Vaccine effectiveness of recombinant and standard dose influenza vaccines against influenza-related hospitalization using a retrospective test-negative design

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BACKGROUND

- Previously, two large studies have evaluated relative vaccine effectiveness (rVE) of recombinant quadrivalent influenza vaccine (RIV4):
  - A pivotal randomized controlled trial (RCT) conducted in the mismatched A/H3N2 predominant 2014-2015 influenza season found significant relative vaccine efficacy for RIV4 compared to SD-IIV4 against laboratory confirmed influenza among older adults 50+ years of age[11]
  - Secondly, a large retrospective cohort study of Medicare beneficiaries in the B-Victoria and A/H1N1 dominant 2019-2020 season, reported significant relative vaccine effectiveness of RIV4 vs SD IIV4 and other differentiated influenza vaccines against influenza related hospital encounters[10]

OBJECTIVE[1]

- This study is a retrospective test-negative case-control study to determine the rVE of RIV4 vs. SD-IIV4 (egg based/cell-based) against influenza like illness (ILI) hospitalization among adults 18–64 and 65+ years of age in the 2018–2019 and 2019–2020 seasons using data from electronic medical records (EMR) from the University of Pittsburgh Medical Center (UPMC) health system.

METHODS[1]

Study Design

A test-negative case-control study estimates VE by comparing the odds of vaccination among patients (cases) hospitalized with ILI with confirmed influenza to the odds of vaccination among controls, i.e., patients hospitalized with ILI who tested negative for influenza.

The hospital system **electronic medical record** and the **state immunization registry** (Pennsylvania Statewide Immunization Information System (PA-SIIS)) were used to confirm influenza vaccination between August 1 and the date of illness/PCR testing.

Seasons

2018/2019 and **2019/2020** influenza seasons

Location

The **UPMC** health system (19 hospitals)

Participants

UPMC Participants ≥18 years (age stratified data not available)	**Cases** hospitalized influenza like illness (ILI) with PCR test-positive influenza **N=1,803**	**Controls** hospitalized influenza like illness (ILI) with PCR test-negative influenza **N=12,787**
	% (n)	% (n)
RIV4	16 (291)	24 (3,047)
SD-IIV4 (egg based/ cell based)	6 (114)	7 (862)
Unvaccinated	78 (1,398)	69 (8,878)

Abbreviations: CDC: Centers for Disease Control and Prevention; CI: confidence interval; EMR: electronic medical records; ILI: Influenza Like Illness; IPW: inverse probability weighting ; PCR: Polymerase Chain reaction; RCT: randomized controlled trials; RIV4: Recombinant quadrivalent Influenza Vaccine; rVE: relative vaccine efficacy/effectiveness; SD-IIV4: standard-dose quadrivalent inactivated influenza vaccine; UPMC:University of Pittsburgh Medical Center; VE: vaccine effectiveness.

References: 1. Zimmerman, R.K., Patricia Nowalk, M., Dauer, K., Clarke, L., Raviotta, J.M., Balasubramani, G.K., 2023. Vaccine effectiveness of recombinant and standard dose influenza vaccines against influenza related hospitalization using a retrospective test-negative design. Vaccine. https://doi.org/10.1016/j.vaccine.2023.06.056 ; 10. Izurieta, H.S., Lu, M., Kelman, J., Lu, Y., Lindaas, A., Loc, J., Pratt, D., Wei, Y., Chillarige, Y., Wernecke, M., MaCurdy, T.E., Forshee, R., 2021. Comparative Effectiveness of Influenza Vaccines Among US Medicare Beneficiaries Ages 65 Years and Older During the 2019–2020 Season. Clinical Infectious Diseases 73, e4251–e4259. https://doi.org/10.1093/cid/ciaa1727 ; 11. Dunkle, L.M., Izikson, R., Patriarca, P., Goldenthal, K.L., Muse, D., Callahan, J., Cox, M.M.J., 2017. Efficacy of Recombinant Influenza Vaccine in Adults 50 Years of Age or Older. N Engl J Med 376, 2427–2436. https://doi.org/10.1056/NEJMoa1608862

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RESULTS: RIV4 VS SD-IIV4[1]

Vaccine effectiveness (VE) of recombinant quadrivalent influenza vaccine (RIV4) and standard dose quadrivalent influenza vaccine (SD-IIV4) and relative VE of RIV4 using propensity scores and inverse probability weighting (IPW)

			Relative vaccine effectiveness (rVE) of RIV4 compared to SD-IIV4, % (95% CI)		
Group	**Adjusted RIV4 VE compared to no vaccination**	**Adjusted SD-IIV4 VE compared to no vaccination**	**Adjusted using a priori variables**	**Adjusted using propensity score**	**Adjusted using IPW**
Overall	**36 (27, 45)**	**24 (6,38)**	21 (-1, 38)	26 (4,43)	**31 (11,46)**
18-64 years	**47 (35,57)**	**27 (8, 42)**	28 (2, 46)	27 (2, 45)	**28 (3, 46)**
≥65 years	**27 (12, 39)**	9 (-42, 42)	22 (-26, 51)	17 (-34, 49)	17 (-36, 48)
High-risk condition	**30 (19, 40)**	21 (-2, 39)	14 (-15, 35)	17 (-13,38)	20 (-7, 40)
No condition	**67 (50, 78)**	27 (-4, 49)	49 (11,71)	58 (23, 77)	**60 (29,78)**
2018-19 season	**31 (15, 45)**	20 (-6, 41)	19 (-17, 44)	28 (-7, 51)	28 (-5, 50)
2019-20 season	**40 (29, 50)**	26 (1, 45)	24 (-6, 46)	29 (-1, 50)	**30 (1, 50)**
Female sex	**40 (28, 50)**	20 (-4, 39)	24 (-5, 45)	26 (-4, 48)	**37 (13, 54)**
Male sex	**31 (16, 44)**	**28 (0,49)**	22 (-15, 48)	28 (-9, 52)	23 (-14, 48)

RIV: Flublok SD-IIV: Fluarix, Afluria, Flulaval, SD Fluzone, Flucelvax.

- Among all adults hospitalized for acute respiratory infections, both RIV4 (first column) and SD-IIV4 (second column) were significantly effective **overall against influenza hospitalizations** compared to unvaccinated patients, **but only RIV4 was effective for all subgroups tested** in this analysis
- Further, the RIV4 rVE vs SD-IIV4 was statistically **significant** (**rVE=31%; 95% CI=11%, 46%**) **demonstrating improved rVE of RIV4** compared to SD-IIV4 amongst all adults overall

LIMITATIONS[1]

- Selection bias among those who received influenza virus testing towards those who are unvaccinated against influenza would have potentially increased the proportion of unvaccinated cases.
- Sample size of SD-IIV4 recipients may have been inadequate to detect meaningful rVE estimates for specific subgroups

CONCLUSIONS[1]

- Adds evidence of the improved performance of RIV4 among adults 18+ and demonstrates better effectiveness over SD-IIV4 (egg-based/cell-based) for adults 18-64 years of age
- Both RIV4 and SD-IIV4 were significantly effective among all adults against influenza hospitalization during the 2018-2019 and 2019-2020 influenza seasons, with RIV4 providing better protection compared to SD-IIV4, whether it was egg-based or cell-based influenza vaccines for all adults 18+

Abbreviations: CDC: Centers for Disease Control and Prevention; CI: confidence interval; EMR: electronic medical records; ILI: Influenza Like Illness; IPW: inverse probability weighting ; PCR: Polymerase Chain reaction; RCT: randomized controlled trials; RIV4: Recombinant quadrivalent Influenza Vaccine; rVE: relative vaccine efficacy/effectiveness; SD-IIV4: standard-dose quadrivalent inactivated influenza vaccine; UPMC:University of Pittsburgh Medical Center; VE: vaccine effectiveness.

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