	17	59 (44–70)
	65 years and above	290	142	49	10,786	4,491	42	44 (28–57)
EU–H[f]	All ages	211	51	24	4,062	1,615	40	50 (27–67)
	18–64 years	59	5	NC	713	132	19	56 (–17–86)
	65 years and above	120	46	38	2,280	1,292	57	45 (14–64)
	Target group[e]	178	51	29	3,553	1,568	44	52 (29–68)
SC–H	All ages	627	130	21	28,494	7,585	27	46 (33–56)
	2–17 years	160	8	5	2,060	130	6	52 (–10–79)
	18–64 years	158	9	6	8,214	721	9	59 (19–80)
	65 years and above	178	70	39	14,991	5,914	39	38 (14–54)
Clade 5a.2a subclade C.1.9								
Primary care								
EU–PC	All ages	149	18	12	5,084	796	16	33 (–17–62)
	18–64 years	84	6	7	2,648	226	9	52 (–23–81)
	Target group[e]	61	15	25	2,321	688	30	7 (–88–54)
UK–PC[g]	All ages	184	58	32	5,355	1,584	30	28 (–3–50)

VE (%) scale: −20 0 20 40 60 80 100

C. Influenza A(H3N2)

Study	Population[a]	Cases n	vacc	%	Controls n	vacc	%	VE (95% CI)[b]
Primary care								
DK–PC	All ages	330	35	11	32,347	6,877	21	47 (20–65)
	18–64 years	181	22	12	16,991	2,435	14	34 (–4–59)
EU–PC[f]	All ages	187	20	11	6,350	1,049	17	29 (–22–60)
	18–64 years	121	10	8	3,312	284	9	–13 (–124–48)
	Target group[e]	62	16	26	2,955	915	31	29 (–39–65)
UK–PC	All ages	292	46	16	12,965	3,314	26	47 (24–63)
	2–17 years	68	6	9	2,656	843	32	83 (59–93)
	18–64 years	197	23	12	7,701	1,072	14	27 (–21–56)
	65 years and above	27	17	NC	26,08	1,399	54	0 (–164–62)
Hospital								
EN–H	All ages	121	25	21	20,703	6,423	31	31 (–13–58)
	18–64 years	64	10	16	6,850	1,187	17	7 (–94–55)
	65 years and above	34	11	NC	10,786	4,491	42	47 (–23–77)
EU–H[f]	All ages	65	25	38	3,350	1,463	44	38 (–11–66)
	65 years and above	42	21	NC	1,964	1,163	59	44 (–11–71)
	Target group[e]	62	25	40	2,969	1,421	48	41 (–6–68)
SC–H	All ages	50	7	NC	26,056	7,556	29	49 (–15–78)
	2–17 years	14	2	NC	2,060	130	6	–124 (–1,026–55)
	65 years and above	14	4	NC	14,991	5,914	39	38 (–124–83)

VE (%) scale: −40 −20 0 20 40 60 80 100

D. Influenza B

Study	Population[a]	Cases n	vacc	%	Controls n	vacc	%	VE (95% CI)[b]
Primary care								
DK–PC	All ages	668	22	3	32,347	6,877	21	74 (59–83)
	18–64 years	382	17	5	16,991	2,435	14	74 (58–84)
EU–PC[f]	All ages	639	24	4	6,529	1,024	16	61 (38–76)
	0–17 years	224	7	3	2,070	250	12	69 (33–88)
	18–64 years	410	14	3	3,420	271	8	53 (16–76)
	Target group[e]	136	14	10	3,003	891	30	57 (22–78)
UK–PC	All ages	184	18	10	12,965	3,314	26	58 (27–76)
	2–17 years	31	5	NC	2,060	843	32	68 (13–88)
	18–64 years	149	10	7	7,701	1,072	14	51 (–3–76)
Hospital								
EN–H	All ages	364	36	10	20,703	6,423	31	74 (63–82)
	2–17 years	120	10	8	3,067	745	24	79 (58–90)
	18–64 years	207	9	4	6,850	1,187	17	79 (56–90)
	65 years and above	37	17	NC	10,786	4,491	42	42 (–19–72)
EU–H[f]	All ages	84	14	17	3,252	1,556	48	82 (66–91)
	65 years and above	35	12	NC	2,112	1,249	59	79 (56–90)
	Target group[e]	73	14	19	3,013	1,514	50	81 (66–91)
NI–H	All adults	31	3	NC	84	26	31	88 (21–99)
SC–H	All ages	112	9	NC	26,056	7,556	29	73 (45–87)
	65 years and above	14	4	NC	14,991	5,914	39	57 (–44–87)

VE (%) scale: −20 0 20 40 60 80 100

CI: confidence interval; DK-H: Denmark hospital study; DK-PC: Denmark primary care study; EN-H: England hospital study; EU: European Union; EU-H: EU hospital multicentre VEBIS study; EU-PC: EU primary care multicentre VEBIS study; NI-H: Northern Ireland hospital study; SC-H: Scottish hospital study; UK-PC: United Kingdom multicentre primary care study; VE: vaccine effectiveness; VEBIS: VE, Burden and Impact Studies.

[a] Age-specific or target group-specific VE was not included for overall or (sub)type-specific VE in some study sites, where sample size did not allow estimation of VE. The definition of 'all ages' differs by study (Table 1), with patients ≥6 months-old in EU-PC, patients ≥2 years-old in UK-PC and EN-H, patients ≥18 years-old in NI-H and patients of all ages in DK-PC, DK-H, EU-H and SC-H.

[b] For details of adjustment variables, see Table 1.

[c] Estimates for DK-PC and DK-H are for any influenza A only, as numbers for influenza B were low.

[d] For EU-PC: those aged 0−17 years are from ≥ 6 months to 17 years.

[e] Groups targeted by seasonal influenza vaccination as defined locally in the studies and study sites.

[f] For EU-PC: three study sites with <10 influenza A(H1N1)pdm09 cases were excluded from A(H1N1)pdm09 VE analysis (3 cases); three study sites with <10 influenza A(H3N2) cases were dropped from A(H3N2) VE analysis (8 cases); two study sites with <10 influenza B cases were not included in B VE analysis (8 cases). For EU-H: one study site with <10 influenza A(H1N1)pdm09 cases was excluded from A(H1N1)pdm09 VE analysis (3 cases); four study sites with <10 influenza A(H3N2) cases were dropped from A(H3N2) VE analysis (6 cases); five study sites with <10 influenza B cases were not included in B VE analysis (19 cases).

[g] The A(H1N1)pdm09 5a.2a C.1.9-specific estimate for UK-PC includes England only.

reduced reactivity of ferret antibodies raised against the vaccine virus with the circulating viruses [14].

Circulating influenza B strains were clade-matched to the clade V1A.3a.2 vaccine virus, which had remained unchanged since the 2022/23 northern hemisphere season. The VE was similarly high in the 2022/23 and 2023/24 seasons [8,9,15,17].

These influenza VE results should contribute to the supporting evidence for the WHO composition meeting for the northern hemisphere influenza vaccine strain selection on 24–27 February 2025.

Conclusion

Influenza vaccination should continue to be promoted in target groups, where feasible, as vaccination against influenza A, the main circulating influenza type, protected from one-third to over one-half of vaccinated individuals. Given that there were signals of lower VE by subtype, and particularly among older adults in some studies, in this time of heightened influenza activity other infection prevention measures should also be strengthened. End-of-season influenza VE with greater sample size, combined with more information on genetic variation of viruses, may help clarify observed differences in age- and study-specific VE.

Ethical statement

The planning, conduct and reporting of the studies was in line with the Declaration of Helsinki [18]. Some countries/studies did not require official ethical approval or patient consent as they are part of routine care/surveillance: DK-H, DK-PC, EN-H, EU-H (Ireland, Malta and Spain), EU-PC (Ireland, Spain), SC-H, UK-PC. In EU-PC (the Netherlands), as the data are initially collected through surveillance, no formal ethical approval was necessary. Verbal informed consent, however, is required from patients for participation in any further research (including VE studies). Other study sites received local ethical approval from a national or regional review board: EU-H (Belgium: the fifth amendment of ethical approval No. 12/310, B.U.N. 143201215671 was approved on 12 October 2022; Croatia: approved by the Ethics Committee of the Croatian Institute of Public Health (class: 030-02/24-01/1, 26 November 2024); Germany: approved by Charité Universitätsmedizin Berlin Ethical Board: references EA2/126/11 and EA2/218/19; Hungary: approved by the National Scientific and Ethical Committee (IV/1885-5/2021/EKU); Lithuania: approved 03 July 2020 by the Lithuanian Biomedical Research Ethics Committee No.: L-20-3/1-2; updated 25 July 2022, 25 January 2023 and 30 October 2024; Romania: CE236/2022; Spain/Navarre: approved by the Navarre Ethics Committee, Ethical Committee for Clinical Research (PI2023/145), which waived the requirement of obtaining informed consent); EU-PC (Croatia: approved by the Ethics Committee of the Croatian Institute of Public Health (class 030-02/22-01/4); France: 471393; Germany: EA2/126/11; Ireland: ICGP2019.4.0; Hungary: as for EU-H; Navarre: as for EU-H; Portugal: approved 14 December 2022 by the Ethics Committee of Instituto Nacional de Saúde Doutor Ricardo Jorge, no registration number given).

Use of artificial intelligence tools

None used.

Data availability

Data are available from the corresponding author on request. The 829 sequences generated in connection with this analysis have been submitted to GISAID.

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Conflict of interest

Authors' contributions

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