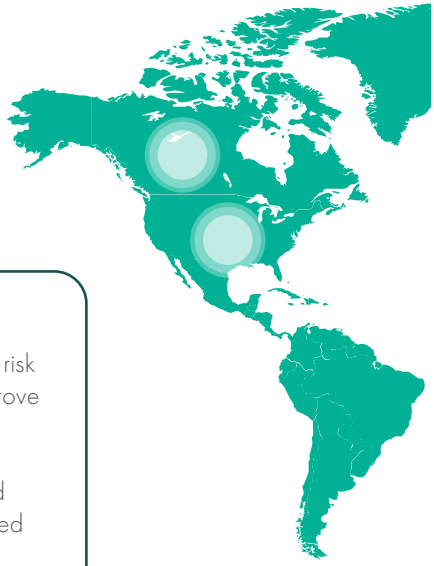
PUBLICATION CARD

Efficacy and effectiveness of high-dose influenza vaccine in older adults by circulating strain and antigenic match: An updated systematic review and meta-analysis

JANUARY 2021

Authors: Jason Lee, Gary Lam, Thomas Shin, Sandrine Samson, David Greenberg, Ayman Chit

Journal: *Vaccine*



INTRODUCTION

- Older adults (≥65 years) are a priority group for annual influenza vaccination due to greater risk of influenza-related complications, and several vaccine options are available that aim to improve immune response and protection for this population.
- The high-dose inactivated trivalent influenza vaccine (HD-IIV3) was licensed by the Food and Drug Administration in 2009 and contains 4 times the hemagglutinin antigen (60 µg) compared to standard dose influenza vaccines (SD-IIV). HD-IIV3 was specifically designed to provide improved immune responses and clinical protection in older adults.

OBJECTIVES

Updated systematic review and meta-analysis of randomized and observational studies to evaluate the relative vaccine efficacy/effectiveness (rVE) of HD-IIV3 compared to SD-IIV in adults aged ≥ 65 years:

- The primary objective was to estimate the pooled rVEs of HD-IIV3 versus SD-IIV3 over all influenza seasons against clinical outcomes related to influenza.
- Secondary objectives of this study were to estimate the rVEs against the same outcomes during A/H3N2- or A/H1N1-predominant seasons, antigenically-matched or mismatched seasons.

STUDY CONDUCT

DESIGN

Systematic review and meta-analysis
15 publications were meta-analyzed, 4 publications on randomized studies and 11 related to observational studies.

PARTICIPANTS

34 million subjects aged ≥ 65 years

SEASONS

10 consecutive influenza seasons
from 2009–10 to 2018–19

LITERATURE SEARCH

May 31st, 2020

KEY FINDINGS

- The data suggest that HD-IIV3 is consistently more effective than SD-IIV at reducing influenza cases as well as influenza-associated clinical complications, irrespective of circulating strain and antigenic match (Table 1).
- The authors also presented rVE of HD-IIV3 and SD vaccine by study type (RCT versus observational studies); statistically significant rVE estimates were shown in 10 out of 14 endpoints, except for some comparisons (e.g. all-cause mortality) with smaller sample size.

Table 1

Outcome	All seasons		Antigenic Similarity with Predominant Circulating Strain[b]				
			Matched Seasons		Mismatched Seasons		
	rVE[c] (95% CI)	p-value	rVE (95% CI)	p-value	n	rVE (95% CI)	p-value
Influenza-like Illness[d]	**15.9%** (4.1-26.3%)	0.01	27.0% (-6.8-50.1%)	0.105	4	14.3% (-3.4-29.0%)	0.107
Influenza Hospitalization[e]	**11.7%** (7.0-16.1%)	<0.001	**10.9%** (2.1-18.9%)	0.016	7	**12.1%** (6.3-17.6%)	<0.001
Pneumonia Hospitalization[f]	**27.3%** (15.3-37.6%)	<0.001	**28.9%** (10.1-43.8%)	0.004	1	-	-
Pneumonia/Influenza Hospitalization[g]	**13.4%** (7.3-19.2%)	<0.001	**13.5%** (5.0-21.3%)	0.002	2	**13.3%** (4.1-21.6%)	0.005
Cardiorespiratory Hospitalization	**17.9%** (15.0-20.8%)	<0.001	**17.4%** (13.5-21.1%)	<0.001	3	**18.6%** (14.1-22.9%)	<0.001
All-cause Hospitalization	**8.4%** (45.7-11.0%)	<0.001	**6.4%** (4.1-8.6%)	<0.001	4	**12.6%** (7.8-17.2%)	<0.001
Post-influenza Mortality	22.2% (-18.2-48.8%)	0.240	-	-	1	-	-
Pneumonia/Influenza Mortality	**39.9%** (18.6-55.6%)	<0.001	-	-	2	**43.2%** (18.1-60.6%)	0.002
Cardiorespiratory Mortality	**27.7%** (13.2-32.0%)	<0.001	-	-	2	**27.3%** (20.3-33.6%)	<0.001
All-cause Mortality	2.5% (-5.1-9.5%)	0.514	0.7% (-4.3-5.6%)	0.768	2	**17.3%** (0.2-31.5%)	0.048

[a]Determined using national CDC viral surveillance data of circulating strains in adults 65 years of age and older.
[b]Based on CDC data on viral antigenic characterization comparing reference vaccine strains to circulating viruses; mismatched seasons includes seasons of antigenic mismatch (2009–10, 2014–15, 2018–19) as well as seasons where egg-adapted vaccine strains may have affected vaccine effectiveness (2012–13, 2016–17, 2017–18).
[c]A random-effects model with DerSimonian-Laird estimators was used to calculate the pooled OR across multiple studies and influenza seasons.
[d]Probable/laboratory confirmed influenza-like illness.
[e]ICD-9-CM 487 coded hospitalizations.
[f]ICD-9-CM 480–486 coded hospitalizations.
[g]ICD-9-CM 480–488 coded hospitalizations.

LIMITATIONS OF RESULTS

- Considerable heterogeneity existed in some comparisons.
- Unmeasured confounders in observational studies were possible.
- Not every endpoint had laboratory confirmation for influenza infection.

KEY MESSAGE

Evidence over 10 consecutive influenza seasons and in more than 34 million individuals aged ≥ 65 years suggests that HD-IIV3 is consistently more effective than SD-IIV at reducing influenza cases as well as influenza-associated clinical complications, irrespective of circulating strain and antigenic match, in both controlled and real-word conditions.

Watch the video summary

Access the article

Glossary: CDC: Centers for Disease Control and Prevention; HD-IIV3: high-dose inactivated trivalent influenza vaccine; RCT: Randomized Clinical Trial; rVE: Relative Vaccine Effectiveness; SD-IIV: standard dose influenza vaccine.

References: Lee J, et al. Efficacy and effectiveness of high-dose influenza vaccine in older adults by circulating strain and antigenic match: An updated systematic review and meta-analysis. *Vaccine* 2021 Jan 7;S0264-410X(20)31146-4.

Declaration: This study was supported by Sanofi Pasteur.