Recombinant or Standard-Dose Influenza Vaccine in Adults under 65 Years of Age

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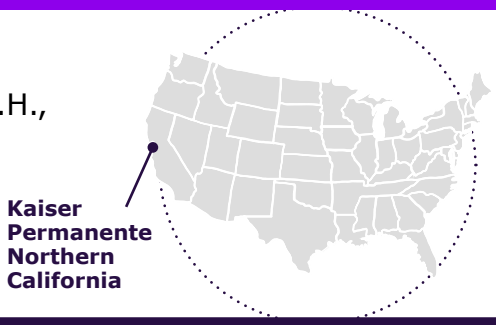

KEY MESSAGES[1]

Recombinant vaccine conferred more protection against PCR-confirmed influenza than egg-based standard-dose vaccine among adults aged 50–64 years (relative vaccine effectiveness rVE 15.3% (95% CI, 5.9 to 23.8; P=0.002) across two influenza seasons (2018–19 and 2019–20)

BACKGROUND

- Every year in the United States, influenza causes mild-to-severe illness in a wide range of people (9–41 million)[2]
- Influenza vaccination is the primary method for preventing influenza-related illness, although the vaccine effectiveness ranges, from ~20% in years in which the vaccine is antigenically mismatched to the circulating viral strain, to 40–60% in years in which the vaccine is antigenically well matched[3,4]
- Recombinant vaccines contain three times the amount of the hemagglutinin protein as standard-dose egg-based vaccines and the recombinant formulation is not susceptible to antigenic drift during manufacturing[1]
- Some studies have shown benefit for the recombinant vaccines as compared with standard-dose vaccines in adults 50 years of age or older[5,6]

OBJECTIVES[1]

- Estimate the **relative vaccine effectiveness (rVE) of recombinant vaccine as compared with standard-dose vaccine** against laboratory (PCR) confirmed influenza and influenza-related hospitalization outcomes in patients aged 50 to 64 years:

Primary	Secondary
PCR-confirmed influenza	PCR-confirmed influenza A PCR-confirmed influenza B Hospitalized PCR-confirmed influenza Hospitalized community acquired pneumonia (CAP) Hospitalized cardiorespiratory events

Study population (adults aged 50–64 years)[a]

[a]Exploratory objectives included 18–64-year-old population and a younger adult population aged 18–49 years (with similar and broader outcomes) – refer to the publication for more details.

METHODS[1]

Location	Data/system	Study Design	Participants	Seasons
Northern California (259 medical clinics; 21 hospitals)	KPNC: Integrated health care system linking medical services, laboratory tests and vaccinations	Cluster-randomized observational study KPNC facilities routinely administrated either the recombinant vaccine (Flublok, Sanofi) or one of the two standard-dose vaccine; each facility alternated weekly between the two vaccine formulations	675,252 older adults aged 50–64 years *(amongst ~1.6 million adults aged 18–64 years)*	3 seasons planned but 2 seasons in final analysis (2018–2019 and 2019–2020)

Declaration: the study was supported by Sanofi (study reference VAP00003)

Abbreviations: CAP: community acquired pneumonia; CI: confidence interval; COPD: chronic obstructive pulmonary disease; KPNC: Kaiser Permanente Northern California; PCR: polymerase chain reaction; rVE: relative vaccine effectiveness.

References: 1. Hsiao A, et al. *N Engl J Med*. 2023;389:2245–55. doi: 10.1056/NEJMoa2302099; 2. CDC. Disease Burden of Flu. Available at: https://www.cdc.gov/flu/about/burden/index.html. Accessed December 2023; 3. CDC. Seasonal flu vaccines. Available at: https://www.cdc.gov/flu/prevent/flushot.htm. Accessed December 2023; 4. CDC. CDC Seasonal Flu Vaccine Effectiveness Studies. Available at: https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm. Accessed December 2023; 5. Dunkle LM, et al. *N Engl J Med*. 2017;376(25):2427–36. doi: 10.1056/NEJMoa1608862; 6. Dunkle LM, Izikson R. *Expert Rev Vaccines*. 2016;15(8): 957–66. doi: 0.1080/14760584.2016.1203261.

Access the publication:

RESULTS[1]

STUDY POPULATION CHARACTERISTICS AMONG ADULTS 50–64 YEARS[a]

Characteristic, No. of participants (%)	Recombinant vaccine n=279,400	Standard-dose vaccine n=395,852
Female	154,860 (55)	220,252 (56)
Race		
White	142,757 (51)	198,434 (50)
Black	13,693 (5)	20,814 (5)
Asian	58,416 (21)	84,154 (21)
Ethnicity		
Hispanic	46,318 (17)	65,868 (17)
Coexisting illnesses		
Asthma	39,909 (14)	56,398 (14)
Diabetes	49,506 (18)	69,924 (18)
COPD	5,628 (2)	7,729 (2)
Coronary heart disease	10,613 (4)	14,883 (4)
Body mass index		
Obese: ≥30 kg/m^2	102,592 (37)	143,787 (36)
Received influenza vaccine in prior year		
Yes	207,236 (74)	290,370 (73)
No. of weeks with outpatient visits in prior year		
1–3	110,148 (39)	157,142 (40)
No. of inpatient stays in prior year		
0	248,335 (89)	352,948 (89)

[a]All detailed subcategories are provided in the publication (only the most relevant/representative ones are shown here).

RELATIVE VACCINE EFFECTIVENESS AMONG ADULTS 50–64 YEARS

	Recombinant vaccine N=279,400	Standard-dose vaccine N=395,852	Relative vaccine effectiveness (95% CI)	P value[x]
Primary endpoint				
PCR-confirmed influenza	559	925	**15.3 (5.9, 23.8)**	**0.002**
Secondary endpoints				
PCR-confirmed influenza A	522	862	**15.7 (6.0, 24.5)**	**0.002**
PCR-confirmed influenza B	37	64	10.3 (−33.9, 39.9)	0.59
PCR-confirmed influenza hospitalization	95	153	15.9 (−9.2, 35.2)	0.19
CAP hospitalization	106	183	16.7 (−5.6, 34.4)	0.13
Cardiorespiratory hospitalization	631	890	2.4 (−8.1, 11.9)	0.64

[x]Test: H0: log-adjusted hazard ratio=0; significant results (p<0.05) are in bold. Adjustment for multiplicity for the secondary outcomes was performed with the use of Holm's adjustment method. The P values that were obtained for the five secondary outcomes were rank-ordered and compared with corresponding adjusted nominal alpha values of 0.01, 0.0125, 0.0167, 0.025, and 0.05.

The post-hoc analysis conducted on combined secondary outcomes hospitalization for PCR-confirmed influenza and hospitalization for community-acquired pneumonia in all adults aged 50–64 years (primary study population) showed a relative effectiveness of 19.7% (95% CI, 2.8–33.7)

KEY FINDINGS[1]

Primary outcomes:

- Recombinant vaccine conferred more protection than standard-dose vaccine against PCR-confirmed influenza in adults aged 50–64 years

Secondary outcomes:

- Recombinant vaccine may confer more protection than standard-dose vaccine against hospitalizations outcomes in adults aged 50–64 years (based on a post-hoc analysis combining secondary hospitalization outcomes)
- The incidence of PCR-confirmed influenza A was lower in the recombinant vaccine group than in the standard-dose group

LIMITATIONS[1]

- There was a difference in the number of people randomized to each group in this real-world study; however, the study population characteristics were well-balanced
- The COVID-19 pandemic reduced the planned study duration from a three-season to a two-season analysis, limiting circulating strains (A/H1N1 and B strains dominant), and the study's power to detect clinically meaningful benefit of recombinant against less frequent and more severe outcomes
- The primary outcome could only be assessed in participants who underwent PCR testing

CONCLUSIONS[1]

- Recombinant vaccine conferred more protection against PCR-confirmed influenza than a standard-dose vaccine among adults aged 50–64 years. This evidence was strengthened by the cluster-randomized study design

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